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Active and healthy aging and quality of life: Interventions and outlook for the future

Edited by
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Active and healthy aging and quality of life: Interventions and outlook for the future

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The association between reproductive history and the multidimensional health of older adults in rural China and its gender differences: Evidence from the Chinese longitudinal healthy longevity survey

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Background: Few studies have examined the association between reproductive history and the multidimensional health of older adults with more diverse reproductive histories and poorer health status in rural China. The purpose of this study is to explore the effect of parity, sex ratio of children and late childbearing on multidimensional health and its gender differences.

Methods: The analytical sample consisted of 3,377 older adults in rural China who participated in the Chinese Longitudinal Healthy Longevity Survey (CLHLS) in 2018. Linear regression models were applied to estimate the relationship between reproductive history and multidimensional health, with separate models for each indicator of health outcomes.

Results: Older adults in rural areas with greater parity were more likely to have better cognitive function (β = 0.409, 95% CI: 0.255–0.563), fewer Activities of Daily Living (ADL) limitations (β = −0.085, 95% CI: −0.137 to −0.034) and symptoms of depression (β = −0.396, 95% CI: −0.577 to −0.216). The social mechanism of intergenerational support from children later in life partly explained the positive effect of parity. Late childbearing had negative effects on cognitive function (β = −1.220, 95% CI: −1.895 to −0.545), ADL (β = 0.253, 95% CI: 0.028–0.478) and symptoms of depression (β = 1.025, 95% CI: 0.237–1.812). Women were more likely to be influenced by the positive effect of parity; the association between late childbearing and health was only significant in the male group.

Conclusions: Parity and late childbearing are associated with cognitive function, activities of daily living, and symptoms of depression in the older adults in rural China. Older adults with more children might be in better health,

and this finding is especially significant in women. However, late childbearing had a negative effect on multidimensional health, especially for men. The social mechanism and gender differences between reproductive history and health need to be further explored.

KEYWORDS

reproductive history, the multidimensional health, gender differences, older adults, cognitive function, activities of daily living, symptoms of depression

Introduction

The world population is rapidly aging, and China is facing the largest and fastest growth in population aging. In 2020, there were 260 million older adults over the age of 60 years in China, accounting for 18.7% of the total population (1). It is estimated that by 2050, the number of older adults over the age of 60 years will increase to a peak of 488 million in China, representing 35.6% of the total population (2). In the process of population aging in China, rural population has an increasingly higher proportion of older adults than the urban (3). According to the Fifth and Sixth National Population Censuses, the population of older adults in rural areas is 15.57 and 44.21 million greater than the population of older adults in urban regions, respectively (4, 5). Improving health status of the older adults in rural areas is an important task to deal with the aging population.

China is an unhealthy aging society. According to the Fourth Sampling Survey on the Living Conditions of Urban and Rural Older People in China in 2015, 31.16% of older adults over the age of 60 years suffered from more than one chronic disease, and 30.27% of the older adults in rural areas reported poor self-rated health. The proportion of partially and completely disabled older adults was 16.5%, and the proportion of older adults who are psychologically lonely made up 30.3% in rural areas (6). The Fourth National Health Service Survey in China in 2003 (7) indicated the prevalence of disability in the population aged 60 years and above was 10.6%, which increased to 16.9% in 2008. The prevalence rates of Activities of Daily Living (ADL) disability appear to be much lower in some developed countries: 5% in Canada, 7% in France, 9% in Italy, and 7% in Sweden when age-standardized (8). Due to China's large population, the total number of disabled older adults will far exceed that of other countries. These data provide strong evidence for the judgment that China is an unhealthy aging society. Given the prevalence rate of ADL disability is significantly higher in rural areas (9), it can be seen that the health status of older adults in rural China is in bad condition. Exploring the determinants of health among the older adults in rural areas and formulating appropriate intervention policies should be the first task for China to address the challenges of the aging population.

In fact, China is a society with a profound tradition of "family culture," reproduction is a life-course event that most Chinese people experience (10). Traditionally, infertility is considered to be one of the most unfilial behavior. Having no children means that nobody inherits property, status, family name, which are of great importance for the Chinese people. Thus, the Chinese people hold a strong belief in the concept of "the more sons, the more blessings" (11). According to Chinese Longitudinal Healthy Longevity Survey in 2018, 97.5% of the participants had at least one child. Today's older adults, most of who were born around the 1950 s, have an average of 3.0–3.5 children (6). The one-child policy, which started in the 1970 s to reduce and control births, has been implemented more loosely in rural than urban areas. As a result, older adults in rural areas have, on an average, 0.5 more children and 0.3 more boys than their urban counterparts. The relationship between reproductive history and health in older adults is an important issue in the study of life course theory. The health outcome of the older adults is a long-term accumulation process, and the early reproductive history has an important influence on the health status of the older adults in later life. To explore the relationship between reproductive history and health is helpful to guide policy direction of reproductive health service and healthy aging.

Many longitudinal studies on the direct effect of reproduction on health have shown that every life course and event from pregnancy onwards has a significant impact on health and wellbeing later in life (10, 12). The "maternal depletion theory" believes that since women are the biological undertaker of reproduction, the processes of pregnancy, childbirth, abortion and breastfeeding have more direct and greater impacts on women's current and long-term physical and mental health, especially women in developing countries with lower socioeconomic status (13–15). Some studies have shown that having more children increases the risk of chronic diseases and disability in elderly women (16–18), whereas others have suggested that women with more children have a lower risk of breast cancer and ovarian cancer (19). In countries where parents receive generous support from the state, greater parity is associated with better health for both men and women (20). A study based on US National Longitudinal Survey of Youth in 1979 showed that late childbearing is associated with better language and cognitive function (21). However, a few studies have shown that late childbirth may cause physical health problems, and older age at last childbirth increases the risk

of women suffering from reproductive diseases such as breast cancer (22, 23). Previous research indicated that the mean age at childbearing of China experienced a decrease between 1990 and 1995, followed by a sustaining growth afterwards (24). 17.28% of women gave birth at an advanced maternal age (≥35) in rural areas, while 12.62% of women in urban areas in 2019 (25). Thus, older adults in rural China had a more complicated reproductive history. The relationship between reproductive behavior and the health of older adults is very complex and needs further analysis (26).

With in-depth exploration of the social mechanism of the indirect effect of reproductive history on health, the focus has been extended to both genders and not confined to elderly women (27, 28). Although the biological undertaker of birth are women, both men and women invest a large amount of economic and emotional resources in bringing up their children, and childbirth will change individual's behavior, psychology, social norms, and economic responsibilities for both men and women (10, 29, 30). Especially in counties where men have the economic responsibilities, they have more financial responsibility and stress and are more likely to smoke, drink, and develop other unhealthy lifestyles (31–33). Of course, it should also be noted that from the perspective of social mechanisms, reproduction does not necessarily have a negative effect on the health of older adults because children also provide financial, daily care, spiritual comfort, and other support to older adults, which helps improve health status later in life (34, 35).

A few studies have explored the effects of reproductive history on the health of older adults in China from both direct and indirect perspectives. In terms of direct effects, elderly women with many children are more likely to suffer from impairment in ADL, poorer self-rated health, and higher mortality (36, 37). Studies indicate that when the number of children ever born or living children is >5, the lifespan of elderly women tends to be longer (38). From the perspective of indirect effects, family provides the most important support to older adults in China, especially in rural areas. Adult children tend to be the main source of external support, such as economic needs, daily care, and spiritual comfort for older adults. Thus, reproduction has a positive, indirect impact on the health of older adults (39).

In general, available research on the effect of reproductive history on the health of older adults in rural China is still limited. Most of the studies concentrated on women and social mechanisms by which reproduction affects the health of the older adults from an indirect perspective (such as economic, caring, and spiritual comfort from children). Few studies have explored the direct impact of reproductive history, and the relevant conclusions are not consistent. Life course theory suggests that early behavior or life events could have a direct or indirect impact on the health status of older adults (40). For the older adults with poor health in rural China, reproduction is a typical and almost inevitable life course event, and its impact on the health of the older adults in rural China is an important topic worth exploring.

The influence of reproductive history on the multidimensional health of older adults includes biological mechanism and social mechanism. Biological mechanism can be regarded as a direct effect of fertility, which refers to the direct physiological impact on women as the bearer of fertility behavior. Specifically, having more children increases the risk of chronic diseases and disability in elderly women (16–18); late childbirth may cause physical health problems and older age at last childbirth increases the risk of women suffering from reproductive diseases such as breast cancer (22, 23). Elderly women with many children are more likely to suffer from impairment in ADL, poorer self-rated health, and higher mortality (36, 37). However, a few studies also showed there was a positive association between reproductive history and multidimensional health. More children is associated with lower risk of breast cancer and ovarian cancer, and better health for both men and women; the lifespan of elderly women that have children more than five tends to be longer (19, 20, 38). Social mechanism refers to the indirect effects of reproductive history on multidimensional health. For example, raising children requires more time and energy, which affects their physical and mental health, and adult children's intergenerational support too may improve their health. Some studies indicated that men have more financial responsibility and stress of bringing up their children and are more likely to smoke, drink, and develop other unhealthy lifestyles (31–33). However, children also provide financial support, daily care, spiritual comfort, and other support to older adults, which help improve health status later in life (34, 35).

Compared with previous studies, there are several contributions of this paper. First, both the direct and indirect effects of reproductive history on the health of the older adults in rural China are investigated in our research. Second, the study population is the older adults of rural China with a more diverse reproductive history and poorer health status, and both women and men are included in our study. Third, based on the parity and timing of reproduction, adding the perspective of sex ratio of born children, we comprehensively investigate the effects of reproductive history on multidimensional health (including cognitive function, physical health, and mental health) of the older adults in rural areas of China.

Methods

Data source and study sample

The data were derived from the Chinese Longitudinal Healthy Longevity Survey (CLHLS), a nationally representative survey jointly performed by the Center for Healthy Aging and Development Studies at Peking University and Duke University.

The CLHLS was first conducted in 1998, followed by seven waves of surveys in 2000, 2002, 2005, 2008, 2011, 2014, and 2018 from 22 sample areas in 31 provincial administrative units. The population of the surveyed region accounts for 85.3% of the total population of the country, which can be regarded as a nationally representative sample (41). Additional details, such as the sampling design, sampling weight, and assessment of data quality, can be found in previous studies (42, 43). We used the latest cross-sectional data from the CLHLS in 2018. Only those individuals aged 60 years and above in rural areas with at least one child were selected for the present analysis. After filtering for missing values, outliers, etc., the present study sample included 3,377 older adults in rural areas.

Measurements

Multidimensional health

Three indicators of health outcomes, cognitive function, ADL, and depressive symptoms were used as dependent variables in our research.

Cognitive function was assessed by 24 items modified from the Mini-Mental State Examination scale (MMSE) (44), which has been proven to be reliable and effective with Chinese older adults (43, 45). It contains a brief set of components to assess orientation, concentration, memory, and language, with total scores ranging from 0 to 30. Higher scores indicate better cognitive function.

The Katz scale was adopted to evaluate ADL, which included six items: bathing, dressing, bathroom use, movement indoors, continence, and eating. Respondents were asked to rate their ability to engage in these ADLs using a three-point scale: (1) not difficult at all, (2) slightly difficult, and (3) unable to do the task. The total scores ranged from 3 to 18, and higher scores indicated more limited functioning for the respondent.

Depressive symptoms were assessed by the Center for Epidemiologic Studies Depression Scale (CES-D) (46). The scale consists of 9 items, including 7 negative feeling items (e.g., lonely and isolated) and 2 positive feeling items (e.g., hopeful about the future). Respondents reported how often they had a particular feeling (1 = always, 2 = often, 3 = sometimes, 4 = seldom, 5 = never). The total scores ranged from 5 to 45, and higher scores indicated more depressive symptoms after reversing the coding of the 7 negative items.

Reproductive history

Information about reproductive history was collected in CLHLS through the following measures. Parity was measured by the number of biological children reported by the respondents, including deceased children. The participants further reported the number of sons that were ever born so we could calculate the sex ratio by dividing the number of sons by parity. Women who give birth over the age of 40 are considered advanced maternal age (26). We define late childbearing as a binary variable, which is set to 0 if the last birth was before the age of 40 or 1 if the last birth was at 40 or above.

Intergenerational support

To capture the indirect effects of reproduction, we were concerned about intergenerational support from children, which might be beneficial to older adults, and included three aspects: economic support, daily care, and spiritual comfort. Economic support is measured by the total value of financial transfers and in-kind assets transfers those older adults received last year from their children. Daily care was assessed by the hours that children spend caring for older adults in the last week. Spiritual comfort was the total score of the following three questions: did you talk to your children frequently? (1 = yes; 0 = no); did you first talk to your children when you needed to tell someone about your thoughts? (1 = yes; 0 = no); did you first ask your children for help when you had problems/difficulties? (1 = yes; 0 = no).

Covariates

All analyses presented here included a series of covariates associated with health as follows according to previous studies (47–51), which provide a good basis for the selection of control variables in this paper: (1) demographic characteristics, including gender, age, education, and marital status; (2) family factors, including family income, number of persons living with you, and housing condition; (3) social support, including medical insurance and the total amount of available social services the participant reported; and (4) lifestyle, including whether they had smoked/drank/exercised in the past (1 = yes; 0 = no) were also queried. Family income was measured by the logarithm of income per capita in the household last year. Housing condition was a dummy variable of whether your home frequently has a mildew odor or a musty smell.

Statistical analysis

We first present the characteristics of the Chi-square tests for categorical variables and *T*-tests for continuous variables were used to test the significance of gender comparisons. Then, the multidimensional health of participants in groups with different reproductive histories was reported. *T*-tests and analyses of variance (ANOVAs) were performed to compare the health outcomes between different reproductive history groups. Finally, linear regression models were used to estimate the relationship

TABLE 1 Descriptive statistics.

Variables	Measurement	*N* (%)/Mean (SD)			*P*-value
		Total ($N = 3,377$)	Women ($N = 2,039$)	Men ($N = 1,338$)	
Age	Continuous measurement	85.42 (11.67)	87.16 (11.93)	82.76 (10.75)	<0.001
Education (years)	Continuous measurement	2.14 (3.20)	1.02 (2.22)	3.86 (3.66)	<0.001
Marital status	Married = 1	1,283 (37.99)	532 (26.09)	751 (56.13)	<0.001
	Other = 0	2,094 (62.01)	1,507 (73.91)	587 (43.87)	
Family income (ln)	Continuous measurement	9.56 (1.77)	9.517 (1.82)	9.64 (1.68)	0.054
Number of persons living with you	Continuous measurement	2.18 (2.03)	2.20 (2.00)	2.15 (2.07)	0.492
Housing condition	Have musty smell = 1	553 (16.38)	341 (16.72)	212 (15.84)	0.499
	No musty smell = 0	2,824 (83.62)	1,698 (83.28)	1,126 (84.16)	
Medical insurance	Yes = 1	2,701 (79.98)	1,666 (81.71)	1,035 (77.35)	0.002
	No = 0	676 (20.02)	373 (18.29)	303 (22.65)	
Social service	Continuous measurement	1.22 (1.45)	1.21 (1.46)	1.24 (1.45)	0.512
Smoked	Yes = 1	964 (28.55)	156 (7.65)	808 (60.39)	<0.001
	No = 0	2,413 (71.45)	1,883 (92.34)	530 (39.61)	
Drank	Yes = 1	822 (24.34)	208 (10.20)	614 (45.89)	<0.001
	No = 0	2,555 (75.66)	1,831 (89.80)	724 (54.11)	
Exercised	Yes = 1	757 (22.42)	391 (19.18)	366 (27.35)	<0.001
	No = 0	2,620 (77.58)	1,648 (80.82)	972 (72.65)	
Cognitive function	Continuous measurement	21.68 (9.60)	19.89 (10.06)	24.40 (8.14)	<0.001
Activities of daily living (ADL)	Continuous measurement	7.41 (2.80)	7.75 (3.08)	6.88 (2.21)	<0.001
Depressive symptoms	Continuous measurement	23.66 (9.79)	24.99 (10.34)	21.63 (8.50)	<0.001

"*N* (%)" means the sample size of a particular category in a categorical variable and its proportion in the total sample. "Mean (SD)" represents the sample mean of a continuous variable and its standard error.

between reproductive history and multidimensional health, with separate models for each indicator of health outcomes. Reproductive history and intergenerational support were separately included in the two models to distinguish between direct and indirect effects. Then, both reproductive history and intergenerational support were included in the third model. Furthermore, we present the gender-stratified results to explore gender differences in the relationship between reproductive history and multidimensional health. Data management and statistical analyses were performed using Stata 15 statistical software (Stata Corp, College Station, TX, USA).

Results

Descriptive characteristics of the study participants ($N = 3,377$) by gender are shown in Table 1. There were 2,039 (60.38%) women and 1,338 (39.62%) men who participated in the study. The average age of the respondents was approximately 85 years. The women in the study population were older than the men by 4 years ($p < 0.001$), had fewer years of education ($p < 0.001$), lower family income ($p = 0.054$), were more likely to be widowed ($p < 0.001$), and were more likely to be without medical insurance ($p = 0.002$). Men tended to smoke ($p < 0.001$), drink ($p < 0.001$), and exercise ($p < 0.001$) in the past. For multidimensional health, women were more likely to be in worse health in terms of cognitive function ($p < 0.001$), ADL ($p < 0.001$), and depressive symptoms ($p < 0.001$).

Table 2 displays the distributions by reproductive history variables and multidimensional health of participants in groups with different reproductive histories. The participants who had 3 to 6 children (categories: 3–4 and 5–6 children) accounted for a large proportion (70.75%) of the whole sample. There were significant differences in cognitive function ($p < 0.001$), ADLs ($p < 0.001$), and depressive symptoms ($p < 0.001$) of older adults with different numbers of children. In brief, the participants with greater parity were more likely to have worse health outcomes. In terms of sex ratio, 43.94% of the sample had more boys, and 34.82% of the sample had more girls. No significant differences were found in the relationship between health outcomes and the sex ratio of their children except cognitive function ($p = 0.075$). Nearly a quarter of older adults had their last birth at 40 years or above, and they had worse conditions of cognitive function ($p < 0.001$), ADL ($p < 0.001$), and depressive symptoms ($p < 0.001$).

Table 3 shows the results from linear regressions assessing the relationship between reproductive history

TABLE 2 Multidimensional health of older adults with different reproductive history ($N = 3,377$).

	Number (%)	Cognitive function		ADL		Depressive symptoms	
		Mean (SD)	*p*-value	Mean (SD)	*p*-value	Mean (SD)	*p*-value
Parity							
1–2	565 (16.73)	23.384 (9.314)	<0.001	7.065 (2.492)	<0.001	22.149 (9.783)	<0.001
3–4	1,372 (40.63)	23.007 (9.013)		7.128 (2.560)		23.023 (9.290)	
5–6	1,017 (30.12)	20.372 (9.781)		7.679 (3.004)		24.572 (9.970)	
7+	423 (12.53)	18.217 (10.078)		8.116 (3.226)		25.551 (10.429)	
Sex ratio of children							
More sons	1,484 (43.94)	21.341 (9.556)	0.075	7.426 (2.822)	0.111	23.854 (9.861)	0.402
Equal number	717 (21.23)	22.332 (9.484)		7.222 (2.627)		23.252 (9.764)	
More daughters	1,176 (34.82)	21.701 (9.716)		7.497 (2.876)		23.663 (9.710)	
Last birth							
After 40 years	792 (23.45)	17.775 (10.460)	<0.001	8.226 (3.330)	<0.001	26.380 (10.844)	<0.001
Before 40 years	2,585 (76.55)	22.872 (8.991)		7.156 (2.568)		22.826 (9.284)	

and multidimensional health after adjusting for covariables. The three health-related outcomes were significantly associated with parity and late childbearing. Older adults in rural areas with greater parity were more likely to have better cognitive function (β = 0.409, 95% CI: 0.255–0.563), fewer ADL limitations (β = −0.085, 95% CI: −0.137 to −0.034), and fewer depressive symptoms (β = −0.396, 95% CI: −0.577 to −0.216). Late childbearing also had a negative effect on cognitive function (β = −1.220, 95% CI: −1.895 to −0.545), ADL (β = 0.253, 95% CI: 0.028–0.478), and depression symptoms (β = 1.025, 95% CI: 0.237–1.812). To capture the indirect effect, we further explored how intergenerational support from children might affect the health of older adults in rural areas in Model 2. The results showed that economic support had a positive effect on health in terms of cognitive function (β = 0.112, 95% CI: 0.041–0.184) and depressive symptoms (β = −0.110, 95% CI: −0.196 to −0.025). Spiritual comfort from children might benefit their parents' health. However, daily care was negatively associated with cognitive function (β = −0.050, 95% CI: −0.055 to −0.044), ADL (β = 0.0263, 95% CI: 0.025–0.028), and depressive symptoms (β = 0.041, 95% CI: 0.035–0.048). The Model 3 included all variables. When intergenerational support was considered, the relationship between parity and health outcomes still passed the significance test with a slight reduction, and the estimated coefficient decreased compared with the Model 1. Late childbearing negatively affected cognitive function (β = −1.071, 95% CI: −1.715 to −0.428) and depressive symptoms (β = 0.927, 95% CI: 0.162–1.692), but the association between late childbearing and ADL became non-significant.

Table 4 displays the results of the gender stratification after controlling for the indirect effect. Women with greater parity were more likely to have better cognitive function (β = 0.339, 95% CI: 0.149–0.528) and fewer depressive symptoms (β = −0.297, 95% CI: −0.525 to −0.069), but these relationships did not pass the significance test in men. Men whose last child was born when they were 40 years old or older experienced cognitive decline (β = −1.926, 95% CI: −2.872 to −0.980) and had more ADL limitations (β = 0.455, 95% CI: 0.177–0.733).

Discussion

In this study, we investigated associations between reproductive history and multidimensional health (cognitive function, ADL, and depressive symptoms) using nationally representative cross-sectional data from older adults in rural China. The results indicated that greater parity was associated with better cognitive function, fewer ADL limitations, and fewer depressive symptoms. This finding was not consistent with several studies (16–18, 27), but the positive effect of greater parity on health was also found in a longitudinal study that showed that elderly women who had five or more children were more likely to live longer in China (38). Having more children means that pregnancy and breastfeeding continue uninterrupted, and it prolongs the cycle of female estrogen in production and stimulates the female biological system, thus promoting survival and health among women (52). In addition, the relationship between parity and health suggests that higher than average reproductive potential may be related to better health (14). Moreover, parity is a positive factor affecting happiness and social support (53, 54), and older adults with more children might be healthier.

To further explore the influence mechanisms, we considered intergenerational support (economic support, daily care, and spiritual comfort from children) to capture the indirect effect of reproduction. The coefficient of parity on multidimensional health is reduced but still significant. This result suggested that

TABLE 3 Linear regression models examining the association between reproductive history and multidimensional health ($N = 3,377$).

	Model 1 direct effect	Model 2 indirect effect	Model 3 overall effect
	β (95% CI)	β (95% CI)	β (95% CI)
Dependent variable: cognitive function			
Parity	0.409***		0.312***
	(0.255–0.563)		(0.163–0.460)
Sex ratio	0.388		0.211
	(−0.623 to 1.401)		(−0.755 to 1.177)
Late	−1.220***		−1.071**
childbearing	(−1.895 to −0.545)		(−1.715 to −0.428)
Economic		0.112**	0.097***
support		(0.041–0.184)	(0.0244–0.169)
Daily care		−0.050***	−0.049**
		(−0.055 to −0.044)	(−0.055 to −0.044)
Spiritual		0.940***	0.924***
comfort		(0.674–1.206)	(0.658–1.190)
Constant	54.330***	49.784***	48.721***
	(51.183–57.476)	(46.800–52.770)	(45.632–51.810)
Dependent variable: ADL			
Parity	−0.085**		−0.054*
	(−0.137 to −0.034)		(−0.101 to −0.008)
Sex ratio	−0.308		−0.192
	(−0.646 to 0.029)		(−0.494 to 0.109)
Late	0.253*		0.162
childbearing	(0.028–0.478)		(−0.038 to 0.363)
Economic		−0.007	−0.005
support		(−0.030 to 0.015)	(−0.028 to 0.017)
Daily care		0.026***	0.026***
		(0.025–0.028)	(0.024–0.028)
Spiritual		−0.198***	−0.194***
comfort		(−0.281 to −0.115)	(−0.277 to −0.111)
Constant	−0.056***	1.934***	2.203***
	(−1.106 to −0.993)	(1.004–2.864)	(1.238–3.167)
Dependent variable: Depressive symptoms			
Parity	−0.396***		−0.296**
	(−0.577 to −0.216)		(−0.472 to −0.119)
Sex ratio	−0.815		−0.656
	(−1.995 to 0.365)		(−1.805 to 0.493)
Late	1.025*		0.927*
childbearing	(0.237–1.812)		(0.162–1.692)
Economic		−0.110*	−0.098*
support		(−0.196 to −0.025)	(−0.184 to −0.012)
Daily care		0.041***	0.041***
		(0.035–0.048)	(0.0339–0.047)
Spiritual		−1.248***	−1.229***
comfort		(−1.564 to −0.932)	(−1.545 to −0.913)
Constant	6.625***	10.730***	11.970***
	(2.956–10.290)	(7.184–14.280)	(8.295–15.64)

The 95% confidence intervals are in parentheses. *p < 0.05; **p < 0.01; ***p < 0.001.

TABLE 4 Linear regression models examining the association between reproductive history and multidimensional health by gender.

	Women ($N = 2,039$)		Men ($N = 1,338$)	
	β	95% CI	β	95% CI
Dependent variable: Cognitive function				
Parity	0.339***	(0.149–0.528)	0.151	(−0.090 to 0.391)
Sex ratio	−0.335	(−1.660 to 0.991)	0.564	(−0.815 to 1.943)
Late childbearing	−0.537	(−1.400 to 0.327)	−1.926***	(−2.872 to −0.980)
Constant	53.015***	(48.861–57.169)	42.973***	(38.223–47.723)
Dependent variable: ADL				
Parity	−0.060	(−0.121 to 0.001)	−0.016	(−0.087 to 0.054)
Sex ratio	−0.180	(−0.605 to 0.245)	−0.025	(−0.430 to 0.380)
Late childbearing	0.005	(−0.272 to 0.282)	0.455**	(0.177–0.733)
Constant	1.377**	(0.045–2.709)	3.348***	(1.954–4.741)
Dependent variable: Depressive symptoms				
Parity	−0.297*	(−0.525 to −0.069)	−0.168	(−0.449 to 0.113)
Sex ratio	−0.070	(−1.663 to 1.523)	−0.998	(−2.611 to 0.614)
Late childbearing	0.587	(−0.451 to 1.625)	1.406*	(0.299–2.513)
Constant	9.137***	(4.146–14.129)	15.170***	(9.611–20.722)

The 95% confidence intervals are in parentheses. *p < 0.05; **p < 0.01; ***p < 0.001.

the positive effect of parity could be partly explained by support from children. Previous studies also confirmed that older adults with more intergenerational support were likely to have fewer depressive symptoms and higher life satisfaction (35, 36, 55). The salience of different mechanisms linked to health may depend on the reproductive culture in different countries (26). China is a country that advocates for filial piety. It is children's responsibility to take care of their parents later in life. Thus, raising children means a long-term investment in the health of older adults in China (56). The more children they have, the more resources they can obtain in their old age. Previous study found a positive "supporting effect" of the parity on parental health. That is, the availability of additional children in old age has a beneficial effect on health during that time (57). In addition, the regression model showed that economic support and spiritual comfort benefit older adults, whereas only daily care had a negative effect on multidimensional health. This finding might be explained by reverse causality, since older adults with cognitive impairment or ADL limitations might need more daily care.

We found no evidence of an association between the sex ratio of children and the multidimensional health among older adults in rural areas, but late childbearing was associated with worse cognitive function and more depressive symptoms. Similar results have been found in several studies that having a child after age 35 years was detrimental to later-life health

(22, 58). In terms of mental health, late childbearing may be associated with greater depression (21).

We finally explored gender differences in the relationship between reproductive history and multidimensional health. Women who gave birth to more children were more likely to have better cognitive function and fewer depressive symptoms. The association between late childbearing and health was only significant in males. It is said that the impact of reproduction on men's health mainly occurs through external social factors, whereas women are influenced by both internal (biological) and external (social) mechanisms (59, 60). In China, men are primarily responsible financially for childbearing. Late childbirth might result in a heavy burden on men, and they would spend more time working and earning money. The working characteristics of men in rural areas, whether they stay in rural areas to engage in agricultural labor or go out to work in urban regions, such as construction workers, are mainly physical labor. The burden of late childbirth has a greater impact on men's health. Therefore, being overworked for a long time may lead to worse health.

Another point should be explained from Table 2. The health of older adults with more children was worse than their counterparts, whereas greater parity resulted in better health after controlling for all covariates in Table 4. This contradictory result might be caused by the fact that older adults who give birth to more children tend to be older. In our sample, only 9.52% of individuals aged 60–70 years had more than five children, but the proportion of participants over 90 years who had five children was 52.25%. It is universally acknowledged that older adults tend to be in worse health. Consequently, when other variables were not controlled, the parity was negatively correlated with health.

The results of regression analysis also showed that age had significant negative impact on the cognitive function ($p < 0.001$), ADL ($p < 0.001$), and symptoms of depression ($p < 0.001$), which suggest that older adults tend to have worse cognitive function, ADL, and symptoms of depression. This finding was consistent with several studies (61–63). As we all know, age plays a fundamental role in the health of older adults. With the increase of age, the function of the body organs of older adults gradually declines, which is reflected by the worse cognitive function, more ADL limitations. and worse symptoms of depression. Therefore, attention should be paid to the health of the oldest-old and provide targeted measures to improve their health.

Nevertheless, the results should be interpreted cautiously due to several limitations. We used only cross-sectional data but not longitudinal data. There may be covariates that affect reproductive decisions and health that were not included in the present study, such as the health status when they were pregnant. Women who give birth to more children might be healthier than others when they are young. In addition, we fail to engage with the possibility of survival bias. Chinese Longitudinal Healthy Longevity Survey (CLHLS) began in 2002. During the following years in 2005, 2008, 2011, 2014, and 2018, there were some lost to follow-ups, deaths, and newly added samples. Since the data of 2018 CLHLS used in our study only contains older adults that survived to 2018, we do not have information for adults that died before this year. It is possible that there is an unobserved mechanism that affects both fertility and health and survival. Finally, for the lack of information in the questionnaire, the paper failed to include some control variables into regression analysis, such as current location of the children. If possible, we will discuss it further in the future.

Conclusions

This study analyzed the association between reproductive history and the multidimensional health of older adults in rural China. Based on cross-sectional data from the CLHLS in 2018, we found that greater parity was associated with better cognitive function, fewer ADL limitations, and fewer depressive symptoms in older adults in rural China. Intergenerational support, including economic support, daily care, and spiritual comfort, partly explained the positive effect of parity. Late childbearing was associated with worse cognitive function and more depressive symptoms. There were gender differences in these relationships. Women were more likely to be influenced by the positive effect of parity, whereas the association between late childbearing and health was only significant in males.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: https://opendata.pku.edu.cn/dataverse/CHADS.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

CY: conceptualization, formal analysis, and funding acquisition. HL: software, writing—review, and editing. FL: writing—review and editing. BW: methodology. EL: funding acquisition, writing—review, and editing. NX: formal

analysis, methodology, and writing—original draft. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Efficacy of vitamin K2 in the prevention and treatment of postmenopausal osteoporosis: A systematic review and meta-analysis of randomized controlled trials

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Introduction: Vitamin K (VK) as a nutrient, is a cofactor in the carboxylation of osteocalcin (OC), which can bind with hydroxyapatite to promote bone mineralization and increase bone strength. However, some studies have been inconsistent on whether vitamin K2 (VK2) can maintain or improve bone mineral density (BMD) and reduce the incidence of fractures in postmenopausal women. Therefore, the main objective of this meta-analysis was to determine the effect of VK2 as a nutritional supplement on BMD and fracture incidence in postmenopausal women.

Methods: We searched PubMed, EMBASE, and Cochrane Library databases (published before March 17, 2022) and then extracted and pooled data from all randomized controlled trials (RCTs) that met the inclusion criteria.

Results: Sixteen RCTs with a total of 6,425 subjects were included in this meta-analysis. The overall effect test of 10 studies showed a significant improvement in lumbar spine BMD (BMD LS) ($P = 0.006$) with VK2. The subgroup analysis of VK2 combination therapy showed that BMD LS was significantly maintained and improved with the administration of VK2 ($P = 0.03$). The overall effect test of the six RCTs showed no significant difference in fracture incidence between the two groups (RR=0.96, P=0.65). However, after excluding one heterogeneous study, the overall effect test showed a significant reduction in fracture incidence with VK2 (RR = 0.43, $P = 0.01$). In addition, this meta-analysis showed that VK2 reduced serum undercarboxylated osteocalcin (uc-OC) levels and the ratio of uc-OC to cOC in both subgroups of VK2 combined intervention and alone. However, for carboxylated osteocalcin (cOC), both subgroup analysis and overall effect test showed no significant effect of VK2 on it. And the pooled analysis of adverse reactions showed no significant difference between the VK2 and control groups (RR = 1.03, 95%CI 0.87 to 1.21, $P = 0.76$).

Conclusions: The results of this meta-analysis seem to indicate that VK2 supplementation has a positive effect on the maintenance and improvement of BMD LS in postmenopausal women, and it can also reduce the fracture incidence, serum uc-OC levels and the ratio of uc-OC to cOC. In conclusion, VK2 can indirectly promote bone mineralization and increase bone strength.

KEYWORDS

vitamin K2, postmenopausal women, osteoporosis, fracture, meta-analysis, randomized controlled trial

Introduction

Osteoporosis (OP) has become a global public health problem, which is mainly characterized by the reduction of bone trabecular number, destruction of bone microstructure and the increase of bone fragility, which predisposes to fractures (1). OP and OP-related fractures are increasingly common in women over 55 years and men over 65 years, especially in older postmenopausal women (2). Hip fracture due to OP in particular can be devastating to the elderly, because it is expensive to treat and carries a high risk of death (3). Postmenopausal osteoporosis (PMOP) is the most common type in primary osteoporosis. When a woman goes through menopause, a sharp drop of estrogen levels will lead to more osteoclastogenesis than osteoblastogenesis, which can lead to the increase of bone resorption, the breakdown of bone metabolism balance, and eventual OP.

Osteocalcin (OC), as a biomarker of bone metabolism, is synthesized and secreted by osteoblasts. It plays an important role in regulating bone calcium metabolism. However, undercarboxylated osteocalcin (uc-OC) has no biological function, because it cannot bind to hydroxyapatite and does not facilitate the deposition of bone calcium. Only with the assistance of VK can uc-OC be converted to carboxylated osteocalcin (cOC), which has a high affinity for calcium and promotes hydroxyapatite formation and bone mineralization (4–7). VK is a fat-soluble vitamin that is a cofactor for the carboxylation of osteocalcin (8, 9). VK includes phylloquinone (VK1) and menaquinone (VK2) (10, 11). VK1 is mainly found in plants, while VK2 is mainly found in some fermented foods, most commonly natto, and VK2 can also be synthesized by intestinal bacteria (12). In addition, there are twelve MK subtypes in VK2, among which MK-4 and MK-7 mainly maintain bone health, as MK-4 and MK-7 can promote bone calcium deposition and increase bone strength (13).

But so far, the answer to the question of whether VK2 significantly maintains or improves bone mineral density (BMD) in various parts of the body and whether it significantly reduces the incidence of fracture is unclear. Some studies (14–20) suggest that VK2 can do this, but some suggest that it cannot (9, 11, 21). However, unlike VK2, the role of vitamin D and calcium in the prevention and treatment of OP has been confirmed by high-quality studies and has been included in guidelines for the prevention and treatment of OP (22, 23). Previous studies have shown that VK2 can promote the mineralization of 1,25 $(OH)_2D_3$-induced in human osteoblasts, and that the effect of VK2 in combination with vitamin D3 or calcium or other anti-osteoporosis drugs (such as alendronate) on bone mass is much greater than that of VK2 alone (24–27). Although previous meta-analyses have evaluated the effects of VK (28–34), to our knowledge, no meta-analysis has examined the effects of VK2 combination therapy and VK2 alone therapy on PMOP. Therefore, we consider it necessary to conduct this systematic review and meta-analysis to determine the role of VK2 in the prevention and treatment of PMOP.

Materials and methods

Search strategy

According to the PRISMA statement, we searched those authoritative literature databases (PubMed, EMBASE, and the Cochrane Library). The search terms used were vitamin K, menaquinone, menatetrenone, postmenopausal and osteoporosis. In order to retrieve these studies comprehensively, we adopted the search method of combining keywords and Boolean Operators. Medical Subject Heading (MeSH) phrases were also used appropriately, and we did not limit the year and language of publication during the search. We have stored the search strategy for the above database in Supplementary material.

Inclusion and exclusion criteria

Based on the principles of PICOS (Population/Intervention/Comparison/Outcome/Study design), the following inclusion criteria were developed: 1. Study design was a randomized controlled trial; 2. Study population was postmenopausal women; 3. Intervention group was VK2 alone or in combination

with other therapeutic measures; 4. Control group was given another drug or placebo; 5. Outcomes should include at least one of the following:(1) percentage change in BMD of lumbar spine, femoral neck, hip, or forearm; (2) Incidence of fractures; (3) percentage change in serum uc-OC; (4) percentage change in serum cOC; (5) percentage change in serum uc-OC to cOC ratio and (6) incidence of adverse reactions.

Studies would be excluded if they fulfilled any of the following conditions: 1. Non-randomized controlled trial; 2. Study was not about VK2; 3. Subjects had renal or immune disease; 4. Subjects were taking anti-osteoporosis drugs or other drugs that affect bone metabolism (such as glucocorticoids or immunosuppressants); 5. Subjects were taking drugs that affect the absorption or metabolism of VK2, such as warfarin.

Study selection

In accordance with the inclusion and exclusion criteria, two reviewers (ML. MA, ZJ.MA) browsed through the titles and abstracts of all studies for initial screening. Then, the full text of the studies was read carefully to identify the final included studies. During the screening process, two reviewers documented the reasons for exclusion of some studies. When two reviewers disagreed on the inclusion or exclusion of studies, a third reviewer (H. DONG) would be invited to discuss and make a final decision.

Data extraction

First, three reviewers (ML. MA, ZJ.MA and H.SUN) extracted and collated the basic information of the final included studies including author, publication year, study type, country, number of study center, sample size, age, follow-up time, intervening measures, as well as other relevant data required for this meta-analysis. Then, three reviewers assessed the quality of the included studies. Some studies presented results in bar or line graphs, without giving specific data. In view of this, we used the online tool for graphical data extraction (Web Plot Digitizer, https://automeris.io/WebPlotDigitizer/). The extracted and collated data were finally rechecked by ML.MA.

Outcomes

The percentage change in BMD (lumbar spine, femoral neck, hip, and forearm) before and after treatment with VK2 or other measures and the incidence of fractures were taken as primary outcomes. Meanwhile, the percentage change of serum uc-OC, cOC, and uc-OC to cOC ratio and the incidence of adverse reactions were taken as secondary outcomes.

Assessment of bias risk for included studies

Two reviewers (YL.HE, SX.LI) independently assessed the risk of bias for all included RCTs using the Cochrane Collaboration's tool. This tool assessed the risk of bias for RCTs through the following seven lists: (1) Random sequence generation (selection bias); (2) Allocation concealment (selection bias); (3) Blinding of participants and personnel (performance bias); (4) Blinding of outcome assessment (detection bias); (5) Incomplete outcome data (attrition bias); (6) Selective reporting (reporting bias); (7) Other bias. Each list has three options: high risk, low risk and unclear risk.

Data synthesis and analysis

We used the STATA software (STATA Software Version 16.0) to assess publication bias and conduct sensitivity analysis, and used the Review Manager Software (RevMan5.3) to make analysis for other data. For continuous outcome variables, we extracted the mean and standard deviation from the included studies and then calculated the weighted mean difference (WMD) and 95% confidence interval (95% CI), and for binary outcome variables, we extracted the number of positive events in both groups then calculated the risk ratio (RR) and 95%CI. The heterogeneity of studies was assessed using I^2 statistics and Cochran's Q Test (35–37). The random-effects model was used when the heterogeneity between studies was large ($P \leq 0.1$, $I^2 > 50\%$) and the fixed-effects model was used when the heterogeneity between studies was small ($P > 0.1$, $I^2 \leq 50\%$). Subgroup analysis was based on VK2 and the studies were then divided into two subgroups: VK2 combined intervention subgroup and VK2 alone intervention subgroup. Sensitivity analysis was performed by removing studies that caused heterogeneity. The continuous variables in this meta-analysis were the percentage change of outcomes before and after treatment, which contributed to the elimination of differences in baseline data.

Results

Search results

We searched a total of 694 studies in PubMed, EMBASE and Cochrane Library databases, and then we removed 213 duplicated studies and obtained 481 studies initially. Next, by reading the titles and abstracts of these studies, we excluded 432 studies again for the following reasons:(1) subjects were uncorrelated with ours; (2) review or meta-analysis; (3) animal studies; (4) outcomes of studies did not meet our needs; (5) study population included either men or non-menopausal women;

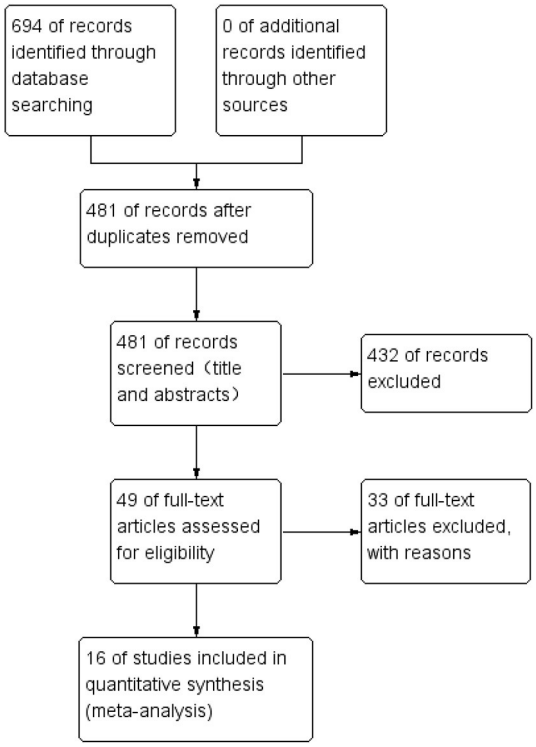

FIGURE 1
Flow diagram of studies selection.

(6) mechanism researches for VK2. Next, the full texts of the remaining 49 studies were read precisely and carefully, and 16 studies (9, 14, 15, 18, 21, 26, 27, 38–46) were finally eligible for the inclusion in this meta-analysis. Another 33 studies were excluded for the following reasons: (1) the intervention was VK1 or partially VK1; (2) non-randomized controlled trials; (3) no access to study data; (4) study data were absolute values, not percentage change. Additionally, the majority of the included studies were conducted in Japan (18, 26, 27, 39–41, 44–46), and others were conducted in Denmark, the Netherlands, Norway, China and Indonesia (9, 14, 15, 21, 38, 42, 43). The screening process of the studies is shown in Figure 1.

Characteristics of the included studies

Through searching and screening, 16 studies were included in this meta-analysis, all of which were RCTs with a total of 6,425 subjects. These studies were mainly distributed in Europe (9, 15, 21, 38, 42) and Asia (14, 18, 26, 27, 39–41, 43–46). Most of them were single-center studies, and only three were multicenter studies (14, 21, 41). The characteristics of the included studies are shown in Table 1.

Quality assessment of the included studies

Two reviewers (YL. HE, SX.LI) independently assessed the quality of each included randomized controlled trial using the Cochrane Collaboration's tool. Although all studies included in this meta-analysis were randomized controlled trials, some studies did not clearly describe how populations were grouped, resulting in a high risk of selection bias (15, 18, 27, 40, 44–46). There were also some studies that did not implement the double-blind method well, leading to a high risk of performance bias (26, 40, 41, 45). The results of bias risk assessment for the included RCTs are shown in Figure 2.

Primary outcomes

Pooled analysis for the changes in BMD

We first analyzed the change in BMD LS before and after treatment with VK2. A total of ten studies (9, 15, 18, 21, 27, 40, 42–44, 46) reported the changes in BMD LS, and the test for the overall effect of these ten studies showed that VK2 maintained and improved BMD LS (MD = 1.02, 95%CI 0.30 to 1.75, P=0.006) compared with the control group (Figure 3A). Subgroup analysis of VK2 combined intervention showed that the effect of VK2 on BMD LS was superior to that of the control group (MD = 1.97, 95% CI 0.20 to 3.74, $P = 0.03$) (Figure 3A). However, the subgroup analysis of VK2 alone intervention showed a similar effect of VK2 and control groups on change in BMD LS ($P = 0.160$) (Figure 3A). In the subgroup of VK2 combined intervention, heterogeneity between studies was eliminated after removing Rønn et al. (9) and Ushiroyama et al. (44) (Figure 3B). And we found that the Z value of the test for overall effect became larger (Z = 4.83), the P-value became smaller ($P < 0.00001$), and the 95% confidence interval was narrow down (1.15 to 2.72) (Figure 3B). These changes further suggest that VK2 combined intervention appears to be better at maintaining BMD LS.

The changes in hip BMD were reported in four studies (9, 21, 39, 42), and the overall effect test showed no significant difference in hip BMD changes in the VK2 group compared with the control group ($P = 0.79$) (Figure 4).

Five studies (9, 15, 21, 27, 42) reported changes in femoral neck BMD, and the overall effect test showed no significant difference in femoral neck BMD change between the VK2 and control groups ($p = 0.24$) (Figure 5).

Four studies (9, 26, 39, 45) reported percentage changes in forearm BMD. Both the overall effect test and the subgroup analysis of VK2 combined intervention showed no significant difference in BMD change between the VK2 and control groups ($P = 0.21$, $P = 0.52$). However, the subgroup analysis of VK2 alone intervention showed that VK2 had a superior effect on

TABLE 1 Characteristics of included studies.

Reference	Study type	Country	Research center	Number	Age	Years of menopause	Osteoporosis	Follow-up	Intervention	Comparison
Rønn et al. (9)	RCT	Denmark	SC	142	67.3 ± 4.4	>2	No	36 M	375μg/day MK-7 + 38μg/day VD3 + 800 mg/day Ca	38μg/day VD3 + 800 mg/day Ca
Rønn et al. (38)	RCT	Denmark	SC	142	60–80	>2	No	12 M	375μg/day MK-7 + 38μg/day VD3 + 800 mg/day Ca	38μg/day VD3 + 800 mg/day Ca
Kasukawa et al. (26)	RCT	Japan	SC	101	>60	-	Yes	12 M	17.5 mg/week risedronate + 45 mg/day menatetrenone	17.5 mg/week risedronate
Koitaya et al. (39)	RCT	Japan	SC	48	58.4 ± 3.8	7.3±3.8	No	12 M	1.5 mg/day MK-4	placebo
Jiang et al. (14)	RCT	China	MC	213	45–75	>5	Yes	12 M	45 mg/day menatetrenone + 500 mg/day Ca	0.5 μg/day alfacalcidol + 500 mg/day Ca
Knapen et al. (15)	RCT	Netherlands	SC	244	55–65	9±6	No	36 M	180μg/day MK-7	placebo
Emaus et al. (21)	RCT	Norway	MC	334	50–60	1-5	No	12 M	360 mg/day MK-7	placebo
Shiraki et al. (40)	RCT	Japan	SC	121	68.6 ± 7.6	19.6 ± 9.3	Yes	6 M	45 mg/day menatetrenone	133.8 mg/day Ca
Inoue et al. (41)	RCT	Japan	MC	4378	>50	20.55±9.89	Yes	48 M	45 mg/day menatetrenone + Ca	Ca
Hirao et al. (27)	RCT	Japan	SC	48	68.5 ± 2.1	-	Yes	12 M	45 mg/day VK2 + 5 mg/day alendronate	5 mg/day alendronate
Knapen et al. (42)	RCT	Netherlands	SC	325	55–75	>2	No	36 M	45 mg/day MK-4	placebo
Purwosunu et al. (43)	RCT	Indonesia	SC	63	60–75	>2	Yes	12 M	45 mg/day menatetrenone + 1500 mg/day Ca	placebo + 1500 mg/day Ca
Ushiroyama et al. (44)	RCT	Japan	SC	172	53.41±5.90	2.50±4.16	Yes	24 M	45 mg/day MK-4 + 1μg/day VD3	1μg/day VD3
Iwamoto et al. (45)	RCT	Japan	SC	72	53-78	>5	Yes	24 M	45 mg/day MK-4	2 g/day Ca
Iwamoto et al. (46)	RCT	Japan	SC	92	55-81	>5	Yes	24 M	45 mg/day menatetrenone + 0.75 μg/day VD3	0.75 μg/day VD3
Iwamoto et al. (18)	RCT	Japan	SC	72	53.82 ± 5.24	5.21±4.18	No	12 M	45 mg/day MK-4	1.0 g/day VD3

RCT, Randomized Controlled Trial; SC, single-center; MC, multiple-center; M, month; VK2, vitamin K2; VD3, vitamin D3; Ca, calcium.

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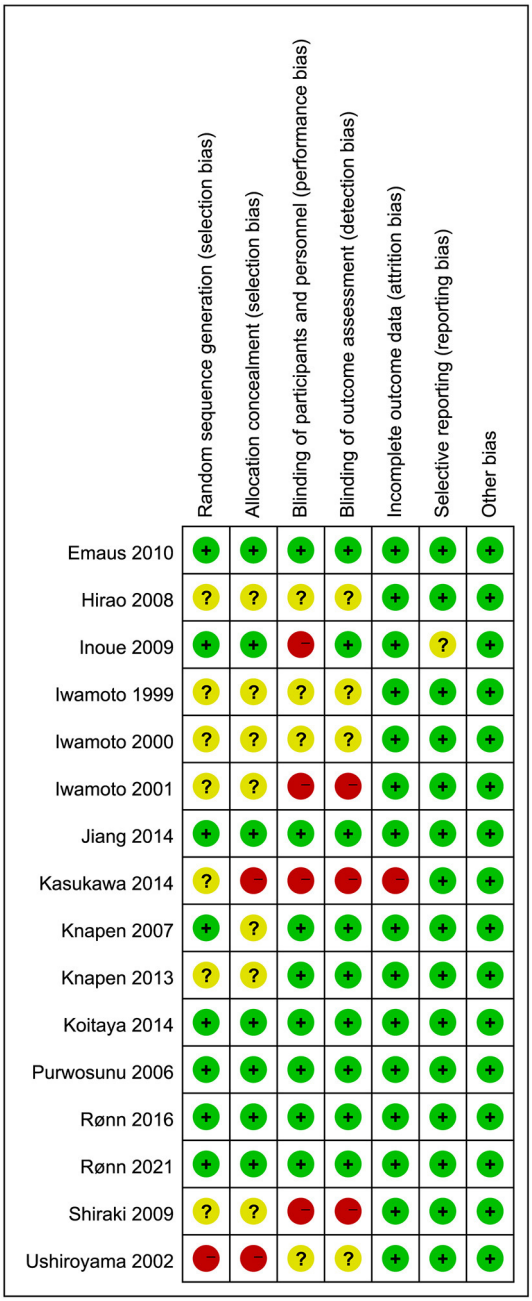

FIGURE 2
Risk of bias summary of included studies.

forearm BMD than controls (MD = 1.42, 95%CI 0.11 to 2.73, $P = 0.03$) (Figure 6).

Pooled analysis for fracture incidence

Six studies (14, 15, 21, 26, 41, 45) reported fracture incidence, and the overall effect test showed that VK2 did not reduce the incidence of fractures (RR = 0.56, 95% CI 0.28 to 1.11, $P = 0.10$) (Figure 7A). However, when the study by Inoue et al. (41) was removed, the subgroup analysis of VK2 combined intervention showed a significant difference in fracture incidence between the VK2 and control groups (RR = 0.25, 95% CI 0.07 to 0.87, $P = 0.03$, $I^2 = 0\%$) (Figure 7B). And the overall effect test also showed that VK2 was effective in reducing the incidence of fractures compared with the control group (RR = 0.38, 95% CI 0.20 to 0.76, $P = 0.006$, $I^2 = 0\%$) (Figure 7B).

Secondary outcomes

Pooled analysis for the change in serum uc-OC

Six studies (14, 15, 26, 27, 38, 39) reported the percentage changes in serum uc-OC. The overall effect test showed a significant difference in serum uc-OC levels between the VK2 and control groups (MD = −39.52, 95%CI−57.25 to−21.79, $P < 0.0001$). Subgroup analyses of both VK2 combined and alone intervention showed that VK2 significantly reduced serum UC-OC levels compared with the control group ($P < 0.05$) (Figure 8).

Pooled analysis for the change in serum cOC

Six studies (9, 14, 15, 26, 27, 39) reported percentage changes in serum cOC that were not significantly different between the VK2 and control groups by overall effect test (MD = 8.45, 95% CI−5.52 to 22.42, $p = 0.24$) (Figure 9).

Pooled analysis for the change in the ratio of serum uc-OC to cOC

Five studies (14, 15, 26, 27, 38) reported the percentage changes in the ratio of serum uc-OC to cOC, and the overall effect test showed a significant difference between the VK2 and control groups (MD = −49.41, 95% CI 64.03 to−34.80, $P < 0.00001$). Similarly, the subgroup analyses of VK2 combined and alone intervention showed that VK2 significantly reduced the ratio of serum uc-OC to cOC ($P < 0.00001$) (Figure 10).

Pooled analysis for the incidence of adverse reactions

The incidence of adverse reactions was reported in five studies (14, 21, 40, 41, 45), and overall effect test showed no significant difference in the incidence of adverse reactions between the VK2 and control groups (RR = 1.03, 95% CI 0.87 to 1.21, $P = 0.76$) (Figure 11).

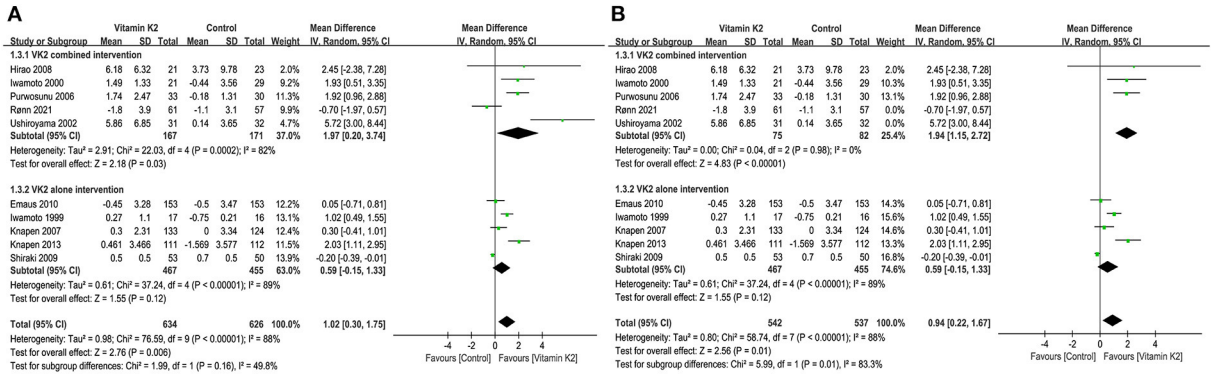

FIGURE 3
(A) Forest plot of the change in BMD LS. **(B)** Forest plot of the change in BMD LS after removed the studies by Rønn and Ushiroyama.

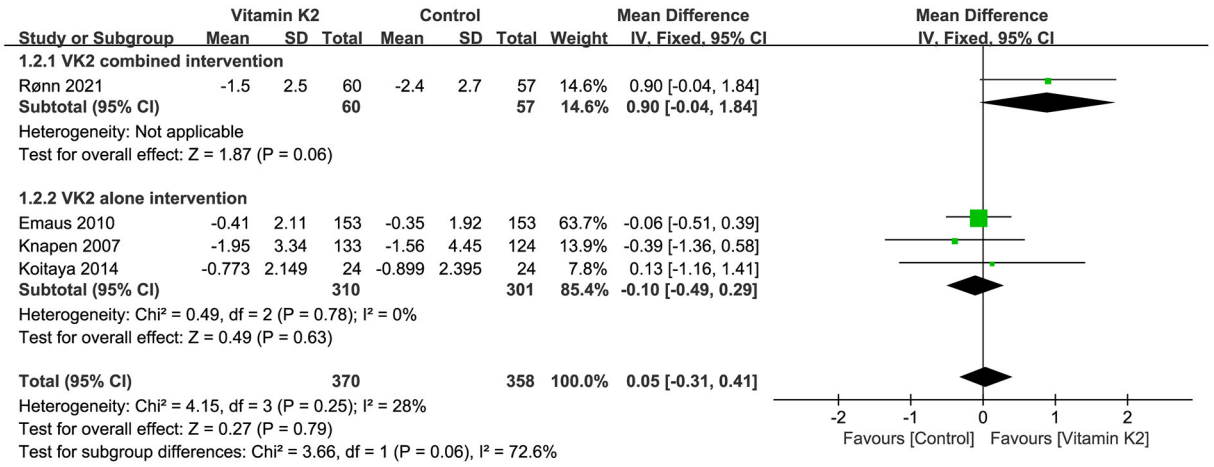

FIGURE 4
Forest plot of the change in hip BMD.

Publication bias and sensitive analysis

We imported the data from 10 studies (9, 15, 18, 21, 27, 40, 42–44, 46) that reported the percentage changes in BMD LS into STATA 16 software and then assessed publication bias by Egger's quantitative test. The results showed no publication bias for the ten studies ($P = 0.134$, 95%CI−1.19 to 7.41), and each study was roughly symmetrically distributed on both sides of the regression line (Figure 12). In addition, we also performed sensitivity analyses for the 10 studies using STATA 16 software to assess the stability of this meta-analysis model, and the results showed that when any of the 10 studies were removed, the dots representing statistical effect of the remaining studies were distributed around the vertical line of the overall statistical effect and within 95% confidence interval (Figure 13).

Discussion

We searched for studies according to the PRISMA statement and screened studies according to the inclusion and exclusion criteria, and ultimately 16 RCTs were included in this meta-analysis. By pooled analysis, we found that VK2 maintained and improved the BMD LS, and the subgroup analysis of VK2 combined intervention yielded the same conclusion, but the subgroup analysis of VK2 intervention alone did not show the difference compared with the control group. In addition, the results of this meta-analysis showed no significant differences between the VK2 and control groups in terms of BMD changes in the hip, femoral neck and forearm. The overall effect test for fracture incidence showed that VK2 reduced fracture incidence after removing study with large

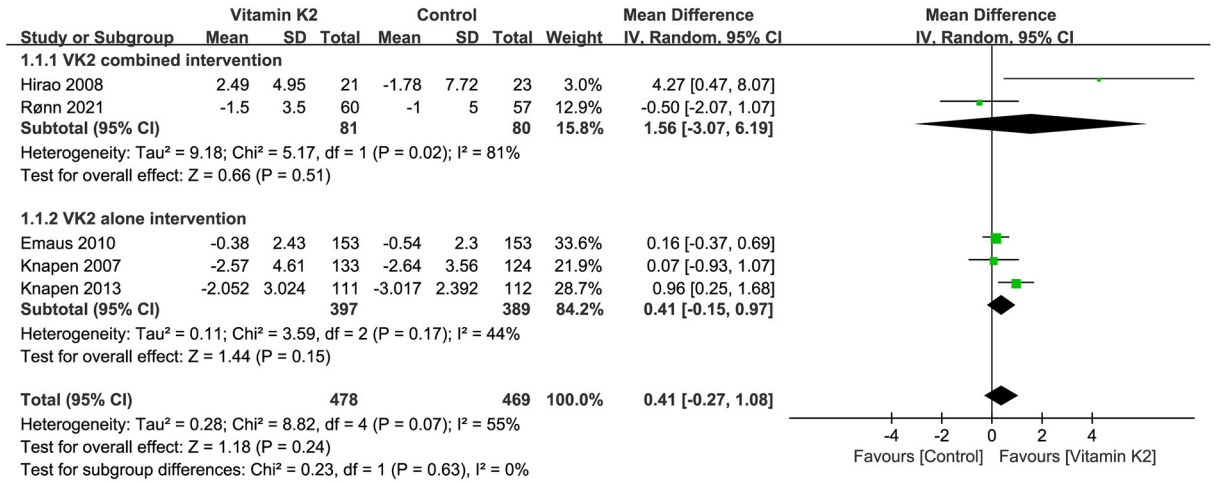

FIGURE 5
Forest plot of the change in femoral neck BMD.

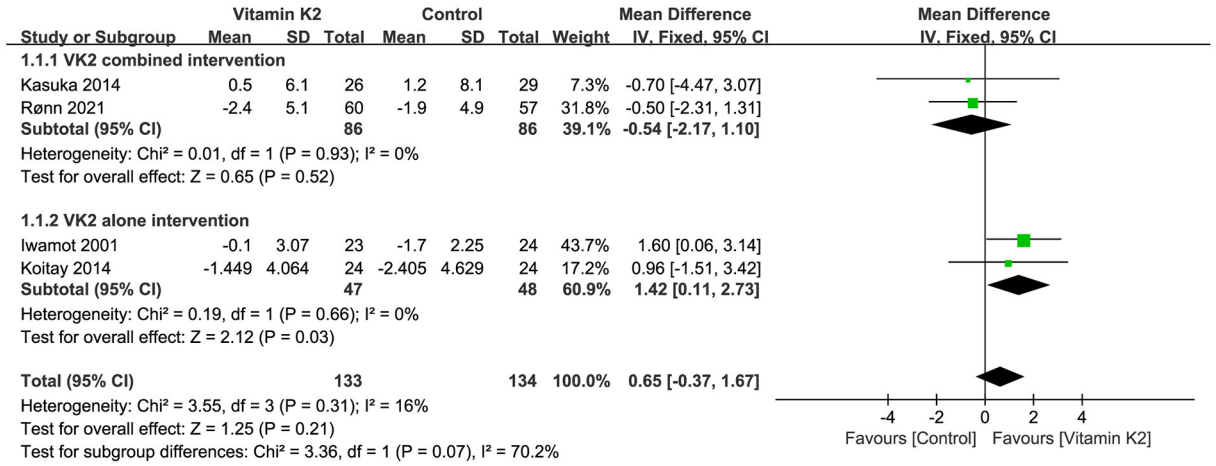

FIGURE 6
Forest plot of change in forearm BMD.

heterogeneity (RR = 0.38,95% CI 0.20 to 0.76, $P = 0.006$, $I^2 = 0\%$) (41).

It is well known that the main aim of prevention and treatment of OP is to prevent fractures, so we took the BMD changes and fracture incidence as the primary outcome indicators in this meta-analysis. However, of all RCTs included in this meta-analysis, only 6 studies (14, 15, 21, 26, 41, 45) reported the incidence of fractures. Therefore, the effect of VK2 on fracture incidence cannot be assessed very accurately in this meta-analysis. The pooled analysis of the 6 studies showed that VK2 cannot reduce the fracture incidence, and subgroup analyses of VK2 combined and alone intervention also showed the similar results. However, when we performed sensitivity analyses on these six studies, we found that the study by Inoue et al. (41) was relatively heterogeneous in comparison with other studies. When the study by Inoue et al. was removed, the result of this meta-analysis showed that VK2 reduced the incidence of fractures. But in fact, the exclusion of the study by Inoue et al. may cause selection bias, because the sample size of this study was very large and the follow-up period was longer (48 months) than other studies. In the study by Inoue et al. there was no significant difference in the incidence of fractures between the VK2 and control groups. However, this study showed a significant reduction in the incidence of new vertebral fractures in patients treated with VK2 who had already had vertebral fractures, and it also showed that VK2 had a positive effect on the elderly population suffering from severe bone loss. Therefore, although the heterogeneity of this study is relatively large, it is undeniably a very valuable study. In view of this, we need to be cautious in excluding this study and

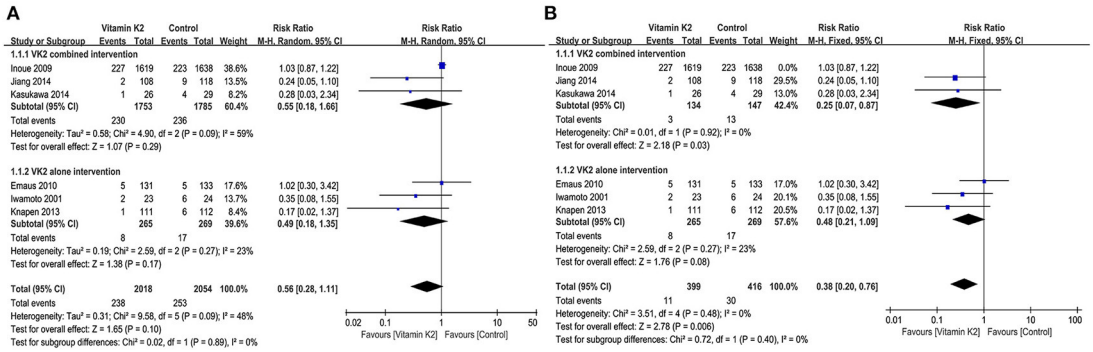

FIGURE 7
(A) Forest plot of the incidence of fractures. **(B)** Forest plot of the incidence of fractures after removed the study by Inoue.

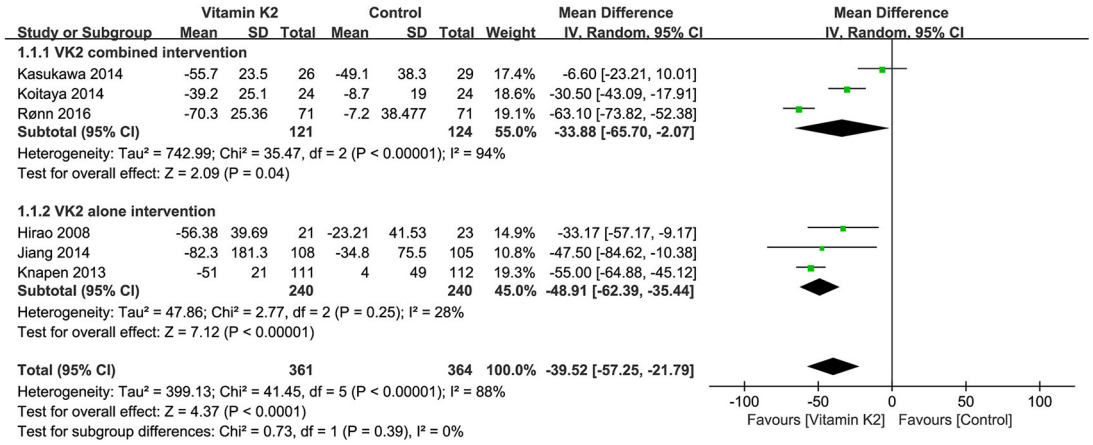

FIGURE 8
Forest plot of the change in serum uc-OC.

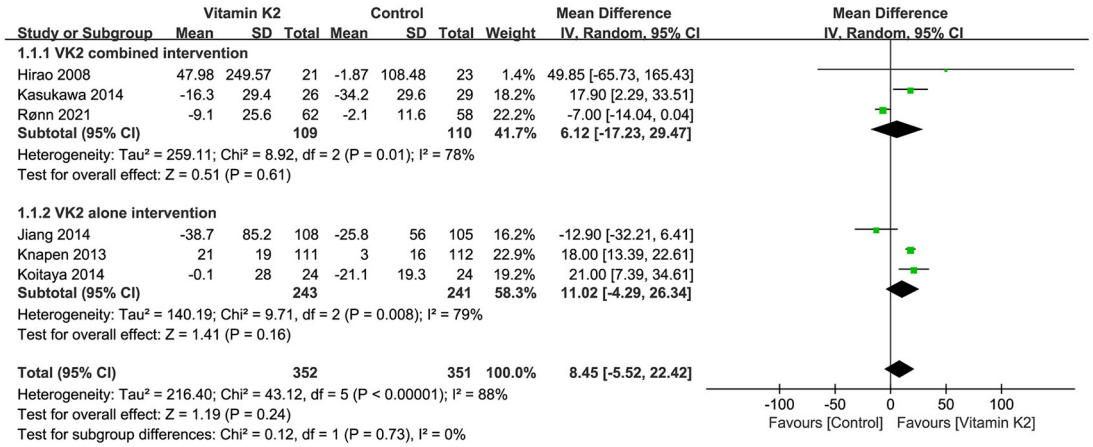

FIGURE 9
Forest plot of the change in serum cOC.

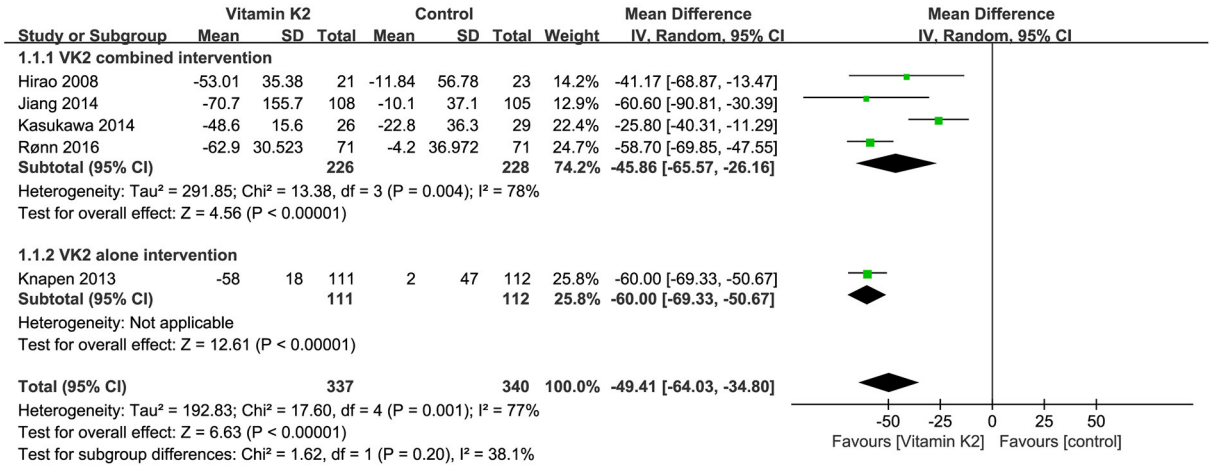

FIGURE 10
Forest plot of the change in the ratio of serum uc-OC to cOC.

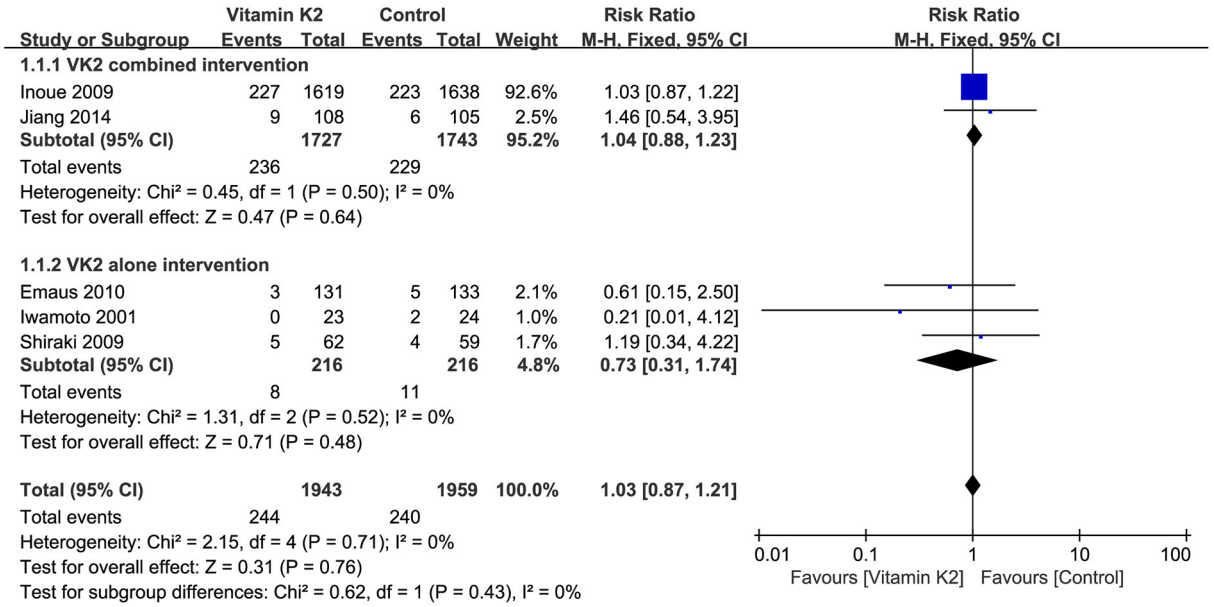

FIGURE 11
Forest plot of the incidence of adverse reactions.

also cautious in drawing conclusion that VK2 can reduce the incidence of fractures.

Osteocalcin (OC), also known as a gamma-carboxyl bone glaprotein (BGP), is a vitamin K-dependent protein that is synthesized and secreted by osteoblasts (47). OC has biological effects in regulating bone metabolism after OC is γ -carboxylated, but the process requires sufficient VK. Depending on the degree of carboxylation of osteocalcin, osteocalcin includes fully carboxylated osteocalcin (cOC) and undercarboxylated osteocalcin (uc-OC), while cOC can bind to hydroxyapatite and thus promote calcium deposition in bones. When serum VK is deficient, the carboxylation ability of osteocalcin will be weakened, serum uc-OC levels will be increased, and cOC levels will be decreased (48, 49). And low serum VK levels and high uc-OC levels are considered as risk factors for hip fracture in older women (50). In this meta-analysis, the overall effect test showed that VK2 significantly reduced serum uc-OC levels and the ratio of serum uc-OC to cOC, while subgroup analyses of the VK2 combined intervention and alone intervention also yielded similar conclusions. However, there was no significant difference in serum cOC levels between the VK2 group and the control

group. Theoretically, when VK2 is maintained at a relatively high levels in serum, the γ-carboxylation of OC would be enhanced, thus contributing to the increase in serum cOC levels and the decrease in uc-OC levels. It should not be forgotten, however, that with increasing serum VK2 levels, more and more OC can become carboxylated and functional. And more of the functional OC can be bound to the bones rather than circulating in the blood, so serum cOC levels may not increase significantly.

Five studies (14, 21, 40, 41, 45) reported the incidence of adverse reactions in evaluating the safety of VK2 in the prevention and treatment of PMOP. The pooled analysis of the five studies showed that VK2 did not increase the incidence of adverse reactions compared to the controls (RR = 1.03, 95% CI 0.87 to 1.21, $P = 0.76$). It suggests to us that the use of VK2 for the prevention and treatment of PMOP is safe in the present situation.

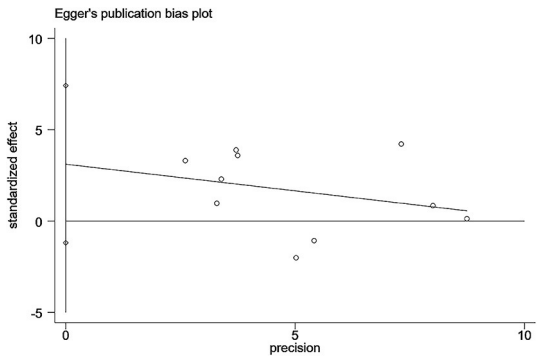

FIGURE 12
Publication bias test for the overall effect test of BMD LS change.

In conclusion, we may conclude that VK2 is effective in the prevention and treatment of PMOP, because VK2 appears to maintain and improve the BMD LS. And VK2 may be particularly effective when used in combination with other preventive or therapeutic measures, such as vitamin D, calcium, or alendronate. The results of this meta-analysis gave us the greatest confidence that VK2 can significantly reduce serum levels of uc-OC. In the effect of VK2, more OC undergoes γ-carboxylation and are converted to cOC, which can promote bone mineralization and increase bone strength. Meanwhile this meta-analysis also suggests that VK2 may reduce the incidence of fractures, but this conclusion needs to be further verified by more multi-center, large sample size and prospective studies.

Although the 16 studies included in this meta-analysis were all randomized controlled trials, the following problems still remained in our meta-analysis: (1) the quality of the included studies was uneven, and there were various biases (selection bias, performance bias, detection bias, etc.); (2) the sample sizes of some RCTs were too small, which might lead to the conclusions that were accidental; (3) the follow-up time of the included studies was different, and we did not perform more detailed groupings; (4) the majority of the included studies were conducted in Japan, and these studies that concluded that VK2 had a positive effect on prevention and treatment of PMOP were

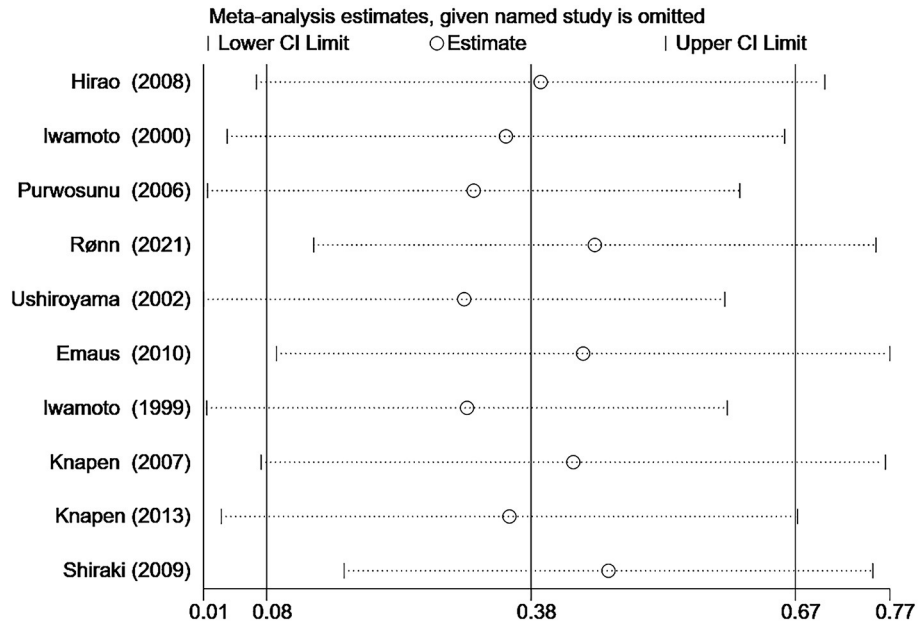

FIGURE 13
Sensitive analysis for the overall effect test of BMD LS change.

also primarily conducted in Japan. Therefore, it remains to be discussed whether the positive effect of VK2 on prevention and treatment of PMOP can be extended to other countries.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

M-lM, Z-jM, and HS carried out the study design, study selection, data extraction, statistical analysis, and drafted the manuscript. BY, B-jR, and W-dZ participated in the study selection, data extraction, and drafted the manuscript. Y-lH and S-xL evaluated the quality of included studies. HD and Y-xW participated in the discussion for any discrepancies and supervised the study. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.979649/full#supplementary-material

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Sleep pattern in relation to recurrent osteoporotic fracture in the elderly

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Background: Previous studies assessed the relationship between individual sleep behavior and fracture risk, rather than taking into account the joint complexity of the sleep behaviors. We aimed to explore the association between sleep pattern and risk of imminent recurrent osteoporotic fracture in older hospitalized patients due to an index osteoporotic fracture, where sleep pattern was evaluated as a combination incorporating five common sleep behaviors (i.e., insomnia, snoring, nocturnal sleep duration, daytime napping, and midnight waking up).

Methods: We used data from a prospective cohort study for analyses. Patients who aged not < 55 years and were admitted to the hospital due to an index osteoporotic fracture were recruited. Sleep pattern was grouped as healthy, intermediate, and poor pattern, based on the categorization of overall sleep scores. We used Cox proportional hazard models to explore sleep pattern in relation to imminent recurrent fracture.

Results: We included a total of 185 elderly hospitalized patients for analyses with mean (± standard deviation) age = 71.5 ± 10.3 years and 87.0% female. During a mean follow-up of 14.7 months, there were 10 (5.4%) recurrent osteoporotic fractures observed. A significantly higher overall sleep score was found in patients with recurrent fractures when compared with those without fractures (3.20 vs. 2.36, $p = 0.038$). Both intermediate ($p = 0.76$) and poor sleep patterns ($p = 0.093$) were non–significantly associated with an elevated risk of fracture when compared with a healthy pattern. Per-one-increase in the overall sleep score was significantly related to an increased risk of fracture: hazard ratio = 1.60 (95% confidence interval: 1.00-–2.55) from the multivariable model.

Conclusion: Per-one-increase in the overall sleep score was found to be significantly associated with a 60% higher risk of imminent recurrent osteoporotic fracture in the elderly, and intermediate and poor sleep patterns were non–significantly related to an increased risk of recurrent fracture. More high-quality evidence is required to further evaluate the relationship between the sleep pattern and the risk of recurrent osteoporotic fracture in the elderly.

KEYWORDS

Recurrent fracture, Elderly, Sleep pattern, osteoporotic fracture, Public Health

Introduction

As the population ages, the risk of osteoporotic fracture remained increasingly high worldwide, posing a significant challenge to the public health and global disease burden (1, 2). The risk of subsequent osteoporotic fracture in the elderly with an index osteoporotic fracture was substantially high, in which their subsequent fracture risk was two to six times higher than their controls who did not have a prior fracture (3). Despite an index fracture resulting in an elevated risk of subsequent fracture, there were <30% of postmenopausal women with an index fracture received anti-osteoporotic medications or prophylactic strategies (4). Therefore, more endeavors were required to enhance the management of osteoporosis and prevention of osteoporotic fracture in the elderly with an index fracture.

The relationship between sleep and osteoporotic fracture in the elderly had been extensively investigated in the literature (5–8). For instance, long sleep duration (hazard ratio = 1.26) and daily napping (hazard ratio = 1.33) were significantly associated with an increased risk of osteoporotic fracture in older women (7), while obstructive sleep apnea resulting in hypoxia was found to be associated with a 30–40% higher risk of fracture in older men (6). However, all the previous studies assessed the relationship between individual sleep behavior and fracture risk, rather than taking into account the joint and intrinsic complexity of the sleep behaviors. It was recommended to treat relevant sleep behaviors as an integrated pattern as appropriate because patients with one sleep characteristic were inclined to maintain another characteristic in general (9). Furthermore, while the previous studies focused on sleep in relation to the onset of osteoporotic fracture, evidence about the relationship between sleep and risk of imminent recurrent osteoporotic fracture in the elderly was limited and sparse. Therefore, in this study, we aimed to explore the association between sleep pattern and risk of imminent recurrent osteoporotic fracture in older patients who were hospitalized due to an index osteoporotic fracture, where sleep pattern was assessed as a combination incorporating five common sleep behaviors (i.e., insomnia, snoring, nocturnal sleep duration, daytime napping, and midnight waking up). Data from a Chinese prospective cohort study that enrolled elderly patients with hospital admission due to an osteoporotic fracture were used for analyses.

Materials and methods

Patients and setting

We recruited elderly patients from the Department of Orthopedics in a general hospital in Zhuhai, China initially from 2020 to September 2021 and extended the enrolment to December 2021 based on the consecutive sampling strategy. Given the official retirement age of 55 years for Chinese women and the high risk of osteoporotic fracture in postmenopausal women, we enrolled the patients aged not < 55 years. The patients were eligible for inclusion if they were admitted to the hospital due to an index osteoporotic fracture that was defined as any fragility fracture (but excluding fractures of face, fingers, and toes) and agreed to participate. The study procedure was similar to previous research conducted by the same authors (10).

Data were gathered *via* an in-person interview with trained research staff, laboratory measurements, and the hospital information system. We performed a follow-up (up to May 2022) by searching patients' medical records and calling them with the use of a telephone. All patients provided written informed consent before the study. This study was reviewed and approved by the Guangdong Second Provincial General Hospital Ethics Committee (No. 20190717-02-YXKXYJ-KT).

Construction of integrated sleep pattern

The individual components and their scoring algorithm for the sleep pattern had been described according to Zeng et al. 2022 (10). In brief, we assigned 1 point to each of the five sleep behaviors if they were defined as *unhealthy* and 0 point if *healthy*, where healthy sleep behaviors included no frequent insomnia, no snoring, appropriate nocturnal sleep duration, appropriate daytime napping, and no frequent midnight waking up.

Patients were asked whether they had difficulty in falling and/or maintaining asleep in the previous 6 months, and if so, to document the *insomnia* frequency (rarely/never, sometimes, 1–3 times per week, and >4 times per week). Those with a response of 1–3 times or > 4 times per week were considered to have frequent insomnia. Regarding the information on *snoring*, patients were asked whether their family members ever told them or they themselves knew they had habitual snoring (yes/no). We documented the daily *nocturnal sleep duration* that patients had recently and categorized them as having appropriate sleep duration if they slept 7–9 h/day. Similarly, we asked whether patients owned habitual *daytime napping* and *midnight waking up* and recorded their duration of daytime napping and frequency of midnight waking up as appropriate. Appropriate daytime napping was defined as a daily napping duration of < 60 min, and no frequent midnight waking up was defined as a waking up frequency of ≤ 2 times each night.

Subsequently, we calculated an overall sleep score by adding up all the points from the five individual behaviors. The overall score had a minimum of 0 and a maximum of 5 points, with a larger score implying aggravated sleep. As recommended by the previous research (9, 11), we grouped patients as having a *healthy sleep pattern* if their overall sleep scores were 0 or 1 point, *intermediate pattern* if 2 or 3 points, and *poor pattern* if 4–5 points.

Outcome assessment

The outcome was whether patients had imminent recurrent osteoporotic fractures after the index fracture during follow-up. We also collected data on the fracture site(s), the date of fracture, and whether the fracture led to hospitalization.

Covariate information

Covariates of consideration were patients' baseline age, sex, smoking and drinking status, body mass index (BMI), lumbar spine T-score, comorbidities including diabetes mellitus and thyroid disease, use of anti-osteoporotic mediations before index fracture, and personal history of osteoporotic fracture in the previous 5 years. Their lumbar spine T-scores, as a measurement of bone mineral density, were evaluated by dual-energy X-ray absorptiometry (DXA) at L_1-L_4 using the same scanner (GE Prodigy, Madison, WI, United States).

Statistical analysis

For descriptive statistics, we presented the results with mean ± standard deviation (SD) for continuous variables, and for categorical variables, we displayed the data with frequency and percentage. To compare differences between patients with and without imminent recurrent osteoporotic fracture, we used the Mann-Whitney *U* test for analysis of continuous variables and Fisher's exact test for categorical variables. Pie charts were used to display the proportions of different sleep patterns in patients with and without recurrent fractures. The Kaplan-Meier method was employed to graph failure curves for imminent recurrent osteoporotic fracture during follow-up.

We used Cox proportional hazard models to explore sleep pattern in relation to imminent recurrent fracture, with hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) reported. We first assessed the relationship between individual sleep behaviors and risk of recurrent fracture. Subsequently, we explored the association between sleep pattern and recurrent fracture risk, treating healthy sleep pattern as a reference. Results were presented from both univariable and multivariable (age- and sex-adjusted) models. As a supplemental analysis, we evaluated the relationship between overall sleep score and risk of recurrent fracture, taking overall sleep score as a continuous exposure variable. Results were shown as a per-one-point increase in the overall sleep score. Given the inconsistent findings on defining appropriate daytime napping, we performed another supplemental analysis by redefining appropriate daytime napping of < 30 min and rebuilding the sleep pattern. Spearman's correlation coefficient was then used to quantify the agreement between the original and the updated sleep pattern. Furthermore, we conducted another analysis by further adjusting for *T*-score in the multivariable model for sleep pattern in relation to the risk of recurrent fracture.

All analyses were performed with the use of STATA version 17 (StataCorp, College Station, TX) and SAS version 9.3 (SAS Institute, Inc., Cary, NC), with the significance level set at 0.05.

Results

We included a total of 185 elderly hospitalized patients due to an index fracture for analyses (Table 1). They had a mean (± SD) age of 71.54 ± 10.32 years and a mean (± SD) BMI of 22.18 ± 3.40 kg/m^2. The majority (87.03%) of included patients were females. There were 14.05% and 43.78% patients taking anti-osteoporotic medication before hospitalization and having a fracture history in the past 5 years, respectively. Their mean (± SD) of lumbar spine T-scores and overall sleep scores were−3.28 ± 1.70 and 2.41 ± 1.19, respectively. During a mean (± SD) follow-up of 14.73 ± 5.01 months, there were 10 (5.41%) recurrent osteoporotic fractures observed. The recurrent fractures included 1 thoracic and 9 lumbar spine fractures, all requiring hospitalization. Supplemental Figure 1 shows the Kaplan-Meier curve for the risk of recurrent fracture.

As shown in Table 1, no significant differences in age, female percentage, or BMI were found between patients with and without imminent recurrent osteoporotic fracture. Similarly, the two groups did not significantly differ in individual sleep behaviors; however, a significantly higher overall sleep score was found in patients with recurrent fractures when compared with those without fractures (3.20 vs. 2.36, $p = 0.038$). According to Supplemental Table 1 and Figure 1, there were 40 (22.86%), 111 (63.43%), and 24 (13.71%) patients having healthy, intermediate, and poor sleep patterns in patients without recurrent fracture, respectively, while the corresponding percentages were 1 (10%), 4 (40%), and 5 (50%) for patients with recurrent fracture. A significant difference in the sleep pattern proportions between patients with and without recurrent fractures was observed ($p = 0.022$).

The relationship between individual sleep behavior and risk of recurrent fracture is demonstrated in Supplemental Table 2. When compared with unhealthy sleep behavior, all the healthy sleep behaviors were related to an increased risk of recurrent fracture (HRs ranging from 1.23 to 2.70), albeit with non–significant results. According to Table 2, both intermediate and poor sleep patterns were non–significantly associated with elevated risk of recurrent fracture when compared with healthy pattern: HR = 1.24 (95% CI: 0.14-−11.15, $p = 0.85$) for intermediate and HR = 6.48 (95% CI: 0.76-−55.54, $p = 0.088$) from univariable model, and HR = 1.40 (95% CI: 0.16-−12.68, $p = 0.76$) for intermediate and HR = 6.45 (95% CI: 0.73-−56.78, $p = 0.093$) from multivariable model. Findings from the three supplemental analyses are shown in Table 3. Per-one-increase in the overall sleep score was significantly related to an increased

TABLE 1 Characteristic descriptions and comparisons between patients with and without imminent recurrent fracture.

Characteristics	Total patients ($n = 185$)	Patients without recurrent fracture ($n = 175$)	Patients with recurrent fracture ($n = 10$)	*P*-value
Age: mean ± SD, in years	71.54 ± 10.32	71.28 ± 10.39	76.10 ± 8.27	0.14[1]
Females: *n* (%)	161 (87.03)	154 (88.00)	7 (70.00)	0.13[2]
Body mass index: mean ± SD, in kg/m^2	22.18 ± 3.40	22.26 ± 3.42	20.72 ± 2.78	0.21[1]
Lumbar spine T-score: mean ± SD	−3.28 ± 1.70	−3.27 ± 1.74	−3.58 ± 0.69	0.73[1]
Current smoker: *n* (%)	18 (9.73)	16 (9.14)	2 (20.00)	0.25[2]
Current drinker: *n* (%)	10 (5.41)	10 (5.71)	0	-[3]
Taking anti-osteoporotic medication before hospitalization: *n* (%)	26 (14.05)	25 (14.29)	1 (10.00)	0.70[2]
Having an osteoporotic fracture in the past 5 years: *n* (%)	81 (43.78)	75 (42.86)	6 (60.00)	0.34[2]
With a diagnosis of diabetes mellitus: *n* (%)	32 (17.30)	31 (17.71)	1 (10.00)	0.53[2]
With a diagnosis of thyroid disease: *n* (%)	17 (9.19)	17 (9.71)	0	-[3]
Healthy sleep behaviors: *n* (%)	145 (78.38)	139 (79.43)	6 (60.00)	0.23[2]
No snoring				
No frequent insomnia	100 (54.34)	96 (55.17)	4 (40.00)	0.52[2]
No frequent midnight waking up	138 (74.59)	132 (75.43)	6 (60.00)	0.28[2]
Appropriate nocturnal sleep duration	136 (73.51)	131 (74.86)	5 (50.00)	0.13[2]
Appropriate daytime napping	86 (46.49)	82 (46.86)	4 (40.00)	0.75[2]
Overall sleep score: mean ± SD	2.41 ± 1.19	2.36 ± 1.17	3.20 ± 1.32	0.038[1]

SD, standard deviation.
[1]Based on Mann-Whitney U test.
[2]Based on Fisher's exact test.
[3]No test performed.

risk of fracture: HR = 1.63 (95% CI: 1.01-−2.62) for univariable model and HR = 1.60 (95% CI: 1.00-−2.55) for multivariable model. The other two analyses yielded largely consistent results with findings from the main analysis.

Discussion

In this study, we evaluated the integrated sleep pattern in relation to the risk of imminent recurrent osteoporotic fracture in elderly patients with hospitalization due to an index fracture. A worsening overall sleep score was found in patients with recurrent fractures when compared with those without recurrent fractures ($p = 0.038$). Per-one-increase in the overall sleep score was significantly related to a 60% higher risk of recurrent fracture. The intermediate ($p = 0.76$) and poor sleep patterns ($p = 0.093$) were non–significantly associated with an increased risk of recurrent osteoporotic fracture when taking healthy sleep pattern as a reference.

We found an incidence of imminent recurrent osteoporotic fracture of > 5% in elderly patients, which was in line with previous studies (3, 12). Despite the progress of osteoporosis management and prophylactic interventions, the control of recurrent fractures remained suboptimal in elderly patients with index fractures (13, 14). Therefore, exploring sleep pattern as a lifestyle in relation to osteoporotic fracture in the elderly may provide some insights into identifying new approaches to enhanced prevention of recurrent fractures.

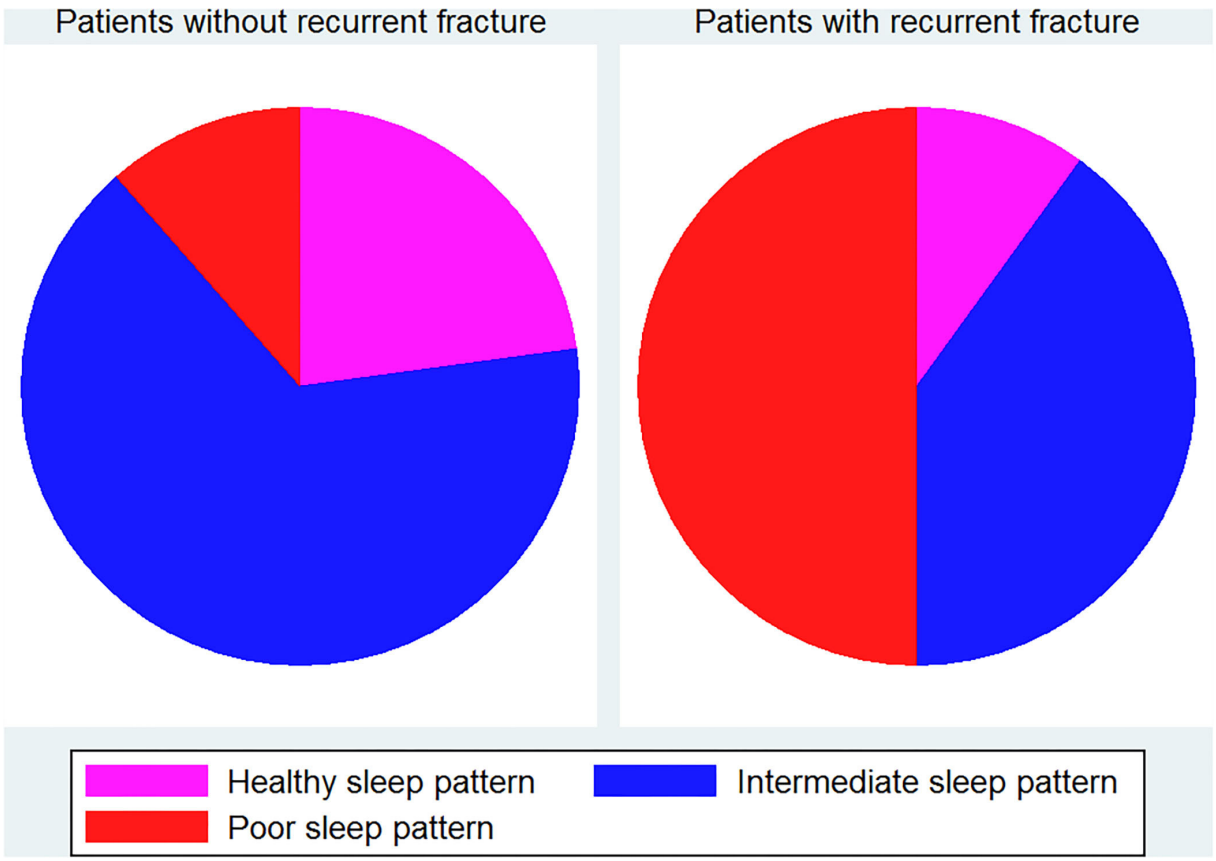

FIGURE 1
Pie charts of sleep pattern in patients with and without imminent recurrent fracture.

Some physiopathological hypotheses, including inflammation, dysregulation of the sympathetic nervous system, and circadian rhythm disorder, had been found to explain sleep and the risk of osteoporotic fracture in the literature (15–17). We observed a significant relationship between overall sleep scores and the risk of recurrent fracture in the elderly (HR = 1.60, 95% CI: 1.00-−2.55 for per-one-increase in the overall score; Table 3), whereas the association between the fracture risk and the sleep pattern was not statistically significant ($p > 0.05$; Table 2). This was due to the categorization of a continuous variable leading to information loss in this study with a small sample size. In contrast, a significantly higher score in patients with recurrent fracture, in combination with the significant association between sleep scores and fracture risk, further suggested the link between the composite of individual sleep behaviors with fracture risk in the elderly.

Unlike previous research that assessed an individual sleep behavior, we used an integrated sleep pattern as a combination of common sleep behaviors for analyses. Specifically, the sleep pattern may be an integrated tool to evaluate both sleep time (including daytime napping and nocturnal sleep duration) and sleep quality (including midnight waking up, insomnia, and snoring). Individual sleep behavior may not substantially influence the recurrent fracture risk in the elderly, while an integrated sleep pattern would show a cumulative and prominent impact on the fracture risk. Therefore, sleep pattern could incorporate the combined and intrinsic influence of each individual sleep behavior, potentially making it a more appropriate measurement to reflect the comprehensive information on sleep than individual behaviors (10, 18). Daytime napping may be a compensation for inadequate nocturnal sleep duration, while insomnia may associate with frequent midnight waking up (9, 19). Although our results were in line with previous studies that an unhealthy behavior, including frequent insomnia, snoring, inappropriate sleep duration, inappropriate daytime napping, and frequent midnight waking up, was related to an increased risk of fracture (as shown in Supplemental Table 2), investigating one specific sleep behavior may thus fail to fully assess the impact of sleep on bone health and fracture prevention in the elderly.

In contrast, there were some scales intending to comprehensively appraise sleep in clinical practice, for instance,

TABLE 2 Relationship between sleep pattern and risk of imminent recurrent fracture.

Sleep pattern[1]	Imminent recurrent fracture	
	Hazard ratio (95% confidence interval)	*P*-value
Model 1[2]		
Healthy	Ref	-
Intermediate	1.24 (0.14–11.15)	0.85
Poor	6.48 (0.76–55.54)	0.088
Model 2[3]		
Healthy	Ref	-
Intermediate	1.40 (0.16–12.68)	0.76
Poor	6.45 (0.73–56.78)	0.093

[1]There were 41 (22.16%), 115 (62.16%), and 29 (15.68%) patients with healthy, intermediate, and poor patterns, respectively.
[2]Model for univariable analysis.
[3]Model adjusted for age and sex.

TABLE 3 Supplemental analysis results for the relationship between sleep and risk of imminent recurrent fracture.

Analysis	Imminent recurrent fracture	
	Hazard ratio (95% confidence interval)	*P*-value
Taking sleep scores as continuous variable		
Model 1[1]	1.63 (1.01–2.62)	0.044
Model 2[2]	1.60 (1.00–2.55)	0.050
Using alternative definition for appropriate daytime napping[3]		
Healthy	Ref	-
Intermediate	1.61 (0.20–13.11)	0.66
Poor	4.23 (0.38–49.97)	0.24
Further adjusting for T-score		
Healthy	Ref	-
Intermediate	1.60 (0.17–14.63)	0.68
Poor	7.60 (0.72–80.01)	0.091

[1]Model for univariable analysis; data shown as a per-one-point increase in the sleep score.
[2]Model adjusted for age and sex; data shown as a per-one-point increase in the sleep score.
[3]Model for univariable analysis; there were 37 (20.00%), 119 (64.32%), and 29 (15.68%) patients with healthy, intermediate, and poor sleep patterns, respectively; Spearman's correlation coefficient with original sleep pattern was 0.76 ($p < 0.001$).

the Pittsburgh Sleep Quality Index. Of note, the requirement of clinical expertise, time, and efforts to complete these scales would preclude their wide application, especially when aiming to monitor sleep for public health. Thus, a simple sleep pattern based on common sleep behaviors and a straightforward scoring algorithm, if externally validated, may own the potential to help with prompt, accurate, and effective assessment of sleep health, especially in population-based studies. Nonetheless, more high-quality evidence is needed to further justify the reliability and validity of sleep pattern and their potential as a sleep evaluation tool.

Our observational study revealed a relationship between the sleep pattern and the risk of recurrent fracture from epidemiological data, which should be interpreted with caution. Confounding bias could not be fully addressed in a non–randomized study (20). For instance, a healthy sleep pattern in the elderly would in general relate to a low degree of frailty, other healthy lifestyles, and/or proactive prevention strategies, which may account for a decreased risk of recurrent fracture to an unknown extent. Unfortunately, we could not adjust for more covariates in models or perform further exploratory analyses, given the small number of fracture events. Therefore, our results were mainly hypothesis-generating, which required more research for exploration.

Strengths and limitations

We targeted the imminent recurrent osteoporotic fracture in the elderly, given the aging population and substantially high risk of fracture recurrence within a short time after an index fracture for older patients. To the best of the authors' knowledge, there were no previous studies exploring sleep pattern in relation to recurrent fractures in the elderly. Findings from this study may generate some evidence for maintaining and improving sleep health to help with osteoporosis management, bone health, and fracture prevention in the elderly.

Several limitations existed in this study. One key limitation was the small sample size of recurrent fracture events, precluding our further analyses and exploration. We assessed the association between baseline sleep before an index fracture and risk of recurrent fracture, failing to take into consideration the change in or transition of sleep information after hospital discharge. Due to the data unavailability during follow-up, the impact of rehabilitation, medications, lifestyle change, and environmental adjustment on the association between sleep and recurrent fracture risk would remain unknown. The only additive algorithm was used to construct the sleep scores and patterns in this study. Furthermore, unquantified and unevaluated confounding factors may bias our findings, which could not be assessed unfortunately in this observational study. Some patients experiencing a recurrent osteoporotic fracture may not be aware of their fracture or receive a fracture diagnosis, which thus underestimated the recurrence of osteoporotic fracture. Moreover, our study sample consisted of hospitalized elderly patients with an index fracture; the generalizability of study results may therefore be weakened. Evidence of sleep pattern in relation to recurrent fractures for older dwellers would be needed to test the generalizability of our findings.

Conclusion

In this study, we evaluated the integrated sleep pattern in relation to the risk of imminent recurrent osteoporotic fracture in elderly patients with hospitalization due to an index fracture. Per-one-increase in the overall sleep score was significantly associated with a 60% higher risk of recurrent fracture, and intermediate and poor sleep patterns were non–significantly related to an increased risk of recurrent osteoporotic fracture. More high-quality evidence was required to further evaluate the relationship between the sleep pattern and the risk of recurrent osteoporotic fracture in the elderly.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving human participants were reviewed and approved by the Guangdong Second Provincial General Hospital Ethics Committee (No. 20190717-02-YXKXYJ-KT). The patients/participants provided their written informed consent to participate in this study.

Author contributions

LL, HZ, and GL contributed equally to this work. LL, HZ, MC, and GL designed the study and collected and analyzed the data. LL, HZ, and GL drafted the manuscript. BZ, XX, and MC provided professional help with manuscript writing and revisions. All authors read and approved the final manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.980352/full#supplementary-material

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Risk factors of falls in elderly patients with visual impairment

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Objective: To examine the risk factors for falls in elderly patients with visual impairment (VI) and assess the predictive performance of these factors.

Methods: Between January 2019 and March 2021, a total of 251 elderly patients aged 65–92 years with VI were enrolled and then prospectively followed up for 12 months to evaluate outcomes of accidental falls *via* telephone interviews. Information of demographics and lifestyle, gait and balance deficits, and ophthalmic and systemic conditions were collected during baseline visits. Forward stepwise multivariable logistic regression analysis was performed to identify independent risk factors of falls in elderly patients with VI, and a derived nomogram was constructed.

Results: A total of 143 falls were reported in 251 elderly patients during follow-up, with an incidence of 56.97%. The risk factors for falls in elderly patients with VI identified by multivariable logistic regression were women [odds ratio (OR), 95% confidence interval (CI): 2.71, 1.40–5.27], smoking (3.57, 1.34–9.48), outdoor activities/3 months (1.31, 1.08–1.59), waking up frequently during the night (2.08, 1.15–3.79), disorders of balance and gait (2.60, 1.29–5.24), glaucoma (3.12, 1.15–8.44), other retinal degenerations (3.31, 1.16–9.43) and best-corrected visual acuity (BCVA) of the better eye (1.79, 1.10–2.91). A nomogram was developed based on the abovementioned multivariate analysis results. The area under receiver operating characteristic curve of the predictive model was 0.779.

Conclusions: Gender, smoking, outdoor activities, waking up at night, disorders of balance and gait, glaucoma, other retinal degeneration and BCVA of the better eye were independent risk factors for falls in elderly patients with VI. The predictive model and derived nomogram achieved a satisfying prediction of fall risk in these individuals.

KEYWORDS

visual impairment, elderly patients, falls, risk factor, prediction tool

Introduction

The population with visual impairment and blindness is projected to be more than doubled by 2050 as a result of shifting demographics and global aging, reaching over 1.5 billion (1). Previous research demonstrated that vision loss is often associated with worse subjective wellbeing (2), poorer daily functions (3), and adverse health consequences among the elderly (4).

Falls are one of the most common leading causes of unintentional injury and death (5). Globally, fall-related death rates are the highest among people with visual impairment and adults aged over 50 (6). The increase in fall risk in the elderly is unavoidable because of the deterioration with age in physical, visual, and cognitive functions. Visual impairment is reported to be an independent risk factor for falls and fractures among older people (7, 8). Therefore, older people with visual impairment should be the main targets of fall risk assessment.

Falls are often caused by more than one risk factor, and this is particularly the case for older people with visual impairment (7). People with poor vision can easily lose stability and change different gaits to avoid obstacles, thus increasing the risk of slips, trips, and falls (9). Even though older people with visual impairment may share risk factors that were previously identified in the general population with those without, they also have their own independent risk factors. Besides, since the main causes of visual impairment, such as cataract (10), glaucoma (11), and retinal degenerations (12), are found associated to fall risk, their respective effects on falls are potentially significant but still understudied.

Even though some patients with eye diseases have undergone ophthalmic surgeries, their visual impairment might still endure. For these patients, post-discharge fall risk assessment and prevention are of great significance in improving patients' quality of life and reducing fall-related injuries and deaths. Although many fall risk assessment scales have been widely used in clinical practice to highlight high-risk groups, to our best knowledge, there is no scale developed specifically for the elderly with visual impairment. Besides, only a handful of cross-sectional studies or studies involving adults have discussed the risk factors for falls in patients with visual impairment (13, 14). Moreover, the associations of eye diseases, ophthalmic surgeries, and other eye-related factors with incident falls in patients with visual impairment are still unclear.

Therefore, this study included elderly patients with visual impairment. In addition to demographics and lifestyle, gait and balance deficits, and systemic conditions, we also examine the associations between eye-related factors and incident falls in visual impairment patients. Based on the result of regression analysis, we further assessed the predictive performance of these factors, and derived a fall risk prediction nomogram for the elderly patients with visual impairment.

Methods

Design and population of the study

This longitudinal study recruited a total of 251 elderly patients with visual impairment, aged 65–92 years. The study was conducted in the Department of Ophthalmology, Guangdong Provincial People's Hospital from January 2019 to March 2021. The procedures adhered to the ethical standards of the Research Ethics Committee of Guangdong Provincial People's Hospital (registration number: KY2020-651-01) and the Helsinki Declaration. Informed consent was obtained from all participants.

Inclusion criteria for patients were diagnosed with visual impairment at discharge and aged $\geq$ 65 years. Visual impairment was defined as the best-corrected visual acuity (BCVA) worse than 0.3 logMAR units (Snellen 20/40) in the better-seeing eye. All patients were able to cooperate in completing the questionnaire survey and follow-up. The exclusion criteria for patients were with (1) falls caused by compression; (2) stroke-related impaired physical mobility; (3) senile dementia; (4) severe systemic diseases (e.g., cerebral infarction, myocardial infarction, heart failure, or connective tissue disorder); (5) endpoints such as loss of follow-up or death occurred during follow-up.

Data collection

The patient information was collected through a detailed interviewer-administered questionnaire during ophthalmic admissions, including demographics and lifestyle, gait and balance deficits, and ophthalmic and systemic conditions. The questionnaires were orally administered to each patient by two trained ophthalmic nurses and the answers were recorded accordingly in data collection sheets. In each survey, the interviewers adopted the same questioning method to reduce bias. In addition, blood test results and surgeries-related data were manually extracted from the electronic medical record system. All the data were double-checked by a professional ophthalmologist (CZ).

The body mass index (BMI) was measured as weight in kilograms divided by the square of height in meters. Smoking status was classified into never-smokers and smokers (including former and current smokers), and alcohol consumption was defined based on self-reported history of alcoholic beverage ingestion. Sleep duration was determined by the average sleep duration over the past month, while nocturnal awakening was further classified as never/occasional or frequent based on self-report. Outdoor participation was referred to the

times of outdoor physical activities and exercise over the past 3 months.

Diabetes was defined as a random glucose level ≥ 11.1 mmol/L, glycated hemoglobin (HbA1c) ≥ 6.5%, use of diabetic medication, or a self-reported history. Hypertension was defined as systolic blood pressure (BP) ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, anti-hypertensive drug use, or a self-reported history. Cardiovascular disease (CVD) was defined based on a self-reported history of angina, stroke, or heart attack. Laboratory tests included glycated hemoglobin, platelets, and serum sodium, potassium, and calcium levels. Health status was divided into good and bad based on the responses of patients when asked "what is your health status as compared to the general health conditions of age-matched individuals".

Difficulty walking was defined as the inability to walk properly due to abnormal and uncontrollable walking patterns. Weakness was defined as self-reported weakness or weakness of the lower extremities. States of balance and gaits were assessed and then classified into normal and abnormal based on the following criteria. Normal balance and gait required natural gaits with eyes open, standing unsupported with eyes closed for over 10 s (safely), and looking behind from both sides with satisfying weight shifts. Meanwhile, disorders of balance and gait (abnormal) represented unsteady gaits and/or standing with eyes open, standing unsupported with eyes closed for <3 s, or failure to look behind (i.e., from one side only, turning sideways only, supervision needed, and assistance needed). Sit-to-stand test was performed to classify patients into independence in standing up and inability to stand up without assistance.

Ophthalmic variables

All patients underwent comprehensive ophthalmic examinations, including (measured on a decimal chart and presented as logMAR), autorefraction, intraocular pressure, slit-lamp examination, and color fundus photography. We also collected information of ophthalmic condition, including glare, visual clarity, use of eye drops, history of eye disease, as well as ophthalmic surgeries. Our study adopted the WHO criteria (International Classification of Diseases 11th edition criteria for vision loss) for visual impairment, i.e., BCVA worse than 0.3 logMAR (Snellen 20/40) in the better eye (15).

Incidence of fall

After discharge, patients were prospectively followed up for 12 months to determine outcomes of accidental falls by interviewing patients or their family members by telephone. In this study, a fall was defined by WHO as "an event which results in a person coming to rest inadvertently on the ground or floor or other lower level", and a faller as an individual who had at least one fall during a 12-month follow-up.

Statistical analyses

Baseline characteristics were tabulated for those with falls at follow-up. Continuous variables with a normal distribution were presented as mean (standard deviation), while those with a non-normal distribution were presented as median (interquartile range). Besides, categorical variables were reported as counts (percentage). Chi-square tests were used to compare categorical variables, while *t*-tests or Wilcoxon rank-sum tests were used to measure the differences in/within continuous variables.

Univariate logistic regressions were applied to identify risk factors for falls in elderly patients with visual impairment. All variables significantly associated with fall ($P < 0.20$) were included in the forward stepwise multivariable logistic regression analysis. Variables with P-values < 0.05 in multivariable analysis were adopted in the final predicted model that laid solid foundations for the following construction of the nomogram for fall risk prediction in elderly patients with visual impairment. Scores for each variable were calculated based on their regression coefficient values. As a result, the total score of each individual could be converted into the predicted probability of fall.

The model performance was assessed by the area under receiver operating characteristic curve (16) that reflects the accuracy of the diagnostic system. Homser-Lemeshow (H-L) was used for calibration and to measure how closely the predicted probabilities agree with the actual outcomes, and a P-value > 0.05 indicated good calibration. Finally, we calculated the sensitivity and specificity of the prediction model.

All statistical analyses were conducted by using Stata version 16.0 (StataCorp, College Station, TX).

Results

Participant characteristics

A total of 251 patients with visual impairment (57.77% women) aged 65–95 years [median (interquartile range): 78.00 (12.00)] were included in the analysis. During a follow-up of 12 months, the incidence of falls among 251 patients with visual impairment was 56.97%. Baseline characteristics and ophthalmic conditions stratified by fall status at follow-up were presented in Tables 1, 2, respectively. Fallers were more likely to be former or current smoker, frequent night awakenings, active outdoor activity, difficulty in walking, inability to stand up without assistance, weakness, disorders of balance and gait, and bad health status at baseline. Besides, fallers at baseline had worse

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TABLE 1 Baseline characteristics stratified by fall status at follow-up.

Baseline characteristics	Total	Fall	Non-fall	*P*-value
N	251	143 (56.97)	108 (43.03)	
Demographic factors				
Age (SD), year†	78.00 (12.00)	78.00 (12.00)	78.00 (11.00)	0.220
Gender, *N* (%)				0.164
Men	106 (42.23)	55 (38.46)	51 (47.22)	
Women	145 (57.77)	88 (61.54)	57 (52.78)	
High (SD), m†	1.60 (0.10)	1.60 (0.10)	1.60 (0.13)	0.426
Weight (SD), kg‡	59.85 (10.17)	59.36 (10.35)	60.51 (9.94)	0.373
BMI (SD), kg/m^2†	23.00 (4.43)	23.05 (4.92)	22.97 (3.87)	0.726
Retire, *N* (%)				0.059
No	20 (5.49)	11 (6.75)	9 (4.48)	
Yes	344 (94.51)	152 (93.25)	192 (95.52)	
Live alone, *N* (%)				0.272
No	18 (7.20)	8 (5.63)	10 (9.26)	
Yes	232 (92.80)	134 (94.37)	98 (90.74)	
Systemic condition				
Hypertension, *N* (%)				0.873
No	113 (45.02)	65 (45.45)	48 (44.44)	
Yes	138 (54.98)	78 (54.55)	60 (55.56)	
Diabetes, *N* (%)				0.908
No	171 (68.13)	97 (67.83)	74 (68.52)	
Yes	80 (31.87)	46 (32.17)	34 (31.48)	
Cardiovascular disease, *N* (%)				0.982
No	207 (82.47)	118 (82.52)	89 (82.41)	
Yes	44 (17.53)	25 (17.48)	19 (17.59)	
Laboratory tests, *N* (%)				0.323
Normal	222 (88.45)	124 (86.71)	98 (90.74)	
Abnormal	29 (11.55)	19 (13.29)	10 (9.26)	
Health status, *N* (%)				**0.016**
Good	201 (80.08)	107 (74.83)	94 (87.04)	
Bad	50 (19.92)	36 (25.17)	14 (12.96)	
Lifestyle factors				
Drinking, *N* (%)				0.326
Never	207 (82.47)	115 (80.42)	92 (85.19)	
Former or current	44 (17.53)	28 (19.58)	16 (14.81)	
Smoking, *N* (%)				**0.026**
Never	216 (86.06)	117 (81.82)	99 (91.67)	
Former or current	35 (13.94)	26 (18.18)	9 (8.33)	
Sleep duration (SD), hours†	6.00 (1.00)	6.00 (1.50)	6.00 (1.00)	0.358
Waking up at night, *N* (%)				**0.007**
Never or occasionally	155 (61.75)	78 (54.55)	77 (71.30)	
Frequent	96 (38.25)	65 (45.45)	31 (28.70)	
Outdoor activities (SD), times/3 months†	0 (0)	0 (0)	0 (0)	**0.002**
Balance-related factors				
Difficulty in walking, *N* (%)				**0.002**
No	195 (77.69)	101 (70.63)	94 (87.04)	
Yes	56 (22.31)	42 (29.37)	14 (12.96)	

(Continued)

TABLE 1 Continued

Baseline characteristics	Total	Fall	Non-fall	*P*-value
Sit-to-stand test				**0.043**
Independent stand up	235 (93.63)	130 (90.91)	105 (97.22)	
Inability to stand up without assistance	16 (6.37)	13 (9.09)	3 (2.78)	
Dizziness, *N* (%)				0.187
No	245 (97.61)	138 (96.50)	107 (99.07)	
Yes	6 (2.39)	5 (3.50)	1 (0.93)	
Weakness, *N* (%)				**<0.001**
No	194 (77.29)	99 (69.23)	95 (87.96)	
Yes	57 (22.71)	44 (30.77)	13 (12.04)	
Disorders of balance and gait, *N* (%)				**<0.001**
No	181 (72.11)	89 (62.24)	92 (85.19)	
Yes	70 (27.89)	54 (37.76)	16 (14.81)	

Data are mean (standard deviation), or median (interquartile range), or *N* (%). BMI, body mass index. All *P*-values were calculated using the ‡*t*-test or †Wilcoxon rank-sum tests for continuous variables and the Chi-square tests for categorical variables. Boldface indicates statistical significance with $P < 0.05$.

BCVA of the better eye and a higher prevalence of cataract, glaucoma, and other retinal degenerations.

Risk factors for falls in elderly visual impairment patients

The results of univariate logistic regression for fall risks in elderly patients with visual impairment were slowed in Table 3. The incident falls were associated with women [odds ratio (OR), 95% confidence interval (CI): 1.47, 0.86–2.37], retirement (0.25, 0.05–1.17), smoking (2.44, 1.09–5.46), outdoor activities/3 months (1.20, 1.01–1.43), waking up frequently during the night (2.07, 1.22–3.52), bad health status (2.26, 1.15–4.44), difficulty in walking (2.79, 1.43–5.44), inability to stand up without assistance (3.50, 0.97–12.61), weakness (3.25, 1.65–6.41), disorders of balance and gait (3.49, 1.86–6.55), cataract (2.06, 1.01–4.22), glaucoma (4.51, 1.80–11.29), and other retinal degenerations (3.26, 1.28–8.31), refractive error (4.73, 1.58–14.16), and BCVA of the better eye (1.88, 1.25–2.81).

The results of stepwise multivariate logistic regression for fall risks in elderly patients with visual impairment were slowed in Table 4. The independent risk factors for falls among elderly patients with visual impairment identified by multivariate logistic regression were women (2.71, 1.40–5.27), smoking (3.57, 1.34–9.48), outdoor activities/3 months (1.31, 1.08–1.59), waking up frequently during the night (2.08, 1.15–3.79), disorders of balance and gait (2.60, 1.29–5.24), glaucoma (3.12, 1.15–8.44), other retinal degenerations (3.31, 1.16–9.43) and BCVA of the better eye (1.79, 1.10–2.91). A nomogram was developed based on these abovementioned multivariate analysis results (Figure 1).

The performance of predictive model

The model performance was assessed by discrimination and calibration. The predictive model and nomogram demonstrated relatively good accuracy in estimating the risk of falls with an AUC of 0.779 (Figure 2). Hosmer-Lemeshow goodness-of-fit tests indicated good calibration ($P > 0.05$). The sensitivity and specificity of the prediction model were 0.824 and 0.650.

Discussion

In this longitudinal study of elderly Chinese patients with visual impairment, we found that gender, smoking, outdoor activities, waking up at night, disorders of balance and gait, glaucoma, other retinal degenerations and BCVA of the better eye were independent risk factors for falls in elderly patients with visual impairment. A nomogram was developed according to the multivariate analysis results. The AUC of the predictive model was 0.779.

Female, smoking, and worse visual acuity were strongly associated with falls in in elderly patients with visual impairment. Our study also found that waking up frequently during the night increased the risk of falls in elderly people with visual impairment. Previous studies have reported that subjective poor sleep quality (17), napping (18), short sleep duration (19, 20), long sleep duration (20), and insomnia (21) were associated with an increased risk of falls and fractures (22, 23). Waking up frequently at night is one kind of sleep disorders that reduce sleep quality (24). Fracture is a risk factor for falls, and poor sleep may disrupt the diurnal rhythm of bone turnover and affect bone metabolism through other mechanisms including hypoxemia, inflammation, increased sympathetic tone, alterations in melatonin, and

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TABLE 2 Baseline ophthalmic conditions stratified by fall status at follow-up.

Baseline characteristics	Total	Fall	Non-fall	*P*-value
Glare, *N* (%)				0.361
No	188 (74.90)	104 (72.73)	84 (77.78)	
Yes	63 (25.10)	39 (27.27)	24 (22.22)	
Visual clarity, *N* (%)				0.099
Both sunny and rainy days	135 (53.78)	72 (50.35)	63 (58.33)	
Sunny days	107 (42.63)	63 (44.06)	44 (40.74)	
Rainy days	9 (3.59)	8 (5.59)	1 (0.93)	
The number of eye drops used[†]	2 (2)	2 (2)	2 (2)	0.504
Cataract, *N* (%)				**0.045**
No	36 (14.34)	15 (10.49)	21 (19.44)	
Yes	215 (85.66)	128 (89.51)	87 (80.56)	
Glaucoma, *N* (%)				**0.001**
No	215 (85.66)	113 (79.02)	102 (94.44)	
Yes	36 (14.34)	30 (20.98)	6 (5.56)	
AMD, *N* (%)				0.643
No	185 (73.71)	107 (74.83)	78 (72.22)	
Yes	66 (26.29)	36 (25.17)	30 (27.78)	
Other retinal degenerations, *N* (%)				**0.010**
No	222 (88.45)	120 (83.92)	102 (94.44)	
Yes	29 (11.55)	23 (16.08)	6 (5.56)	
Refractive error, *N* (%)				0.075
No	102 (40.96)	65 (45.77)	37 (34.58)	
Yes	147 (59.04)	77 (54.23)	70 (65.42)	
Intraocular lens implantation, *N* (%)				0.661
No	71 (28.29)	42 (29.37)	29 (26.85)	
Yes	180 (71.71)	101 (70.63)	79 (73.15)	
Glaucoma surgery, *N* (%)				0.463
No	247 (98.41)	140 (97.90)	107 (99.07)	
Yes	4 (1.59)	3 (2.10)	1 (0.93)	
Vitreoretinal surgery, *N* (%)				0.415
No	184 (73.31)	102 (71.33)	82 (75.93)	
Yes	67 (26.69)	41 (28.67)	26 (24.07)	
Anterior segment surgery, *N* (%)				0.648
No	240 (95.62)	136 (95.10)	104 (96.30)	
Yes	11 (4.38)	7 (4.90)	4 (3.70)	
BCVA of the better eye (SD), logMAR[†]	1.07 (0.99)	0.83 (0.45)	1.25 (1.23)	<0.001

Data are mean (standard deviation), or median (interquartile range), or *N* (%). BCVA, best-corrected visual acuity. All *P*-values were calculated using the [†]Wilcoxon rank-sum tests for continuous variables and the Chi-square tests for categorical variables. Boldface indicates statistical significance with P<0.05.

predispose individuals to fracture (24). Besides, sleep disorder may also lead to decreased muscle strength and physical function, as well as slower walking speed, which have been linked with falls and fractures (25, 26). Due to frequent waking up at night, the sleep quality of elderly patients with visual impairment may decrease and the body may not get adequate rest, which lead to reduced reaction ability, limb weakness, or influence bone turnover, thus increasing the risk of falling.

Our study found that disorders of balance and gait were associated with a higher risk for falls in elderly patients with visual impairment. Disorders of balance and gait are particularly important in the elderly because they compromise independence and contribute to the risk of falls and injury (27). It has been shown that when walking at a constant speed, the elderly with slower step speed and frequency, shorter stride length and stride length, longer foot support time and greater gait variability are more likely to fall (28–30). In addition, visual impairment itself

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TABLE 3 Univariate logistic regression for fall risk in elderly patients with visual impairment.

Variables	Odds ratio (95% CI)	*P*-value
Gender		
Men	(Reference)	
Women	1.43 (0.86–2.37)	**0.165**
Retire		
No	(Reference)	
Yes	0.25 (0.05–1.17)	**0.079**
Outdoor activities, times/3 months	1.20 (1.01–1.43)	**0.036**
Smoking		
Never	(Reference)	
Former or current	2.44 (1.09–5.46)	**0.029**
Waking up at night		
Never or occasionally	(Reference)	
Frequent	2.07 (1.22–3.52)	**0.007**
Health status		
Good	(Reference)	
Bad	2.26 (1.15–4.44)	**0.018**
Difficulty in walking		
No	(Reference)	
Yes	2.79 (1.43–5.44)	**0.003**
Sit-to-stand test		
Independent stand up	(Reference)	
Inability to stand up without assistance	3.50 (0.97–12.61)	**0.055**
Weakness		
No	(Reference)	
Yes	3.25 (1.65–6.41)	**0.001**
Disorders of balance and gait		
No	(Reference)	
Yes	3.49 (1.86–6.55)	**<0.001**
Visual clarity		
Both sunny and rainy days	(Reference)	
Sunny days	1.25 (0.75–2.09)	**0.389**
Rainy days	7.00 (0.85–57.52)	**0.070**
Cataract		
No	(Reference)	
Yes	2.06 (1.01–4.22)	**0.048**
Glaucoma		
No	(Reference)	
Yes	4.51 (1.80–11.29)	**0.001**
Other retinal degenerations		
No	(Reference)	
Yes	3.26 (1.28–8.31)	**0.013**
Refractive error		
No	(Reference)	
Yes	4.73 (1.58–14.16)	**0.006**
BCVA of the better eye	1.88 (1.25–2.81)	**0.002**

BCVA, best-corrected visual acuity. Boldface indicates statistical significance with $P < 0.20$.

TABLE 4 Stepwise multivariate logistic regression for fall risk in elderly patients with visual impairment.

Variables	Odds ratio (95% CI)	*P*-value
Gender		
Men	(Reference)	
Women	2.71 (1.40–5.27)	**0.003**
Smoking		
Never	(Reference)	
Former or current	3.57 (1.34–9.48)	**0.011**
Outdoor activities, times/3 months	1.31 (1.08–1.59)	**0.006**
Waking up at night		
Never or occasionally	(Reference)	
Frequent	2.08 (1.15–3.79)	**0.016**
Disorders of balance and gait		
No	(Reference)	
Yes	2.60 (1.29–5.24)	**0.007**
Glaucoma		
No	(Reference)	
Yes	3.12 (1.15–8.44)	**0.025**
Other retinal degenerations		
No	(Reference)	
Yes	3.31 (1.16–9.43)	**0.025**
BCVA of the better eye	1.79 (1.10–2.91)	**<0.001**

BCVA, best-corrected visual acuity. Boldface indicates statistical significance with $P < 0.05$.

may interfere with balance when walking and standing, because visual motion signals provide direct information regarding head movements (31, 32). Our study indicated that the association between disorders of balance and gait and falls were independent on visual acuity. Therefore, assessment of balance function and gait abnormalities is also an important part of determining the risk of falls in elderly patients with visual impairment.

Our study found that higher levels of outdoor activity were associated with a greater risk of falls in elderly patients with visual impairment. Activity limitation due to a fear of falling is very common in older adults with visually impairing eye disease, thus this compensatory strategy may protect against falls (33). But previous studies have demonstrated that fear of falling often results in decreased activities of daily living, leading to frailty, and decreased muscle strength and tone, which may also play a role in future falls (34–37). Besides, a U-shaped relationship was identified by a prospective cohort study between bouted physical activity and fall incidence, and both physical inactivity and high activities increase the risk of falls in older adults (38). The type of exercise was also associated with fall risk. Therefore, the effect of outdoor activities on the risk of falls in the elderly with visual impairment requires further study.

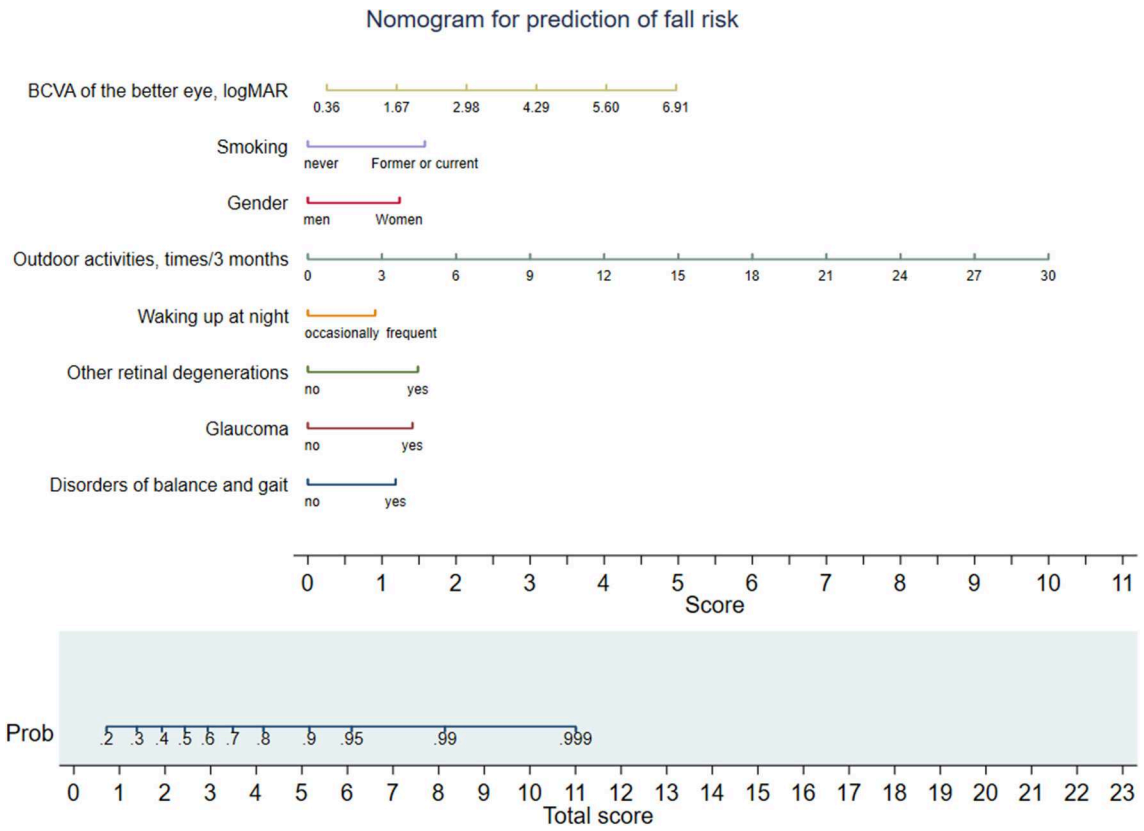

FIGURE 1
Nomogram for fall risk prediction of elderly patients with visual impairment. Different values of each variable correspond to different positions in the nomogram. Draw a line from the position of cach variable to the points axis for acquiring points of this variable. Points of different variables are summed to yield a total score that can be converted into predicted probability of fall based on the total score axis of the nomogram. BCVA, best-corrected visual acuity.

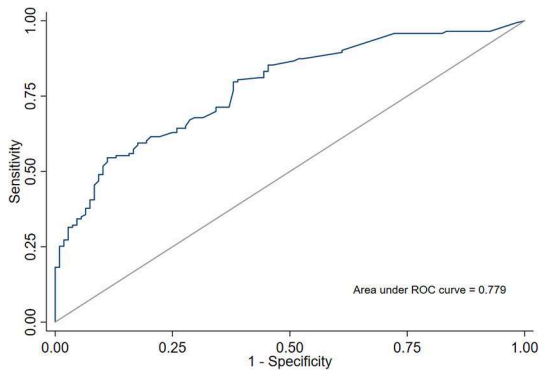

FIGURE 2
ROC curve and area under receiver operating characteristic curve (AUC) of a predictive model for fall risk in elderly patients with visual impairment.

In this study, glaucoma and other retinal degenerations increased the risk for falls among elderly people with visual impairment. It has been noted that individuals with visual field damage were associated with more falls (11, 39). Inferior peripheral visual field damage and preserved inferior central visual field sensitivity were associated with increased fear of falling in glaucoma (40). At worse levels of visual field damage, patients with glaucoma demonstrated an exacerbated decline in walking speeds (ie, stride velocity and cadence) in older adults with glaucoma (41). And fear of falling and changes in gait are both risk factors for falls. Previous studies showed that age-related macular degeneration is associated with falls, postural instability, and reduced gait speed (12, 42). The differences between these studies and our results may be due to the small sample size and selection of the visually impaired population. Other retinal degenerations, such as retinitis pigmentosa, which leads to general nyctalopia and is followed by a gradual narrowing of the visual fields, may also be associated with falls in older patients. Previous studies were unable to distinguish between falls caused by visual impairment or by the eye disease itself, but our results demonstrated that glaucoma and other retinal degeneration are associated with falls. Therefore, for the elderly with visual impairment, special attention should be paid to those with glaucoma and other retinal degenerations.

In addition, to our best knowledge, there is no fall risk assessment scale that specifically targets the elderly with visual impairment to highlight the high-risk groups. Prediction models and nomograms based on predictors/risk factors of diseases can provide patients with accurate prediction tools to be used in safety management for individuals (43–45). We contributed a predictive model and nomogram based on these abovementioned risk factors for falls, and older patients with visual impairment may get a predicted probability of fall based on the total score axis of the nomogram. Future studies are needed to further validate and improve the predictive performance of this model. Our model provides a convenient method for the assessment and prevention of falls in patients with visual impairment. For patients with visual impairment who are at high risk of falling, doctors and nurses can enhance targeted education and guidance to improve patient quality of life and outcomes.

This study had uniquely examined whether a variety of fall-related factors and eye-related factors were independent risk factors for fall in patients with visual impairment, and assessed the predictive performance of these factors. The present study has several limitations. Firstly, the risk factors included in our analysis are limited. Further studies are needed to investigate the effects of other factors on the risk of falls, such as medication use. Secondly, the present study was also limited by its relatively limited sample size, and further studies with larger sample sizes would help confirm the findings of our research. Thirdly, we did not assess the performance of predictive models in patients with different degrees of visual impairment due to the small sample size. Finally, we did not compare the study on risk factors of falls in elderly peoples before and after ophthalmic surgery because of failure to review the history of falls.

In conclusion, gender, smoking, outdoor activities, waking up at night, disorders of balance and gait, glaucoma, other retinal degenerations and BCVA of the better eye were independent risk factors of falls in elderly patients with visual impairment. The predictive model and derived nomogram achieved a satisfactory prediction of fall risks in the target population. The results of this study laid solid foundations for the advanced individualization of fall interventions.

Data availability statement

The data used during the current study are available from the corresponding authors on reasonable request.

Ethics statement

The studies involving human participants were reviewed and approved by Research Ethics Committee of Guangdong Provincial People's Hospital. The patients/participants provided their written informed consent to participate in this study.

Author contributions

SO, GW, and YH: conception and design. XZ, HL, and YF: data collection and collation. GW and SO: data analysis and interpretation. SO, GW, ZL, and CZ: manuscript writing. YH and HY: data interpretation and final review of the manuscript. All authors revised and approved the submitted manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The relationship between real-life social support and Internet addiction among the elderly in China

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Internet addiction among the elderly is a novel issue in many countries. However, extant research about excessive use of the Internet is focusing on adolescents and younger adults. There are few studies to explore the topic of the elderly's Internet addiction. The purpose of this study is to investigate the relationship between real-life social support and Internet addiction among older adults during the COVID-19 pandemic. This article adopted a self-reported questionnaire *via* internet links to collect data. A total of 303 valid samples about Internet addiction for the elderly were obtained in China. The results suggested that real-life social support is significantly and negatively related to Internet addiction among the aged. Moreover, the findings revealed that real-life social support could mitigate Internet addiction by increasing the levels of hopefulness and decreasing the feeling of loneliness. We expect that this study can enrich the understanding of the problematic Internet usage within older populations. Finally, the contributions, practical significance, and limitations of this study were discussed.

KEYWORDS

real-life social support, Internet addiction, hopefulness, loneliness, the elderly

Introduction

Internet usage in China has increased significantly in recent years. A report from China Internet Network Information Center suggested that by June 2021, the number of netizens in China exceeded 1 billion. And the number of aged 60 and above was about 123 million, accounting for 12.2% of the total number of Internet users and an increase of 1.9% over 10.3% in June 2020. More specifically, a growing number of older netizens begin using the Internet, smart devices, and social network services in China, with the development of information and communication technology and the successful implementation of the aging strategy. However, the wide usage of internet was accompanied by the concern of the excessive use of internet among the elderly. For example, China's Internet Life of the Elderly 2020 report suggests that more than 100,000 are online almost all day, and 0.19% of seniors spend more than 10 h a day online on some apps. Moreover, the average senior user over the age of 60 spends 64.8 min per day on the Internet, and each senior user logs into applications an average of five times per day.

Not only that, but a survey from China reported that almost half of the older respondentias will have negative psychological states such as anxiety or uneasiness when smartphones cannot be connected to the network, which are typical of Internet addiction withdrawal reactions (1). As we can see, problematic smartphone use (PSU)/ Internet addiction (IA) is not only limited to young people, but the elderly who are idle at home may also suffer from Internet/ smartphone dependence (2).

However, to our knowledge, very few studies have considered the issue of IA among the elderly, especially netizens who started to be exposed to digital technologies until a later stage of life. That is, the elderly's Internet addiction is a novel issue emerging in the digital age (3), which is worth studying since it is closely related to spending their meaningful and healthy later life (4). Only a handful of studies analyzed the antecedent of addictive use of social media in elderly groups. For instance, Özbek and Karaş (5) proposed that the probability of social media addiction is higher among the older populations with low levels of education and income, living in villages and towns. Moreover, women are vulnerable to reporting higher levels of social media addiction than those men. But social support from family and from a significant other had significant effects on the addictive use of social media among the elderly. Busch et al. (2) conducted a cross-sectional survey and investigated smartphone usage among older adults, and the results revealed social influence, habit, and self-control are strong predictors of problematic smartphone use in the aged 60 years and older. Other studies indicate that perceived social isolation is associated with problematic social media use among older adults (6).

Even though previous literature has revealed the benefits of internet use by the old and indicated that encouraging older adults to use the internet may help decrease isolation and depression (7), improve the cognitive health (8), and learn about the risk of disease (9), there will be harmful impacts of excessive use of Internet among the elderly. Prior studies have suggested that Internet addiction can damage the mental health and physical health of individuals (10–13). For older adults, their physical functions are in a state of decline, and excessive use of the Internet can cause greater physical and mental harm than other groups, such as causing eye problems, cervical spondylosis, cardiovascular and cerebrovascular diseases, and insomnia (14). In addition, the Internet is full of false information such as rumors, and if deceived, it may also lead to psychological damage such as depression among the elderly (14). A report from China also indicated that Internet addiction not only affects the physical and mental health of the elderly, such as cervical spondylosis, lumbar spondylosis, and emotional changes, but also affects the daily life of the elderly, such as weakening oral expression and vulnerability to Internet fraud (15). Based on the above considerations, older people are in a worse position physically, mentally, and cognitively compared to younger people, we need to pay more attention to Internet addiction in older adults. However, to the best of our knowledge, it is apparent that the field lacks a coherent understanding of how antecedents exert an effect on IA among the aged. Thus, it is necessary to reveal the mediating mechanisms the above factors could induce IA in the elderly, which will give us a real insight into the causes of the IA and contribute to proposing effective intervention strategies.

Remarkably, although researchers have investigated that social support is negatively related to the elderly's IA (5), few studies have focused on the mechanisms of the relationship between social support, especially the real-life social support (RLSP), and IA in senior citizens. RLSP is significant in later life since it is a fundamental need for the older populations to keep in touch with society, cultivate positive emotional experiences, overcome feelings of loneliness, sustain their state of psychological wellbeing, and improve their levels of hope for the future (16, 17). Prior studies suggested that offline social support protects mental health and reduces the likelihood of Internet addiction (18). Then, can RLSP weaken the IA in the elderly? And what is the internal mechanism of this effect? No prior research has investigated these research issues. To address the research gap and provide important practical implications, we focus on the influence of RLSP on IA, and also explore the paths that RLSP indirectly affects IA in the elderly. That is, the mediating role of hopefulness and loneliness, which is beneficial for opening the "black box" of the influence of RLSP on IA.

Taken together, the principal aim of this study is to explore the relationship between RLSP and IA among those aged 55 years and above during the period of the COVID-19 pandemic. Next, the other purpose of this study is to discuss the mediating role of hope and loneliness in the relationship between RLSP and IA. Figure 1 is the conceptual model.

Literature review and hypothesis

Internet addiction

Although numerous studies had been conducted by researchers in the field of Internet addiction over the past decade, there is no clear agreement on which term to use for Internet-use-related problems (19). Diverse terms in the extant studies such as problematic smartphone use, smartphone addiction, excessive Internet use, Internet addiction, Internet dependency, etc. have been adopted and characterized as unsatisfactory Internet use behavior. Meanwhile, prior literature has not formed a unified view about the definition of these terms (20). Young (21) suggested that Internet addiction presented some special characteristics including the inability to stop the desire to use the Internet excessively and the extreme tension felt when losing the Internet. Davis (22) argued that pathological Internet use describes the set of symptoms, i.e., cognitive, emotional, and behavioral symptoms, and cognitive symptoms

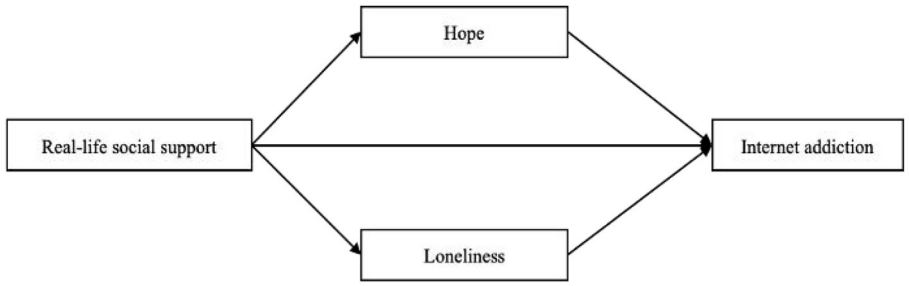

FIGURE 1
The conceptual model of this study.

are prominent among these symptoms, which could induce behavioral symptoms of PIU.

Regardless of the terminology used, they all describe behaviors characterized by symptoms that are similar to those of other addictive behaviors (2). In line with these prior studies, this article adopted the term IA and referred to it as excessive smartphone usage and probably to have difficulty in social or psychological life with five vital symptoms: (1) compulsive use (2) withdrawal symptoms (3) tolerance symptoms (4) interpersonal and health-related problems (5) time management problems. In addition, Internet addiction can cause harm to both individuals and society by preventing people from working or studying (23).

The relationship between real-life social support and Internet addiction

Social support, a multifaceted concept, is defined as the aid individuals received or perceived from their network members (24). Several opposing types of social support are distinguished in prior literature, i.e., real-life vs. virtual social support (25), visible vs. invisible social support (26, 27), instrumental vs. emotional social support (24). Remarkably, real-life social support, consisting of material assistance and direct services, becomes increasingly vital and plays a protective role in the field of mental disorders such as loneliness and suicidal ideation in the overlapping context of the post-epidemic era and the digital age (28). Particularly, RLSS is a basic but critical need for the elderly during the COVID-19 pandemic, which mainly depends on the following reasons. On the one hand, some evidence has shown that senior citizens are more likely to have a higher rate of COVID-19 infection compared to younger people, they, therefore, could be in a stressful situation where they are concerned about their health. On the other hand, the social range becomes increasingly narrower for the elderly who gradually separated from society as a result of retirement, having a strong need for RLSS. The main sources of RLSS for the elderly are family members and friends. Especially, the frequency of interaction with neighbors and other friends experiences a decreasing trend for older adults under the strict limitation of social distance during the COVID-19 pandemic, and family members become the only source that older people received social support and personal contact. This means that those aged 55 and older are likely to lack real-life social support.

Compensatory Internet use theory suggests that Internet use is a coping strategy for real-life problems (29). More specifically, the elderly with low levels of RLSS could receive online social support and maintain online relationships *via* using a smartphone or smart network services to fulfill their needs for social support (30). However, upon reviewing the literature, we found this also yielded some results contrary to expected such as problematic smartphone use, and even Internet addiction. Namely, an individual who continually achieves social networks *via* smartphone is more likely to be immersed in a virtual life and forget about the physical world around them, a behavior that may result in Internet addiction (31). Related research has well-documented that the old population with low levels of RLSS shows a higher rate of smartphone addiction (32). For example, Özbek and Karaş (5) argued that elderly individuals who are at risk for lack of RLSS are more likely to turn to excessive use of social media. Meshi and Ellithorpe (18) speculated that problematic social media use was significantly associated with decreased real-life social support and increased social support on social media. In contrast, Real-life social support provides a powerful source in preventing and solving sociological or psychological problems and in dealing with difficult situations (20). The elderly with high levels of RLSS could receive concrete aid and emotional support from the real world, which is more likely to exert an effective function on negative events. That is RLSS may be helpful at the functional level for those aged 55 years older. More specifically, some literature has indicated that RLSS is negatively related to Internet addiction (33).

Therefore, we propose the following hypothesis:

Hypotheses 1: Real-life social support is negatively related to Internet addiction among the elderly.

Hope as a mediator between real-life social support and Internet addiction

Hope is "a positive motivational state that is based on an interactively derived sense of successful (1) agency (goal-directed energy) and (2) pathways (planning to meet goals)" (34). Ersek (35) indicated that hope is "a multidimensional life force that focuses on positive expectations of the future and is always influenced by others." It is noted that hope for the future is an individual's view and attention to the future and the pursuit of making things better can lead to a sense of social wellbeing, which is a Widely concerned topic in positive psychology.

Hope is an essential need for the elderly (36), and particularly, it was found to be an effective protective mechanism to counteract the negative influences of changes and losses caused by COVID-19. Based on this beneficial effect on the aged, previous research focused on factors that could cultivate and facilitate the level of hope among the elderly. For example, available social support (such as instrumental support from family, and emotional support from friends), as a critical protective factor, contributes to the wellbeing, maintaining positively mental levels, and finding sources of hope for older adults (37). Doolittle and Farrell (38) present that increasing RLSS is more likely to reduce psychological stress and give them more hopefulness when the older population faces the challenge in daily life. High-quality social relationships with their family members and friends could forest a sense of purpose, which is a determinant of promoting hope (39). Taken together, social support was a powerful predictor of hope among the elderly (40). That is, sufficient real-life social support can decrease depression, improve one's general level of happiness and promote the establishment of positive quality, including hope (41).

According to the hope theory, hopefulness focuses on future- and goal-oriented cognition, which could effectively buffer some risky behavior and negative influences. Based on this theory, extant studies have found that hopefulness plays an important role in dealing with psychological distress among individuals who experience some traumatic events (42). Specifically, a person with high levels of hope may better adapt to life challenges, nurture positive psychology, and develop effective strategies when facing additional and tough problems (43–45). Particularly contrasted to the elderly with low levels of hope, hopeful the aged consider their skills to deal with the difficulties and envision a positive future, which may, in turn, lead to lower anxiety and fewer negative outcomes. Following the above logic, older adults with high levels of hope have a set of psychological resources to adequately cope with the Internet usage stress caused by a great deal of fake information and rumor on the Internet during the spread of COVID-19 and the conduction of lockdown. Addiction is a major type of Internet usage stress. Seif et al. (46) also proposed that the elderly full of hope is more likely to have higher self-esteem and adequately cope with the problem of Internet use. Specifically, hope could exert a negative effect on Internet addiction during the COVID-19 pandemic.

Overall, given the positive effect of social support on the hope and the negative role of hopefulness in Internet addiction, we propose the following hypothesis:

Hypotheses 2: The relationship between real-life social support and Internet addiction in the elderly is mediated by hope.

Loneliness as a mediator between real-life social support and Internet addiction

Loneliness has increasingly become a universal human experience, particularly in the digital age (47). There is a consensus that loneliness is a multi-dimensional concept. Researchers have provided various definitions of loneliness in past years. For example, Peplau and Perlman (48) proposed that loneliness is an unpleasant experience, it occurs when there is an incongruence between ideal and achieved personal relationships. Weiss (49) suggested that loneliness consisted of social and emotional aspects. Social loneliness stems from social isolation, whereas emotional loneliness is derived from the deficiency of a close emotional attachment. Although loneliness is distinguished into different types based on various perspectives, it shares a common core that is deficient.

The stress process framework shed light on the that disadvantaged individuals such as the elderly are the most vulnerable to social stressors. We could therefore suggest that those aged 55 and older are more likely to be loneliness compared with other groups, because of many factors, i.e., spousal loss, lack of close friends, and limited social support (50–52). RLSP among the elderly is a critical determinant in the development of successful aging and relieving loneliness. Previous research has revealed the effect of real-life social support for decreasing loneliness in later life among the elderly. For example, Coyle and Dugan (53) imply that the narrowing of social networks contributes to increased social isolation and loneliness. Social isolation is always regarded as a risk factor, while social support can play a protective role in aged later life (54). One possible scenario is that the loss of real-life social support due to the policy of epidemic prevention and control strengthens senior adults' feelings of social isolation and marginality. That is to say, those with higher levels of social network support may have additional material and emotional resources to cope with loneliness.

To reduce loneliness, the elderly is more likely to be attracted to use the Internet for social interaction to strengthen existing friendships and meet their social needs. To be specific, the lonely elderly use video chats or online social media sites to stay in

contact with family and friends during the period of lockdown. However, earlier research implies that loneliness increases the risk of experiencing negative outcomes of Internet use (55). Özdemir et al. (19) found that higher loneliness resulted in low self-control, which subsequently led to Internet addiction. Moreover, it was reported that high levels of smartphone addiction were correlated with low self-esteem, loneliness, depression, and shyness (56).

In conclusion, loneliness is associated with Internet addiction (57, 58).

Overall, given the negative effect of real-life social support on loneliness and the positive role of the loneliness in aggravating Internet addiction, we propose the following hypothesis:

Hypotheses 3: Loneliness mediates the negative relationship between social support and Internet addiction among the elderly.

Methods

Sampling

The data used in this paper were collected *via* a Chinese professional market research company which has built a massive database including numbers of the older population. This database accumulates about 500,000 elderly users in China, as well as their children's relationship network. The market research company selected a sample of 500 people by systematic random sampling according to our needs. Specifically, random sampling was conducted on the basis of taking into account the eastern, central, and western regions in China, as well as the rural elderly and the urban elderly. If it is difficult for the elderly interviewees to fill in the questionnaire, that could be filled in by their children on behalf of the elderly interviewees. Ultimately, 426 of the elderly completed the self-reported questionnaire (response rate = 85.20%). The questionnaire was designed with screening questions, such as attention detection items. Participants who failed to satisfy these screenings would be considered invalid. After removing a number of unqualified ones, we finally obtained 303 valid samples (valid rate = 71.13%), which formed the basis of data analysis in this paper. The survey was collected from January 2022 to February 2022. Participants were given a reward of Renminbi (RMB) 5 when they completed the questionnaire. This fee does not include payments to the research company. Moreover, we did not involve any sensitive topics that may make the participants feel uncomfortable in our questionnaire. All participants were informed of the research process and provided written informed consent in accordance with the Declaration of Helsinki.

A comparison of *t*-test of the valid responding and invalid responding elderly people from the sampling frame indicated no significant differences in terms of key demographic characteristics (i.e., age, gender, education level, and personal income), suggesting that non-response bias may not be a major concern in this research.

In addition, we employed the Heckman two-stage model to assess sample representativeness (59). We recoded the question "How many hours a day do you surf the Internet (the options ranged from 0 to 24 h)" into a dummy variable (i.e., internet access), with 0 h a day coded 0, and others coded 1. We select internet access as the dependent variable in the first stage. We next bring the predicted inverse Mills ratio from the first-stage regression in the second stage of the model. The coefficient of Heckman's lambda is insignificant ($\beta = 0.219$, $p = 0.770$), which means that there is no sample selection bias.

Measurement

Real-life social support

We measured the real-1ife social support by the six-item scale from the Multidimensional Scale of Perceived Social Support (MSPSS). Sample items include statements like "I can get emotional help and support from my family when I need it," and "My friends try to help me." The items ranged from 1 (strongly disagree) to 5 (strongly agree). All statements on this scale are positive. That means higher scores indicate more social support and lower scores indicate less.

Hope

Hope is assessed with the 6 item State Hope Scale developed by Snyder et al. (60). Sample items include statements like "I can think of many ways to reach my current goals" and "At this time, I am meeting the goals that I have set for myself." Respondents were asked to select the number that best describes how they think about themselves right now. All adopted a five-point Likert scale, ranging from 1 (definitely false) to 5 (definitely true), with higher scores representing higher levels of hope.

Loneliness

We used the ULS-8 Loneliness Scale (61), which is a simplified version of the UCLA Loneliness Scale (ULS-20), to assess participants' loneliness. Respondents are asked to indicate the frequency of how often they experience the following "I lack companionship," "There is no one I can turn to," "I am an outgoing person" and so on. Each item was measured on a five-point scale (1 = never, 5 = daily). The higher the score was, the greater the loneliness was.

Internet addiction

We used the revised Internet Addiction Scale developed by Mak et al. (62) to measure IA among the elderly. The scale of IA comprised a total of 18 items including four

dimensions: Compulsive Use of Internet and Withdrawal Symptoms of Internet Addiction (Sym-CW, 6 items), Tolerance Symptoms of Internet Addiction (Sym-T, 4 items), Interpersonal and Health-Related Problems of Internet Addiction (RP-IH, 4 items), and Time Management Problems (RP-TM, 4 items). The respondents are asked to answer the following questions about Internet use according to their practical status. Each item was measured on a five-point scale from 1 (strongly disagree) to 5 (strongly agree). Higher scores indicate a more severe level of Internet addiction.

Control variables

To control for alternative explanations, we take demographic information of the participants, including age, gender, education level, personal income, self-rated health, taking care of a grandchild, and living situation. Age was measured in years (range = 55–90), and gender was represented by a dichotomous variable (1 = male, 0 = female). Education level was represented by four categorical variables-primary degrees or below (reference group), secondary degrees, high school degrees, and junior college degrees or above. Self-rated health indicated participants' ratings of their overall health, ranging from 1 (poor) to 5 (excellent). Taking care of a grandchild was represented by a dichotomous variable (1 = yes, 0 = no). Also, the living situation is a dummy variable (1 = living alone, 0 = living with a significant other. The level of individual income per month was represented by four categorical variables: < RMB 1,000 (reference group), RMB 1,000–2,000, RMB 2,000–5,000, and more than RMB 5,000.

Common method bias tests

Harman's single factor test was conducted to check for the potential effects of common method bias. All scale items were subjected to exploratory factor analysis in SPSS to test for common method variance. The results showed that in the unrotated factor structure, the variance explained was 30.65%, which did not reach 50% (63), so there was no serious common method bias in the sample data.

In addition, we used confirmatory factor analysis to test for common method bias in MPLUS software. We analyzed all scale measures inside a factor, and the results showed a poor model fit (RMSEA = 0.182; CFI = 0.396, TLI = 0.339; SRMR = 0.145), which indicated that all measures should not belong to the same factor (64). Thus, common method bias was unlikely to be of great concern in the sample data. In addition, there was no significant difference between our sample and the non-response sample in terms of age, gender, education level, and *t*-test. Therefore, the effect of non-response bias is very limited (65).

TABLE 1 The validity and reliability of variables.

Variables	Factor loadings	CR	AVE
A. Four first-order factors of internet addiction $\chi^2_{(126)} = 342.411, p < 0.001$; **CFI = 0.949; TLI = 0.939; RMSEA = 0.075; SRMR = 0.047**			
Sym-CW	0.814	0.923	0.665
	0.767		
	0.864		
	0.791		
	0.840		
	0.815		
Sym-T	0.860	0.885	0.659
	0.895		
	0.678		
	0.798		
RP-IH	0.768	0.870	0.625
	0.830		
	0.806		
	0.757		
RP-TM	0.828	0.871	0.628
	0.798		
	0.806		
	0.735		
B. Overall model $\chi^2_{(242)} = 585.267, p < 0.001$; **CFI = 0.918; TLI = 0.906; RMSEA = 0.068; SRMR = 0.054**			
Real-life social support	0.617	0.863	0.515
	0.709		
	0.753		
	0.632		
	0.797		
	0.776		
Hope	0.735	0.838	0.464
	0.752		
	0.664		
	0.588		
	0.647		
	0.689		
Loneliness	0.709	0.894	0.515
	0.855		
	0.696		
	0.687		
	0.839		
	0.631		
	0.638		
	0.651		
Internet addiction	0.743	0.881	0.653
	0.678		
	0.935		
	0.853		

CR, composite reliability; AVE, average variance extracted.

Analytic strategy

To test our three hypotheses, we implement several quantitative methods, including descriptive statistics, correlations analysis, and multivariable approaches. Multivariable approaches contained OLS regression, confirmatory factor analysis (CFA), and Bootstrap method.

Results

Reliability and validity tests

We assessed the reliability and validity of latent variables with confirmatory factor analysis (CFA). First, we ran a CFA model of the four first-order factors of Internet addiction (i.e., Sym-CW, Sym-T, RP-IH, and RP-TM) (see Table 1, Model A). Then we conduct an overall CFA model that includes all latent variables, in which Internet addiction was treated as a second-order factor with four summated indicators of the first-order factors (see Table 1, Model B).

Based on the fit index of Model A and B (see Table 1), we found that the adjusted measurement models had a good model fit (66). As the Table 1 shows, all composite reliability (CR) values exceeded the 0.70 benchmark (67); all average variance extracted (AVE) values were above the cutoff value of 0.50 (68). Moreover, we compared the square root of the AVE value of each variable with the variables' correlations with other factors to estimate discriminant validity. The square root of the AVE value was greater than the between variable pairs, which supports the criterion for discriminant validity (65). Overall, the measures of key variables contained competent reliability and validity.

Descriptive analysis

Table 2 shows the result of descriptive statistics about sample demographics and correlations among all variables, including the means, standard deviations, and correlation coefficients. Of the 303 usable samples, there are 149 male and 154 female participants. The average age is 69.1 years old (SD = 7.14). Only 28 participants live alone among 55 years and older, others live with a significant other. With regards to self-rated health, the proportions of those self-rated healthier and those self-rated unhealthier are more than 50% and <10%, respectively. The number of older people with primary degrees or below is the largest, accounting for 42.9%. Also, about 40.92% of the participant could earn RMB 2,000–5,000 per month, but 21.45% income is < RMB 1,000 per month.

Besides, there remains a close relationship among these core variables in the present study. Namely, real-life social support is associated with Internet addiction among the elderly ($r = -0.307$, $p < 0.01$), loneliness ($r = -0.375$, $p < 0.01$), and hope ($r = 0.423$, $p < 0.01$). As we expected, hope is significantly correlated with Internet addiction of the old ($r = -0.239$, $p < 0.01$) and loneliness is significantly related to the elderly's Internet addiction ($r = 0.272$, $p < 0.01$) as well. This will help us to understand (1) what is the relationship between real-life social support and Internet addiction in the elderly population? (2) And how does real-life social support affect Internet addiction in older adults?

Hypothesis testing

We conducted a hierarchical regression to assess the association between the factors in our models. Hypothesis 1 of this study predicts that real-life social support could reduce the probability of Internet addiction among the elderly. As shown in Table 3, RLSS is negatively related to Internet addiction ($\beta = -0.356$, $p < 0.01$, Model 3), supporting Hypothesis 1.

To examine the indirect effects of RLSS on Internet addiction *via* hope and loneliness, we estimated mediated path models. First, the control variables and independent variables are entered into Model 1. The regression result of Model 1 indicates that RLSS has a negative relationship with loneliness ($\beta = -0.230$, $p < 0.01$). Second, Model 4 is that we add the mediating variable based on Model 1. The result represents that loneliness is positively correlated with Internet addiction, as RLSS is controlled ($\beta = 0.321$, $p < 0.01$). Meanwhile, RLSS is negatively related to Internet addiction ($\beta = -0.282$, $p < 0.01$) after controlling loneliness. Therefore, according to the causal steps approach used by (69), we propose that loneliness plays a mediating role in the link between RLSS and IA, supporting Hypothesis 2.

Similarly, RLSS is positively associated with hopefulness ($\beta = 0.383$, $p < 0.01$, Model 2), while hopefulness negatively predicted Internet addiction among the older population after RLSS was controlled in the regression model 5 ($\beta = -0.214$, $p < 0.01$, Model 5). That is, the indirect effect of RLSS on the elderly's IA *via* hope is significant and negative, which supports Hypothesis 3.

Moreover, we adopted PROCESS macro model template 4 for SPSS 26.0 with 5,000 bias-corrected bootstrap samples and 95% confidence intervals (CIs) to further examine the main and mediating effects of this study. When the 95% confidence interval (CI) does not contain zero, this means the statistical significance is achieved. That is the hypothesis is supported. Results are presented in Table 4. Real-life social support is negatively associated with Internet addiction in the elderly [$\beta = -0.376$, SE = 0.066, 95% CI = (-0.486,−0.225), CI does not include zero], and Hypothesis 1 is tested again. Furthermore, the results of the test of the mediation model indicate that hope mediates the relationship between RLSS and Internet addiction [$\beta = -0.084$, SE = 0.033, 95% CI = (−0.162, −0.028), CI does

TABLE 2 Descriptive and correlations among all variables.

Variables	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
(1) Hope	1										
(2) Loneliness	−0.254***	1									
(3) Real-life social support	0.423***	−0.375***	1								
(4) Internet addiction	−0.239***	0.272***	−0.307***	1							
(5) Age	0.087	−0.095*	0.070	−0.303***	1						
(6) Gender	0.013	0.021	−0.022	0.015	0.005	1					
(7) Education level	0.148***	−0.019	−0.048	0.204***	−0.180***	0.169***	1				
(8) Personal income	0.216***	−0.138**	0.050	0.134**	−0.123**	0.128**	0.600***	1			
(9) Self-rated health	0.251***	−0.268***	0.133**	0.000	−0.087	0.075	0.149***	0.196***	1		
(10) Taking care of grandchild	0.019	0.048	−0.045	0.138**	−0.155***	−0.093	0.012	0.039	0.057	1	
(11) Living situation	−0.066	0.138**	−0.124**	−0.074	0.171***	−0.630	−0.116**	−0.135**	−0.080	−0.111*	1
Mean	3.455	2.481	3.862	2.046	69.073	0.492	2.132	2.578	3.601	0.422	0.092
SD	0.595	0.447	0.610	0.757	7.142	0.501	1.146	1.029	0.835	0.495	0.290

N = 303. *P < 0.1, **P < 0.05, ***P < 0.01. Gender: 1-male, 0-female; Education level: 1-primary degrees or below, 2-secondary degrees, 3-high school degrees, 4-associate degrees or above; Ling with children: 1-yes, 0-no; Taking care of grandchildren: 1-yes, 0-no.

TABLE 3 Regression coefficients in the mediation model.

	Loneliness	Hope	Internet addiction			
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Independent variable						
Real-life social support	−0.230***	0.383***	−0.356***	−0.282***	−0.274***	−0.207***
Mediators						
Loneliness				0.321***		0.309***
Hope					−0.214***	−0.203***
Control variables						
Age	−0.007*	0.009*	−0.025***	−0.023***	−0.023***	−0.021***
Gender	0.043	−0.023	−0.014	−0.028	−0.019	−0.032
Education level	0.021	0.047	0.079*	0.072*	0.089***	0.082*
Personal income	−0.052*	0.072*	0.031	0.048	0.047	0.062
Self-rated health	−0.117***	0.121***	−0.014	0.024	0.012	0.047
Taking care of grandchild	0.045	0.045	0.123	0.109	0.133	0.118
Living situation	0.152*	0.017	−0.110	−0.159	−0.106	−0.153
Constant	4.285***	0.608	4.924***	3.549***	5.054***	3.724***
R^2	0.219	0.259	0.204	0.232	0.225	0.251

N = 303. *p < 0.1, ***p < 0.01.

not include zero]. In parallel, loneliness plays a mediating role in the association between RLSS and IA [β = −0.085, SE = 0.032, 95% CI = (−0.154, −0.030), CI does not include zero]. Hence, these findings provided effective support for Hypothesis 2 and 3.

Discussion

With the further promoting of information technology and strictly controlling of COVID-19, the increasingly older population engages in online entertainment instead of offline activities in China. Although a large number of studies focus on the negative effects of Internet use or smartphone use among the elderly, e.g., inducing depression and reducing subjective wellbeing (70), few studies investigate the problem of Internet addiction for the aged 55 years and older. It is important to consider the ramifications of Internet abuse for senior citizens, as the Internet has rapidly become an essential tool in their daily life. To fill this gap, this study indicates the significance of real-life social support during the period of prevention and

TABLE 4 Direct and indirect effects of social support *via* hope and loneliness on internet addiction.

Paths	Effect	SE	LLCI	ULCI
Total effect	−0.376	0.066	−0.486	−0.225
Direct path				
RLSP→IA	−0.207	0.074	−0.352	−0.062
Indirect path				
RLSP → Hope → IA	−0.084	0.033	−0.162	−0.028
RLSP → Loneliness →IA	−0.085	0.032	−0.154	−0.030

RLSP, real-life social support; IA, Internet addiction. Bootstraps resample = 5,000, Control variables are included in the analysis.

control of the COVID-19 epidemic and attempts to reveal the underlying mechanism in the relationship between RLSS and IA among senior citizens. Specifically, this article examined a theoretical model that demonstrated the mediating role of hope and loneliness in the relationship between real-life social support and Internet addiction.

This study yields several notable findings regarding the link between RLSS and IA among adults aged 55 years and older. The present study initially revealed that real-life social support is negatively related to Internet addiction for the elderly. Specifically, older adults with higher levels of real-life social support might decrease the probability of Internet addiction during the COVID-19 pandemic. This finding is congruent with the prior literature, which has found social support to be a strong indicator of Internet addiction behaviors (71). One possible scenario is that higher RLSS could effectively meet the social and emotional needs of the elderly, and help the aged affirm and express their identity, accordingly, affecting their physical and psychological health positively. Virtually, the older population is required to abide by coronavirus rules that stay home as much as possible and avoid physical contact with neighbors and strangers for reducing the chance of infection when the COVID-19 pandemic is in China. Accordingly, the frequency of interaction with neighbors and friends showed a dramatically decreased trend, especially for the senior adults with lower RLSS. They thereby have to seek and obtain alternative resources and support *via* online interaction, which will intensify their dependence on smart devices and pose a threat of Internet addiction.

The findings also present that hope mediates the relationship between RLSS and IA among senior citizens. More specifically, this result suggests that the aged with high levels of social support from their family members and close friends will have a promising prospect for the retired life, which extremely reduces the chance of Internet addiction. One possible reason for this finding is that RLSS is easily perceived and visible, which could help the elderly to protect against psychological distress and attain some coping strategies. Especially, they might obtain a large amount of information, resources, and emotional support from their family and friends, consequently, focusing on how to improve the quality of individual life instead of social media exposure frequently during the period of the COVID-19 pandemic.

Furthermore, the results of this study reveal another mediating mechanism of how RLSS exerts an effect on Internet addiction among the aged. That is loneliness plays a mediating role in the association between RLSS and IA. RLSS provides powerful sources for preventing and solving psychological problems, such as loneliness (54), while the feelings of loneliness exert a catalytic effect on Internet addiction. To our knowledge, this study is earlier to investigate the mediating role of loneliness in the relationship between RLSS and Internet addiction.

It is also interesting that the findings suggest age significantly and negatively predicts the level of IA. Compared with the oldest old, younger elderly are excelled at utilizing the smart devices and various phone applications. Therefore, there is a real possibility to use the smartphone excessively. In addition, the education level has a positive relationship with IA for those 55 years and older. A possible explanation for this could be that the aged with a higher degree have reserved funds of knowledge and have a strong learning capacity. They thereby could adapt and integrate into the digital society, and show a narrower digital divide, which also enhances the probability of Internet addiction than low education counterparts. Taken together, Internet addiction is also a differentiated problem within the older age group. However, this variation in IA among the elderly is rarely explored in existing research.

Practical implications

From a practical perspective, the findings of our study have important implications for both the field of aging study and the digital society.

First, we should not unilaterally suppose that only adolescents is likely to encounter a problem of Internet use such as addictive behaviors. It is more likely to be a prevalent problem among senior citizens with the development of successful aging and information technology. The negative effect of "Internet addiction on the elderly tends to be more terrible compared to younger." One possible explanation is that older adults, as the disadvantaged cohort, are prone to experiencing psychological trouble and fall into loneliness during the prevention and control of the COVID-19. They are more likely to increase the frequency of social media use to relieve feelings of loneliness, inducing the problem of Internet addiction. Meanwhile, the elderly have difficulty independently addressing the problem behavior such as Internet addiction as a result of a lack of digital literacy. Therefore, it is necessary to develop digital literacy and addiction prevention programs should aim to inform users about the risks associated with excessive SNS use (72, 73).

Second, this study reveals that real-life social support plays a crucial role in preventing problem behavior such as Internet addiction. Real-life social support is a major resource associated with wellbeing in the face of stress (74). This is especially important for older people who are disadvantaged and the most vulnerable to social stressors (75). However, it is a common phenomenon that individuals anywhere (i.e., in restaurants, coffee houses, etc.) are absorbed in using their smart devices in real life, instead of interacting face-to-face with each other (71). Taken together, we argue that older adults should draw attention to the importance of participating in social activities in an offline environment, which is more likely to facilitate the social relationships with their friends, reducing their dependence on smart devices (33). In addition, family is still the fundamental source of safety. Thus, the quality of relationships formed with the family is expected to be effective in gaining social support.

Third, this research also reveals that hope and loneliness play importantly mediating roles in the relationships between real-life social support and Internet addiction among the elderly. Thus, the community may target the aged to help them increase positive psychological experience and foster hopefulness (76). For instance, interventions should be focused on developing some positive coping skills for social distance during the period of pandemic prevention and control (e.g., doing exercise regularly at home, getting some sunlight, reducing social media exposure, etc.). Furthermore, it is an effective approach to giving emotional support to older people to enhance their positive psychological quality, including hope.

Limitations and future research

This study also presents some limitations. First, our participants all come from China and the study is not national representative, which to some extent influences our findings' generalizability. Thus, our findings are limited in terms of external validity and universality. However, it is true that the digital level has presented a significantly increasing trend in China and a large number of retired older adults have been exposed to digital services. Moreover, prior reports and studies have suggested the existence of the elderly's Internet addiction (1). Thus, we argue that our sample is a good and typical case for studying the association between real-life social support and Internet addiction among the elderly. Future research should pay more attention to the Internet addiction of the aged 55 years and older in other contexts such as developed countries where they rank highly on digitalization indexes or the country where the rate of aging is growing faster. And future research could be national representative to conduct empirical tests, which helps to provide more rigorous evidence for the external validity and universality of the research conclusions.

Second, we take all samples as the object of study and do not make a further distinction as a result of the relatively small sample. As is well known, there are large differences among the elderly. For example, whether the negative relationship between social support and the Internet is different in the aged group having various social and economic statuses. Hence, future research should adopt a perspective of comparative analysis and focus on the heterogeneity of Internet addiction among the elderly. Moreover, future research wants to delve deeper into the results by using a bigger sample size.

Thirdly, social support is a multidimensional concept that is generally defined as the tangible or intangible resources that individuals receive from their social network (77). We principally employed offline social support to measure the perceived social support in the aged 55 years and older in the present study. But what we cannot ignore is that online social support in the digital age is increasingly crucial for the elderly during the period of the COVID-19 pandemic (78). We are uncertain whether the relationship between the various dimensions of social support and Internet addiction presents great contrasts. These constitute new avenues of research with a promising future in this field of study.

Fourth, since this paper is a cross-section study of questionnaire data, it does inevitably exist endogeneity issue. Thus, the lack of examination of the endogeneity problem is a shortcoming of our paper. Future research could test and control the endogeneity problem by longitudinal tracking survey or instrumental variable method.

Conclusion

Although numerous older people already spend much time on the Internet and have shown some features of Internet addiction during the period of the COVID-19 pandemic, we have had little knowledge of the relationship between real-life social support and the Internet addiction, and also, there is few evidence to reveal the underlying mechanisms that real-life social support could exert effects on the Internet addiction among the senior adults. This article shows that real-life social support is a vital driver of Internet addiction among older adults during the period of the COVID-19 pandemic. Moreover, this study presents a theoretical framework to better clarify that hope and loneliness play a mediating role in the relationship between real-life social support and Internet addiction. We hope our findings could encourage researchers to pay attention to the problematic Internet use among the aged groups in the digital and aging era and inspire practitioners to design more effective settings to reduce online time and the possibility of Internet addiction among those aged 55 and older.

Data availability statement

The datasets presented in this article are not readily available due to confidentiality requirements.

Queries regarding the datasets should be directed to yangyangwhu@whu.edu.cn.

Ethics statement

The studies involving human participants were reviewed and approved by School of Sociology, Wuhan University. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

YJ contributed to writing original draft, conceptualization, data curation, formal analysis, and methodology. TL contributed to resources, data collection, and supervision of the article. YY contributed to data curation, methodology, review, and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Multidimensional energy poverty and depression among China's older adults

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Older adults often face more pronounced energy inequality in their daily lives, which is one of the reasons for their accumulation of stress or anxiety and may further aggravate their depression. Analyzing the relationship between energy poverty and the depression level of China's older adults will provide policy enlightenment for solving the problems of older adults' relative poverty, energy poverty, and mental poverty and thus promote happy and healthy aging. In this paper, using the data of China Health and Retirement Longitudinal Study in 2018, we used the entropy weighting method to objectively assign weights to 10 indicators reflecting the status of energy poverty and construct a multidimensional energy poverty index for older adults. First, we analyzed the relationship between multidimensional energy poverty and the depression levels of older adults using multiple linear regression model and quantile regression models. Next, we used instrumental variable linear regression model and instrumental variable quantile regression models for endogeneity tests. Then, we performed a robustness check by replacing the core explanatory variable. After that, we conducted heterogeneity analyses by residential area, type of residence, and solitary status. Finally, we analyzed the mediating role of life satisfaction using structural equation modeling. Multidimensional energy poverty has aggravated depression among older adults, and the effect is greater for older adults with higher depression levels. The effect of multidimensional energy poverty on depression is greater for older adults in western China, urban areas, and those who live alone. Multidimensional energy poverty has aggravated depression among older adults by reducing their life satisfaction.

KEYWORDS

multidimensional energy poverty, depression level, life satisfaction, older adults, China

Introduction

After years of arduous efforts in the battle against poverty, China has made remarkable achievements in poverty alleviation. After achieving moderate prosperity in all respects in 2021, China has entered a stage of poverty mainly characterized by relative poverty. This means that poverty alleviation will change from a tough battle to a prolonged campaign, focusing on solving the problem of relative poverty and thus providing a "Chinese solution" for other developing countries to tackle poverty. According to the seventh national census, the number of older adults aged 60 and above

in China was 260 million in 2020, accounting for 18.7% of the total population (1). The scale and proportion of older adults in China have been increasing over the years. China has entered a moderately aging society, and at the same time is facing the problem of "aging before getting rich." With the change in the direction of poverty alleviation and the acceleration of population aging, the problem of poverty among older adults in China has become increasingly prominent. Compared with other poor populations, the elderly find it more difficult to overcome poverty due to their declining physical functions, single source of income, and declining function of family care. Moreover, they are generally suffering from material, energy, health, and spiritual poverty (2).

As an important dimension of poverty, energy poverty is mainly reflected in the low level, poor structure, and weak capacity of energy use for domestic purposes, resulting in negative impacts on individual health and socioeconomics (3). According to the energy ladder hypothesis, older adults are more likely to suffer from energy poverty after retirement as their income level and socioeconomic status decrease significantly, which further affects their health status (4). Improving energy poverty is an important element of China's sustainable development and the establishment of a social equity system (5). With the deepening understanding of energy poverty in the international community, the United Nations and other international organizations have made the elimination of energy poverty an important development goal.

The United Nations designated 2012 as "the International Year of Sustainable Energy for All" and proposed the "Sustainable Energy for All" initiative, calling for global concerted action to safeguard the right of everyone to have access to modern, clean, and efficient energy for living and to jointly address energy poverty (6). The United Nations Sustainable Development Goal 7 for 2030 is to "ensure access to affordable, reliable, sustainable and modern energy for all" (7), including expanding access to electricity and clean cooking fuels, which is a common task for all countries and everyone. There are still 770 million people worldwide who do not have access to electricity—mostly in developing countries in Africa and Asia. Furthermore, more than 2.5 billion people do not have access to clean cooking fuels, and cooking with traditional biomass, coal, or kerosene causes 2.5 million premature deaths each year, thereby slowing social and economic development and increasing inequality. The outbreak of the coronavirus disease has led to an increase in energy prices, reducing households' ability to purchase energy and reversing the recent progress in areas such as expanding access to electricity and cooking fuels (8). Although China has experienced unprecedented economic growth, it is still a developing country with a very large population, so it is imperative for China to address energy poverty. Access to modern forms of energy is critical to the development, health, education, and other socioeconomic aspects of a country and can help residents improve their living standards and health.

Lewis first introduced the concept of energy poverty, that is, household inability to afford adequate warmth, to illustrate how inadequate energy use affects people's living standards (9). Leach validated the above concept of energy poverty by arguing that low-income households spend a higher proportion of their total household income on energy consumption than middle-income households (10). Boardman proposed the "10% indicator" from the perspective of affordability, arguing that a household can be considered energy poor if its energy consumption expenditure accounts for 10% or more of its total income (11). Many researchers have used this indicator to measure energy poverty (12–14). However, Papada et al. argued that the "10% indicator" is not a good measure of energy poverty because it neglects the fact that some households do not have sufficient access to energy due to their low income (15). Hills proposed the "low-income-high-costs" indicator and defined energy poverty as when residual household income is below the official poverty line while basic energy costs for household living needs are higher than the average (16). This indicator has been used by many researchers (17–19). However, the double relativity of this indicator makes it difficult to isolate the causal relationship in the analysis (20). Nussbaumer et al. (22) first proposed the concept of multidimensional energy poverty and defined it as the inability to obtain clean energy with sustainable human development and social prosperity as the starting point. They constructed a macrolevel multidimensional energy poverty index (MEPI) based on the dual-cutoff approach proposed by Alkire and Foster (21). This index measures energy poverty from several perspectives and has been used by many researchers to measure multidimensional energy poverty in different regions (23–26).

Some scholars have analyzed the health effects of energy poverty. Nawaz et al. found a significant positive impact of energy poverty on the multidimensional health poverty index (consisting of three dimensions—child health, general health, and infectious disease prevalence) of Pakistanis (27). Zhang et al. concluded that energy poverty has an important and significantly negative impact on the average health status of Chinese households (28). Zhang et al. (30) constructed a multidimensional poverty index from five dimensions—cooking, clothing, travel, housing, and education/entertainment and concluded that energy poverty has impaired Chinese residents' physical and mental health (29). Brown et al. measured the health status of Australian residents from different perspectives and found a strong correlation between energy poverty and adverse health status (31). Hailemariam et al. found that energy poverty has increased the possibility of Australian residents suffering physical violence (32). Prakash et al. concluded that energy poverty is positively correlated with obesity among Australian residents (33). Zhang et al. used instrumental variable quantile regression (IVQR) to find a significantly positive impact of energy poverty on depression at the high quantile of depression scores among rural Chinese residents but found no impact at the low and middle quantiles

(34). Nie et al. concluded that energy poverty has led to higher depression levels among Chinese adults (35). Lin and Okyere found that energy poverty in Ghana heightenes one's chances of being mentally unhealthy; among the indicators of multidimensional energy poverty, deprivation in household appliance ownership (refrigerator ownership) has the most significant impact on household heads' depression levels (36). From these aforementioned studies, it is clear that there are few studies on the association between multidimensional energy poverty and older adults' mental health, which is the focus of this study.

Other effects of energy poverty have also been analyzed. Getie found that energy deprivation directly or indirectly affects the living standards of individuals in Ethiopia (37). Bukari et al. found that energy poverty significantly increases household health expenditures in Ghana (38). Liu et al. found that energy poverty significantly reduces Chinese residents' subjective wellbeing, with regional, urban–rural, and income heterogeneity. They also found that greater intensity of energy poverty exerts a greater impact on residents' wellbeing (39). Druica et al. believed that energy poverty has a significant impact on the life satisfaction of citizens in many countries (40). From the perspective of different developing countries, Banerjee et al. found that energy poverty reduces the average years of education for citizens (41). Xiao et al. found that energy poverty has a significantly negative impact on individual development through health status (42). Cheng et al. believed that consistent with the disadvantage theory of entrepreneurship, the higher the share of household income spent on energy consumption or energy poverty, the higher the likelihood of becoming an entrepreneur (43). Rafi et al. believed that energy poverty has a significantly negative impact on the human capital development of Indian children (44).

So far, there are few studies on the mechanism by which multidimensional energy poverty affects depression among older adults. Nie et al. concluded that self-rated health and household food expenditure play mediating roles in the impact of energy poverty on depression levels among Chinese adults (35). Some studies have revealed that energy poverty affects residents' welfare and living standards (37–39), and decreases their life satisfaction (40), which increases depression among older adults (45).

Depression is a very common psychological disorder among older adults in China and is affected by a number of social and biological factors. Older adults often face more pronounced energy inequality in their daily lives, which is one of the reasons for their accumulation of stress or anxiety and may further aggravate their depression. This issue needs to be addressed. However, most existing studies have focused on the impact of energy poverty on the health of the population but have paid less attention to the association between energy poverty and the mental health of older adults. Therefore, from the perspective of multidimensional energy poverty, this paper analyzes the relationship between energy poverty and the depression level of China's older adults and explores the heterogeneity across different older adult populations and possible influencing mechanisms. Theoretically, this study improves the existing theoretical system of research on the impact of energy poverty on older adults' mental health. It provides practical policy insights for China to address the problems of relative poverty, energy poverty, and mental poverty of older adults to promote happy and healthy aging.

Materials and methods

Data

The data are sourced from the 2018 China Health and Retirement Longitudinal Study (CHARLS)—an interdisciplinary survey project hosted by the National School of Development of Peking University and executed by the Institute of Social Science Survey. The survey aims to collect a set of high-quality microdata of Chinese households and individuals aged 45 years and above to analyze the aging of China's population and promote interdisciplinary research on aging. The survey contains the personal characteristics, health status, energy poverty, and other statuses of older adults, which can satisfy the needs of this study. In this study, older adults aged 60 and above were selected as the study population. After eliminating samples with missing values of variables, the final sample size is 6,222.

Variables

Explained variable

Many studies have shown that the reliability and validity of the CES-D 10 scale are not decreased with the reduction of items (46, 47). Huang et al. found that CES-D 10 scale has high reliability and good discriminant validity, and can effectively measure the level of depression in middle-aged and elderly people in China (48). In the questionnaires of China Health and Retirement Longitudinal Study (CHARLS) and Chinese Longitudinal Healthy Longevity Survey (CLHLS), CES-D 10 is a very important scale to evaluate depression level and has been widely used.

The explained variable is the depression levels among older adults, reflected by the depression scale (CES-D 10), including a total of 10 questions: "I am bothered by small things;" "I have difficulty concentrating when doing things;" "I feel depressed;" "I find it hard to do everything;" "I am hopeful about the future;" "I feel scared;" "I have trouble sleeping;" "I am happy;" "I feel lonely;" and "I don't think I can continue my life." In this study, the eight questions reflecting negative emotions were assigned values based on the responses as follows: "rarely or

not at all" = 0, "not too much" = 1, "sometimes or half of the time" = 2, and "most of the time" = 3. The two questions reflecting positive emotions, that is, "I am hopeful about the future" and "I am happy" were assigned opposite values. The values of the 10 questions were eventually summed to obtain the scores of depression levels, ranging from 0 to 30. A higher depression score indicates a higher depression level and worse mental health status.

Core explanatory variable

The core explanatory variable is the MEPI of older adults, and we adopted the framework proposed by Nussbaumer et al. to measure it (22). MEPI under this framework is defined as multiple deprivations of modern energy services for a decent life. we chose ten indicators of energy deprivation embodied in four dimensions: ① access to travel: "own a car;" ② access to entertainment: "own a TV," "own a computer (tablet);" ③ access to modern housing appliances: "own a refrigerator (freezer)," "own a washing machine," "own an air conditioner," "own an air purifier," "own bathing facilities," "have heating facilities;" ④ access to clean cooking fuel: "main fuel used for cooking is clean energy." They were measured on a binary scale, where "yes = 0" or "no = 1." Compared with the six indicators used in Nussbaumer et al. (22) and the nine indicators used in Zhang et al. (30), we expanded the number of indicators to ten. MEPI was constructed from the above 10 indicators through the Entropy Weight Method, an objective weighting method. A larger MEPI indicates deeper energy poverty experienced by older adults.

Table 1 presents the data statistics and weights for each dimension. Among the samples in this study, 4.74% of the older adults owned a car, 85.71% owned a TV, 10.41% owned a computer (tablet), 75.35% owned a refrigerator (freezer), 67.18% owned a washing machine, 34.96% owned an air conditioner, only 1.67% owned an air purifier, 59.31% owned bathing facilities, 14.56% had heating facilities, and 63.40% of the elderly used clean energy as their main fuel for cooking. We can see that the weight of the variable will increase if the proportion of the older adults who do not own an energy service decreases. "Own an air purifier" had the lowest weight, 0.0024; "Own a TV" had the highest weight, 0.2730.

TABLE 1 Data statistics and weights for each dimension of energy poverty.

Variables	Yes	No	Weights
Own a car	295 (4.74%)	5,927 (95.26%)	0.0068
Own a TV	5,333 (85.71%)	889 (14.29%)	0.2730
Own a computer (tablet)	648 (10.41%)	5,574 (89.59%)	0.0154
Own a refrigerator (freezer)	4,688 (75.35%)	1,534 (24.65%)	0.1965
Own a washing machine	4,180 (67.18%)	2,042 (32.82%)	0.1563
Own an air conditioner	2,175 (34.96%)	4,047 (65.04%)	0.0603
Own an air purifier	104 (1.67%)	6,118 (98.33%)	0.0024
Own bathing facilities	3,690 (59.31%)	2,532 (40.69%)	0.1261
Have heating facilities	906 (14.56%)	5,316 (85.44%)	0.0221
Main fuel used for cooking is clean energy	3,945 (63.40%)	2,277 (36.60%)	0.1410

Control variables

After reviewing relevant studies and the survey data used (34–36, 49, 50), this study selected the following as control variables: gender, age, marital status, education level, type of residence, work status, physical health, self-rated health, number of household members, availability of health insurance, availability of endowment insurance, and residential area. Educational level was divided into primary school or below, middle school, and high school or above. Work status included unemployed, agricultural work, and non-agricultural work. Physical health status was reflected by activities of daily living scores, ranging from 0 to 18. According to the geographical location and level of economic development, the residential area was divided into western region (including Sichuan, Guizhou, Yunnan, Tibet, Shaanxi, Gansu, Qinghai, Ningxia, Chongqing, Xinjiang, and Guangxi), central region (including Shanxi, Inner Mongolia, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, and Hunan), and eastern region (including Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Hainan).

Mediator variable

Studies have demonstrated that energy poverty impacts residents' life satisfaction (39, 40), and life satisfaction often has a very important impact on residents' depression. Thus, this study selected life satisfaction as a mediator variable to examine its mediating role between multidimensional energy poverty and older adults' depression. The value range of life satisfaction is 1–5, and the satisfaction decreases as the value increases.

Instrumental variable

The existing literature has demonstrated the rationality of community (village) level indicators as instrumental variables for individual indicators (39, 51). Therefore, in this study, the "MEPI at community level," i.e., the mean of the MEPI of all older adults in the same community, was selected as an instrumental variable. The reason for this is that the multidimensional energy poverty index of the

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TABLE 2 Variables and data statistics.

Continuous variables	Mean	Standard deviation	Min	Max
Depression level	9.750	6.835	0	30
MEPI	0.322	0.261	0	1
Life satisfaction	2.748	0.803	1	5
Age	66.678	6.326	60	95
Activities of daily living	0.772	1.718	0	18
Self-Rated health status	3.209	0.972	1	5
Number of household members	0.849	1.445	0	12

Categorical variables	Categories	*n*	Percentages (%)	Average depression level
Gender	Female	3,378	54.29	10.594
	Male	2,844	45.71	8.748
Marital status	No spouse	1,227	19.72	11.015
	With spouse	4,995	80.28	9.439
Education level	Primary school or below	4,691	75.39	10.360
	Middle school	957	15.38	8.439
	High school or above	574	9.23	6.953
Type of residence	Rural	3,750	60.27	10.678
	Urban	2,472	39.73	8.342
Work status	Unemployed	3,086	49.60	9.665
	Agricultural work	2,738	44.01	10.122
	Non-agricultural work	708	11.38	7.881
Medical insurance	No	178	2.86	10.522
	Yes	6,044	97.14	9.727
Endowment insurance	No	578	9.29	10.401
	Yes	5,644	90.71	9.683
Residential area	Western region	1,803	28.98	11.104
	Central region	2,373	38.14	9.808
	Eastern region	2,046	32.88	8.490

As some older adults are engaged in both agricultural and nonagricultural work, the sum of the percentages for all work status is >100.

community as a whole is closely correlated with the MEPI of older adults but does not significantly correlate with their other characteristics.

Data statistics

Table 2 presents the variables and data statistics. The average depression level of the older adults was 9.750, the mean of MEPI was 0.322, and the average life satisfaction was 2.748, which was between "very satisfied" and "somewhat satisfied." In terms of control variables, the average age was 66.678 years old, the average activities of daily living were 0.772, the average self-rated health status was 3.209 between "fair" and "poor," and the average number of household members was 0.849; Among the samples, 54.29% of the elderly were female, 19.72% did not have a spouse, 75.39% had only primary school education or below, 60.27% lived in rural areas, 49.60% were unemployed, 2.86% had no medical insurance, 9.29% had no endowment insurance, and 28.98% of the older adults lived in western region of China.

Models

Linear regression model

In this paper, we regarded the depression levels among older adults as the explained variable and the MEPI as the core explanatory variable, added various control variables to establish a multivariable linear regression model, in which we used the ordinary least squares (OLS) to analyze the association between multidimensional energy poverty and the depression levels of older adults.

$$Y_i=\alpha_0+\beta_{00}X_i+\sum\beta_{0j}Z_{ij}+\varepsilon_{0i} \quad (1)$$

In Equation (1), Y_i is the i-th older adult's depression level; α_0 is the constant term, and ε_{0i} is the error term. X_i is the core explanatory variable, representing the MEPI of i-th older adult, respectively, and β_{00} is its coefficient. Z_{ij} is the j-th control variable for the i-th older adult, and β_{0j} is the coefficient of each control variable.

Quantile regression model

As the depression levels of older adults are highly heterogeneous and the same multidimensional energy poverty index may have different impacts on older adults with different depression levels, this paper used QR models to analyze the different relationships between multidimensional energy poverty and the depression levels of older adults at different quantile points to verify whether the findings of the multivariable linear regression model are robust.

$$Q_{iq}\left(Y_i\right) = \alpha_q + \beta_{0q}X_i + \sum \beta_{jq}Z_{ij} \tag{2}$$

In Equation (2), $Q_{iq}\left(Y_i\right)$ denotes the conditional quantile of depression level given the distribution of core explanatory and control variables, where q denotes the quantiles, and 10, 25, 50, 75, and 90% quantiles are selected successively in this paper. The definitions of the remaining variables and parameters are the same as those of the multivariable linear regression model.

Instrumental variable linear regression model

Because of the possibility of omitted variables and measurement errors, this study used two-stage least squares (2SLS) to deal with endogeneity in the instrumental variable linear regression model.

$$Y_i = \alpha_1 + \beta_{10}\hat{X}_i + \sum \beta_{1j}Z_{ij} + \varepsilon_{1i} \tag{3}$$

$$X_i = \gamma_0 + \delta_{00}I_i + \sum \delta_{0j}Z_{ij} + u_{0i} \tag{4}$$

Equation (4) is the first-stage regression, and I_i is the instrumental variable, i.e., the community-level MEPI. Equation (3) is the second-stage regression, and $\hat{X}_i$ is the fitted value of the first-stage regression.

IVQR model

As mentioned above, multidimensional energy poverty is endogenous, and the results of the QR models may also be biased. Therefore, in this paper, instrumental variable was added to the QR models, and the IVQR models were used to deal with the endogeneity problem. The specific solution process is based on the study of Chernozhukov and Hansen (52, 53).

$$Y = X'\alpha\left(U\right) + Z'\beta\left(U\right), U|Z, I \sim \text{Uniform}\left(0, 1\right) \tag{5}$$

$$X = f\left(Z, I, V\right) \tag{6}$$

In Equation (5), Y represents the depression levels of older adults; Z represents the control variables, and X represents the endogenous variable. U is a random variable that follows a uniform distribution of $(0, 1)$. In Equation (6), I is the instrumental variable; V is the unobserved disturbance vector, and V and U are correlated, thus giving rise to endogeneity.

Structural equation modeling

In this paper, we used life satisfaction as a mediator variable and developed a SEM to analyze the mechanism through which multidimensional energy poverty impacts the depression level of older adults. The mediating effect model is as follows:

$$Y_i = \alpha_2 + cX_i + \sum \beta_{2j}Z_{ij} + \varepsilon_{2i} \tag{7}$$

$$M_i = \alpha_3 + aX_i + \sum \beta_{3j}Z_{ij} + \varepsilon_{3i} \tag{8}$$

$$Y_i = \alpha_4 + c'X_i + bM_i + \sum \beta_{4j}Z_{ij} + \varepsilon_{4i} \tag{9}$$

where Y_i, X_i, and M_i denote the explained, core explanatory, and mediator variables, respectively. Equation (7) represents the regression equation of the explained variable and the core explanatory variable; Equation (8) represents the regression equation of the mediator variable and the core explanatory variable, and Equation (9) represents the regression equation of the explained variable and both the mediator and core explanatory variables.

Results

The relationship between multidimensional energy poverty and depression level

This paper established a multivariable linear regression model as the baseline model to analyze the relationship between multidimensional energy poverty and the depression level of older adults. According to Model 1 in Table 3, the MEPI of older adults is significantly and positively associated with their depression levels at the 1% level; the depression level increases by 2.416 units with each unit increase in the MEPI. We performed a multicollinearity test to eliminate the multicollinearity problems of the multivariable linear regression model.

As the depression levels among older adults are highly heterogeneous, the same multidimensional energy poverty

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TABLE 3 Regression results of the relationship between multidimensional energy poverty and depression levels.

Variables	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
	OLS	QR				
		Q10	Q25	Q50	Q75	Q90
Core explanatory variable						
MEPI	2.416***	1.096***	2.071***	2.452***	2.998***	3.406***
	(0.337)	(0.360)	(0.399)	(0.409)	(0.546)	(0.792)
Control variables						
Gender	−1.464***	−0.677***	−0.933***	−1.536***	−1.725**	−1.529***
(Female)	(0.161)	(0.180)	(0.158)	(0.221)	(0.243)	(0.351)
Age	−0.082***	−0.038***	−0.056***	−0.086***	−0.111***	−0.103***
	(0.013)	(0.014)	(0.013)	(0.019)	(0.020)	(0.030)
Marital status	−0.895***	−0.319	−0.566**	−0.976***	−0.907***	−1.827***
(No spouse)	(0.212)	(0.237)	(0.244)	(0.278)	(0.325)	(0.488)
Middle school	−0.697***	0.101	−0.059	−0.620***	−1.343***	−1.740***
(Primary school or below)	(0.205)	(0.210)	(0.231)	(0.214)	(0.309)	(0.453)
High school or above	−1.473***	−0.536**	−0.914***	−1.445***	−1.858***	−2.807***
(Primary school or below)	(0.254)	(0.208)	(0.233)	(0.286)	(0.415)	(0.626)
Type of residence	−0.948***	−0.574***	−0.883***	−1.235***	−1.083***	−1.092***
(Rural)	(0.182)	(0.168)	(0.174)	(0.217)	(0.232)	(0.385)
Agricultural work	0.306*	0.164	0.215	0.405*	0.210	0.165
(Unemployed)	(0.174)	(0.162)	(0.193)	(0.221)	(0.274)	(0.418)
Non-agricultural work	−0.458**	−0.403	−0.182	−0.536**	−0.687*	−0.344
(Unemployed)	(0.232)	(0.272)	(0.238)	(0.271)	(0.390)	(0.674)
Activities of daily living	0.786***	0.566***	0.810***	0.977***	0.963***	0.749***
	(0.055)	(0.086)	(0.073)	(0.082)	(0.079)	(0.088)
Self-rated health status	1.942***	0.928***	1.339***	2.041***	2.501***	2.411***
	(0.085)	(0.070)	(0.081)	(0.096)	(0.111)	(0.210)
Number of household members	−0.172***	−0.079	−0.100**	−0.209***	−0.178**	−0.187
	(0.051)	(0.055)	(0.047)	(0.064)	(0.083)	(0.117)
Medical insurance	0.296	−0.432	0.421	0.268	−0.681	0.637
(No)	(0.459)	(0.372)	(0.441)	(0.699)	(0.717)	(0.758)
Endowment insurance	−0.073	0.030	−0.023	−0.265	−0.239	−0.373
(No)	(0.276)	(0.283)	(0.249)	(0.366)	(0.319)	(0.615)
Central region	−0.864***	−0.521***	−0.772***	−0.897***	−1.183***	−0.671
(Western region)	(0.194)	(0.188)	(0.228)	(0.269)	(0.297)	(0.447)
Eastern region	−1.630***	−1.063***	−1.294***	−1.632***	−2.085***	−1.762***
(Western region)	(0.198)	(0.216)	(0.207)	(0.264)	(0.323)	(0.448)
Constant	10.452***	3.215***	5.120***	10.052***	15.973***	19.431***
	(1.168)	(1.117)	(1.136)	(1.678)	(1.939)	(2.981)
R^2/pseudo R^2	0.238	0.075	0.103	0.144	0.164	0.152

Robust standard errors in Model 1 are given in parentheses, and the goodness-of-fit statistical measure is R^2; bootstrap standard errors in Models 2–6 are given in parentheses, with a sample size of 100, and the goodness-of-fit statistical measure is pseudo R^2; *, **, *** represent the significance levels of 10, 5, and 1%, respectively.

status may have different impacts on older adults with different depression levels. The QR models were also developed to analyze the association between MEPI and the depression level of older adults in different quantiles. According to Models 2–6 in Table 3, the association between MEPI and the depression level of older adults remains significant at the 1% level with coefficients of 1.096, 2.071, 2.452, 2.998, and 3.406, respectively. The coefficients are greater for older adults with higher depression levels. The results of the multivariable linear regression model and QR models indicate that multidimensional energy poverty

TABLE 4 Estimation results of instrumental variable regression models.

Variables	Model 7	Model 8	Model 9	Model 10	Model 11	Model 12
	2SLS	IVQR				
		Q10	Q25	Q50	Q75	Q90
MEPI	4.213***	2.171***	2.958***	4.120***	5.510***	6.824***
	(0.683)	(0.735)	(0.654)	(0.682)	(0.914)	(1.228)
Control variables	Yes	Yes	Yes	Yes	Yes	Yes
Constant	10.078***	2.234*	4.967***	9.004***	13.834***	18.399***
	(1.181)	(1.193)	(1.062)	(1.106)	(1.474)	(1.978)

Standard errors in Models 7–12 are given in parentheses; *, *** represent the significance levels of 10 and 1%, respectively.

TABLE 5 Regression results by replacing core explanatory variable.

Variables	Model 13	Model 14	Model 15	Model 16	Model 17	Model 18
	OLS	QR				
		Q10	Q25	Q50	Q75	Q90
Multidimensional energy poverty status	1.036***	0.516**	0.837***	0.972***	1.161***	1.378***
	(0.170)	(0.212)	(0.206)	(0.210)	(0.239)	(0.343)
Control variables	Yes	Yes	Yes	Yes	Yes	Yes
Constant	10.657***	3.386***	5.242***	10.361***	15.985***	17.893***
	(1.169)	(1.177)	(1.273)	(1.606)	(1.930)	(2.907)
R^2/pseudo R^2	0.236	0.075	0.102	0.142	0.162	0.151

Robust standard errors in Model 13 are given in parentheses, and the goodness-of-fit statistical measure is R^2; bootstrap standard errors in Models 14–18 are given in parentheses, with a sample size of 100, and the goodness-of-fit statistical measure is pseudo R^2; **, *** represent the significance levels of 5 and 1%, respectively.

TABLE 6 Estimation results of instrumental variable regression models by replacing the core explanatory variable.

Variables	Model 19	Model 20	Model 21	Model 22	Model 23	Model 24
	2SLS	IVQR				
		Q10	Q25	Q50	Q75	Q90
Multidimensional energy poverty status	2.459***	1.143***	1.649***	2.399***	3.296***	4.152***
	(0.401)	(0.409)	(0.366)	(0.395)	(0.541)	(0.733)
Control variables	Yes	Yes	Yes	Yes	Yes	Yes
Constant	10.249***	2.680**	5.301***	9.182***	13.825***	18.256***
	(1.184)	(1.198)	(1.068)	(1.103)	(1.455)	(1.951)

Standard errors in Models 19–24 are given in parentheses; **, *** represent the significance levels of 5 and 1%, respectively.

aggravates depression among older adults and is detrimental to their mental health.

Treatment of endogeneity

We performed a Hausman test in the linear regression model, which showed a chi-square value of 8.95, rejecting the original hypothesis at the significance level of 5%, and therefore considered MEPI as an endogenous variable. Obviously, due to the possibility of omitted variables and measurement errors, there was also endogeneity in the quantile regression model. We mentioned above the rationality of community (village) level indicators as instrumental variables for individual indicators (39, 51), so the MEPI at the community level of older adults was selected as an instrumental variable to deal with endogeneity. As a whole, the MEPI at the community level is closely correlated with the individual MEPI of older adults but does not significantly correlate with their other characteristics, which satisfies the correlation between the instrumental variable

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TABLE 7 Estimation results of the multivariable linear regression model by residential area.

Variables	Model 25	Model 26	Model 27
	Western region	Central region	Eastern region
MEPI	2.702***	2.290***	2.317***
	(0.610)	(0.537)	(0.615)
Control variables	Yes	Yes	Yes
Constant	8.707***	10.986***	9.020***
	(2.229)	(1.983)	(1.870)
N	1,803	2,373	2,046
R^2	0.218	0.229	0.229

Robust standard errors in Models 25–27 are given in parentheses; *** represents the significance level of 1%.

TABLE 8 Estimation results of multivariable linear regression model by type of residence.

Variables	Model 28	Model 29
	Rural	Urban
MEPI	1.787***	3.445***
	(0.421)	(0.567)
Control variables	Yes	Yes
Constant	11.944***	8.060***
	(1.544)	(1.847)
N	3,750	2,472
R^2	0.207	0.245

Robust standard errors in Models 25–27 are given in parentheses; *** represents the significance level of 1%.

TABLE 9 Estimation results of multivariable linear regression model by solitary status.

Variables	Model 30	Model 31
	Solitary (number of household members equal to 0)	Non-solitary (number of household members >0)
MEPI	3.224***	1.297**
	(0.433)	(0.539)
Control variables	Yes	Yes
Constant	8.911***	13.475***
	(1.447)	(2.015)
N	3,962	2,260
R^2	0.254	0.222

Robust standard errors in Models 30 and 31 are given in parentheses; **, *** represent the significance levels of 5 and 1%, respectively.

and the endogenous explanatory variable and the exogeneity between the instrumental variable and the disturbance term. Then we conducted a weak instrumental variable test, and the result showed that the F statistic at the first stage was 1,808.76 (much larger than 10), which excluded the existence of weak instrumental variable. The coefficients of Models 7–12 in Table 4 are 4.213, 2.171, 2.958, 4.120, 5.510, and 6.824, respectively, which are all larger than the corresponding coefficients of Models 1 to 6 in Table 3 and significant at the 1% level. The effect of multidimensional energy poverty on the depression level of older adults becomes significantly larger after treating for endogeneity.

Robustness test

Referring to the studies of Zhang et al. (30) and Mendoza et al. (54), when $MEPI \geq 0.3$, older adults are in a multidimensional energy poverty status; otherwise, they are not in a multidimensional energy poverty status. In this paper, we used multidimensional energy poverty status as the replaced core explanatory variable to conduct a robustness check. According to Table 5, after replacing the core explanatory variable, the coefficients of Models 13–18 are 1.036, 0.516, 0.837, 0.972, 1.161, and 1.378, respectively; after treating for endogeneity, the coefficients of Models 19–24 in Table 6 are 2.459, 1.143, 1.649, 2.399, 3.296, and 4.152, respectively. According to the results of the robustness check, the relationship between multidimensional energy poverty status and the depression level of older adults remains significant.

Heterogeneity analysis

According to the models in Table 1, residential area, type of residence, and the number of household members all have significant correlation with the depression level of older adults. Thus, we used the multivariable linear regression model to analyze heterogeneity by residential area, type of residence, and solitary status (number of household members).

According to Models 25–27 in Table 7, the coefficients of the MEPI are 2.702, 2.290, and 2.317 in the western, central, and eastern regions, respectively, and all are significant at the 1% level. According to Models 28 and 29 in Table 8, the coefficients of MEPI are 1.787 and 3.445 in rural and urban areas, respectively, and both are significant at the 1% level. According to Models 30 and 31 in Table 9, the coefficients of MEPI on the depression level of solitary and non-solitary older adults are 3.224 and 1.297, respectively, and both are significant at the 5% level.

Mediating effect analysis

In this study, structural equation model was used to analyze the mediating effect of life satisfaction between

TABLE 10 Results of SEM.

Variables	Life satisfaction	Depression level
Life satisfaction		2.604***
		(0.105)
MEPI	0.161***	1.998***
	(0.045)	(0.322)
Control variables	Yes	Yes
Constant	3.101***	2.375**
	(0.169)	(1.147)

Bootstrap standard errors are given in parentheses, with a sample size of 500; **, *** represent the significance levels of 5 and 1%, respectively.

TABLE 11 Direct effect, indirect effect, and total effect.

Effect	Coefficient	Bootstrap standard error	95% confidence interval	*P*-value
Direct effect	1.998	0.322	[1.367, 2.629]	<0.001***
Indirect effect	0.418	0.115	[0.192, 0.644]	<0.001***
Total effect	2.416	0.341	[1.748, 3.085]	<0.001***

*** represents the significance level of 1%.

multidimensional energy poverty and the depression level of older adults. The evaluation criteria of SEM fitting indices are as follows: RMSEA (Root mean squared error of approximation) = 0.000 < 0.05, SRMR (Standardized root mean squared residual) = 0.000 < 0.05, CFI (Comparative fit index) = 1.000 > 0.90, and TLI (Tucker-Lewis index) = 1.000 >0.90, which indicates that the model is well-fitted. According to Table 10, the coefficient of MEPI on life satisfaction is 0.161; and the coefficients of life satisfaction and MEPI on depression levels are 2.604 and 1.998, respectively, and both are significant at the 1% level. According to the results in Table 11, the mediating effect of multidimensional energy poverty on the depression level of older adults is 0.418; the direct effect and total effect are 1.998 and 2.416, respectively, and all of them are significant at the 1% level. The mediating effect of life satisfaction accounts for 17.3% of the total effect.

Discussion

In this paper, based on the data of CHARLS in 2018, 10 indicators reflecting the energy poverty status of older adults are synthesized into a MEPI using EWM. First, we analyzed the relationship between multidimensional energy poverty and the depression level of older adults using multiple linear regression and QR models. Next, we used instrumental variable linear regression model and IVQR models for endogeneity treatment. Then, we performed a robustness check by replacing the core explanatory variable. After that, we conducted heterogeneity analyses by residential area, type of residence, and solitary status. Finally, we adopted the SEM to analyze the mediating role of life satisfaction.

Multidimensional energy poverty has aggravated depression among older adults, and similar results have been obtained by other studies (29, 30, 35, 36). After retirement, older adults are removed from their previous positions and have substantially lower incomes and socioeconomic status (55). They then face more pronounced energy inequality in their daily lives, which is one of the reasons for their accumulation of stress or anxiety. As multidimensional energy poverty deepens in older adults, they suffer more pronounced energy inequality and perceive more stress or anxiety. They feel that they are in a lower social class or society is not fair (39), which aggravates their depression. And multidimensional energy poverty will damage physical health, cause poor people to feel low-spirited, lack of happiness, and affect the level of mental health (29). Moreover, multidimensional energy poverty also causes a decline in the quality of life or welfare of older adults, which affects their subjective life satisfaction and may further aggravate their depression. In addition, this effect becomes more significant as depression among older adults increases, which is to some extent the same as the findings of Zhang et al. (34) and Zhang (56). Older adults with severer depression are more fragile and sensitive psychologically and are more easily influenced by the external environment; thus, they are more severely impacted by energy poverty.

Compared with the central and eastern regions, the western region has a low level of socioeconomic development and sparsely populated areas with a significant gap in energy infrastructure development, and the older adults there face higher multidimensional energy poverty. Thus, multidimensional energy poverty has the greatest effect on depression among older adults in the western region, whereas there is little difference in its impact on older adults in the central and western regions, which is inconsistent with the findings of Zhang and Shu (29) and Zhang et al. (30).

The effect of multidimensional energy poverty on depression among urban older adults is greater than that among rural older adults, which is mainly due to the large wealth gap among urban older adults, which is a view shared by several studies (29, 30). Although compared with those in rural areas, urban older adults have lower levels of multidimensional energy poverty, they face greater energy inequality. Urban older adults live in highly modernized and fast-paced cities. Once they have a large gap in energy use with that of others, they experience many inconveniences and relatively large psychological disparities.

The effect of multidimensional energy poverty on depression among solitary older adults is greater than that among non-solitary ones, which is a finding that has not been revealed in existing studies. Compared with solitary older adults, non-solitary older adults have more family members; moreover, their families have higher demand and the willingness and

ability to pay for all forms of energy and thus face relatively less energy poverty, which benefits them. Furthermore, family members help older adults to learn to operate various energy-related appliances and devices, and they become more proficient at using them. Due to these two reasons, the effect of multidimensional energy poverty on depression among non-solitary older adults is less significant.

Nie et al. believed that energy poverty affects residents' depression levels through self-rated health and food expenditures (35). In contrast, the present study holds that multidimensional energy poverty decreases older adults' life satisfaction and then increases their depression levels. Energy plays a vital role in the lives of older adults, affecting their access to travel, entertainment, housing appliances, cooking, and other aspects. The elderly are vulnerable to suffer from energy poverty due to inadequate energy infrastructure and family affordability and energy availability constraints, which prevent them from obtaining clean and efficient energy to meet their basic needs. Studies have revealed that energy poverty affects residents' welfare and living standards (37–39), thus decreases their life satisfaction (40), which will increase depression among older adults (45). To sum up, life satisfaction plays a mediating role between multidimensional energy poverty and depression among older adults.

This study has the following limitations. First, this paper analyzed the static relationship between multidimensional energy poverty and the depression level of older adults using cross-sectional data without considering how this association changes over time. Second, energy poverty contains many dimensions and indicators. Second, this paper only synthesized 10 indicators that reflect older adults' energy poverty status to construct a multidimensional poverty index, which may lead to a certain degree of measurement error. Third, multidimensional energy poverty may impact the depression level of older adults through a number of mechanisms, but this paper only considered life satisfaction as a mediator variable.

Conclusions

The main findings of this study are as follows: ① Multidimensional energy poverty has aggravated depression among older adults, and the effect is greater for older adults with higher depression levels. Older adults with deeper multidimensional energy poverty perceive more stress or anxiety, which aggravates their depression. ② Multidimensional energy poverty has a greater effect on depression among older adults in the western region. The lower level of economic development and relatively backward energy infrastructure in the western region contribute to the deeper multidimensional energy poverty among older adults. ③ The effect of multidimensional energy poverty on depression among urban older adults is more significant. The wide wealth gaps in urban areas cause relatively large psychological disparities among older adults with higher energy poverty. ④ The effect of multidimensional energy poverty on depression among solitary older adults is more significant. Solitary older adults have deeper multidimensional energy poverty and do not have family members to support them in energy use. ⑤ Multidimensional energy poverty aggravates depression among older adults by reducing their life satisfaction.

Based on the above findings, this paper puts forward the following suggestions: ① Investment in energy infrastructure should be increased to ensure that all older adults have access to affordable, reliable, sustainable and modern energy. ② Promote the strategy of coordinated regional development, increase support for the western and other backward regions, make up for shortcomings in energy infrastructure development, and narrow regional disparities. ③ Improve the accessibility of energy services and promote the equalization of energy services in both urban and rural areas. In addition, greater emphasis should be placed on improving the equity of energy accessibility in urban areas. ④ Communities (villages) should increase their attention and livelihood support for older adults living alone, help them reduce multidimensional energy poverty, and guide them to use various energy-related appliances and devices. ⑤ Energy price concessions or quantity concessions should be implemented for older adults to alleviate their energy poverty and thus improve their life quality.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: China Health and Retirement Longitudinal Study (CHARLS), http://charls.pku.edu.cn/en.

Ethics statement

The studies involving human participants were reviewed and approved by Ethical Review Committee of Peking University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

JH and WZ conceived the idea. WZ drafted the manuscript. JH, WZ, and YJ participated in the discussion and put forward valuable opinions. YJ revised and polished this article. All authors have contributed to the article and agree to submit this version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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A study on digital inclusion of Chinese rural older adults from a life course perspective

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Digital inclusion is viewed as a crucial strategy for promoting social inclusion and addressing issues related to aging. This study focuses on the digital inclusion practices of rural senior citizens and introduces a life course research perspective to move the study of influencing factors from the proximal to the distal end. The motivations, trajectories, and barriers to digital inclusion among rural elderly groups are presented through participant observation and semi-structured interviews with 34 elderly people in a village in northern China. It was discovered that digital inclusion or exclusion is the cumulative result of life events, social roles, and personal agency in the life course, while it is difficult for the elderly to break away from traditional culture and social relations in rural areas in the digital age. The digital practice is not only an inner adjustment in the process of life stage transition for rural seniors but also an individual pursuit of active aging.

KEYWORDS

smartphone, digital inclusion, digital divide, rural elderly, life course

Introduction

China has 264 million people over the age of 60 by the end of 2020, representing 18.7% of the total population (1). As the population continues to age, policy development and academic research have focused on the issues facing older adults. Among these, the social exclusion and inclusion of the elderly have been major social concerns. With the advancement of information and communication technology, older people face social exclusion in the information age (2). As a result, the concept of digital inclusion is created, emphasizing that "all people should be integrated into the digital trend for personal and social success" (3). The gradual digitization of public services such as daily consumption, medical care, and pensions, as well as daily expenses, makes it imperative for the elderly to adopt new technologies. Some theories, such as post-metaphorical culture, the digital divide, and cultural feedback, as well as specific practices, such as new media workshops and digital back-feeding, have been utilized to assist older individuals in mastering information and communication technology (ICT) and promoting their re-socialization.

With the help of the Digital Village Strategy, the Internet penetration rate in China's rural areas has skyrocketed to 55.9% (1). Based on the author's empirical observation, rural seniors face greater challenges in digital practice than urban seniors due to

disparities in economic status, literacy level, social relationships, and life background. However, we know very little about the plight of this more vulnerable group facing changes in information technology. What motivates rural seniors to engage in digital activities? What difficulties and obstacles do they encounter during digital practice? While the majority of recent studies point to age and other objective factors as barriers to digital inclusion, the subjective experience of older people should also be considered. The problem of digital inclusion was not created overnight, and its cumulative nature is emphasized. In light of this, this paper employs a life course perspective to investigate the digital practices of rural seniors and analyzes the key findings.

Literature review

From social inclusion to digital inclusion

As the majority of countries and regions gradually enter an aging society, researchers have become aware of several issues that may arise in the survival of the elderly population. Among these issues, the identity change and role adjustment of the elderly group after retirement have garnered considerable attention. In sociology and gerontology, there are two opposing viewpoints on the question of whether or not older people should be socially active. Among them, disengagement theory, also known as social withdrawal theory, proposes that older adults should withdraw from society and return to a peaceful later life as the decline of ability and role loss, whereas activity theory proposes that older adults should actively participate in society to alleviate the emotional depression resulting from the disruption of social roles (4). Fryer (5) coined the term "digital refugees" to refer to older individuals who have subjectively fled or been objectively excluded from the digital world.

Similar to the above-described activity theory, research in the field of communication emphasizes the significance of communication practices in successful aging. Social exclusion, which occurs when individuals or groups are completely or partially excluded from social participation (6), is still unavoidable due to the limitations of the technological environment, social capital, and individual agency. This perspective defines social inclusion as the active promotion of participation opportunities at all levels (7). At the level of the individual, social inclusion is a better adaptation to society and longevity. And for the government, social inclusion is a crucial strategy for addressing the aging population issue.

With a deeper understanding of older adults, some academics have concluded that the term "digital vulnerable group" is a more accurate descriptor, revealing the hope and potential within this demographic (8). In the dual context of a mediated and aging society, digital inclusion can contribute to achieving active aging, maintaining psychological health (9), improving quality of life (10), managing loneliness among older adults (11), enhancing subjective well-being (12). In contrast, older age groups' disconnected behavior and the digital generation gap can have negative consequences. Some researchers are aware that the digital generation gap in Chinese society is exacerbating the digital intergenerational conflict and sparking new conflicts within families and among social groups (13).

The majority of researchers refer to internet use as active aging (14), and argue that the digital inclusion of older people has positive contemporary significance. Active Aging is an updated version of the concept of healthy aging introduced by the World Health Organization in 2002, which aims to improve the quality of life of older people and provide them with the best opportunities for health, participation, and security. Internet use aims to promote the participation and inclusion of older people in society, which is consistent with the objectives of active aging. In response, the Chinese government has elevated "Digital China" to a major strategic decision, with a focus on the construction of smart cities and digital villages to accommodate the social reality that digital technology is being integrated into all areas.

Not only is the learning and use of ICT by older people driven by the objective environment, but it is also viewed as an inherent need for social inclusion and environmental adaptation (15). Although a few scholars emphasize anti-connectivity (16) and advocate for the right to disconnect (17), the majority of studies still uphold a technology-for-good stance, defining lack of internet access or low internet use as a problem to be solved (18). Under this premise, researchers have investigated how to assist older individuals in adopting new information and communication technologies.

Influence factors for the elderly to use smartphones

The elderly lag behind younger generations in terms of ICT adoption and use (19), and they participate in fewer online activities (20). According to social cognitive theory, older adults' digital inclusion is the result of the interaction between the individual, behavior, and environment (21). Enjoyment to use, expressiveness (22), Self-actualization (23), and connectedness to others (24) among older people themselves facilitate digital practices. Simultaneously, several factors impede the use of smartphones by older people, including both objective and subjective factors. For instance, Lin et al. (25) noted that the phone's Hardware and Software interface caused difficulties in use. According to He and Zhang (26), the digital divide among older adults is caused by a lack of age-appropriate information technology, the neglect of older audiences in online content, the limitations of older adults' characteristics, etc. Additionally,

TABLE 1 Basic information of participants.

Age group	No	Age	Whether to use smartphones	Usage period (year)	Number of App usage
Younger-old group	FM2	65	Yes	1	1
	FM5	66	yes	2	4
	M10	66	yes	1	2
	FM12	60	yes	8	12
	M13	65	yes	2	2
	FM14	63	yes	1	1
	M17	65	yes	0.5	1
	M18	66	no	/	/
	M19	61	yes	5	6
	M22	66	yes	3	3
	M23	66	yes	3.5	4
	M24	60	yes	0.5	2
	FM31	62	yes	5	7
	FM34	63	yes	4.5	5
Middle-old group	FM1	72	yes	1	2
	FM3	73	no	/	/
	FM7	73	yes	1.5	1
	M8	71	yes	6	3
	M9	71	yes	6.5	7
	FM11	69	yes	2	2
	M15	73	yes	3.5	4
	M16	72	yes	1	1
	FM21	72	yes	2	1
	M25	67	yes	1.5	1
	FM26	67	yes	2	2
	FM27	72	yes	1	1
	M28	68	yes	3	4
	M30	68	yes	2	2
	FM33	67	yes	3	2
Senior-old group	FM6	75	yes	1	2
	M20	74	no	/	/
	M29	76	yes	0.5	1
	FM4	76	no	/	/
	FM32	80	No	/	/

FM represents female, M represents male.

subjective factors, such as reluctance to adopt digital tools (27), lack of confidence (28), and lack of knowledge (29) are also playing a hindering role.

The mainstream literature depicts older individuals as non-users, hostile to technology, and a homogenous population (30). Several qualitative investigations enhance our understanding of the inner lives of older persons. Twenty one digital elders were questioned by (31) about how ICTs influenced their routines and habits. The researchers found that digital seniors have the freedom to determine when and for what purposes ICT use is suitable. Zhou (8) discovered in his study of the adoption of WeChat among older persons that poor demand, limited energy, and technical panic contributed to the non-use or limited usage of new media. This study stressed that subjective needs and perceptions were more influential than objective criteria in the adoption of new media by older persons. In addition to institutional and structural factors, demographic variables and individual psychological and cognitive levels contribute to the digital divide (32). This research also implies that age is not the most critical factor determining digital inclusion in older age groups.

According to Mead (33), our information society is a post-metaphorical civilization in which newer generations teach older generations. Zhou (34) focuses on the pervasive phenomena of cultural feedback in changing societies, and her study demonstrates that cultural feedback has a direct relationship with electronic media. With the intergenerational amplification of the digital gap, Zhou (35) observed that a cultural feedback revolution is occurring within families. Studies on the forms, qualities, challenges, and uses of digital feedback have increasingly proliferated since then (36, 37). Social support is also required for the digitalization of the elderly outside of the home environment. Age-appropriate modifications of digital devices, such as larger fonts, memory-friendly interfaces, and learning interfaces, can accommodate the declining physical functions of older adults (38), and media literacy education can concentrate on developing their engagement and interaction skills (39).

Foremost, Literature on the digital divide indicates that older persons continue to lag in Internet access, digital skills, and digital literacy. These studies shed light on the challenges older persons encounter while using digital technology, but they disregard the impact of interrelated parts of the life course. In addition, the internal heterogeneity and diversity of older persons have been simplified, whilst their subjective experiences and perceptions as users of modern technology are frequently disregarded. In addition, the majority of past research has taken a quantitative approach, which might make it difficult to see the forest for the trees. Therefore, researchers must provide older persons, who are the topic of digital exclusion, with the opportunity to be heard (40). Despite recent qualitative research analyzing the new media use behaviors of older persons in their daily lives (41), which reveals some colorful stories behind the quantitative data, the longer-term and more complicated individual experiences have not yet gotten adequate attention.

Based on this, the study focuses on the front-end variables of digital inclusion behavior, which analyze the effect of the entire life course on the use of digital devices among the elderly and considers the following questions.

RQ1: What are the distinguishing aspects of smartphone use among rural seniors with distinct life courses?

TABLE 2 Different levels of digital inclusion among rural elderly.

Inclusion level	No	Description
Lower	FM1, FM2, FM7, FM14, M17, M24, M25, FM27, M29, M30	Only can make phone calls, send voice messages *via* WeChat, and browse short videos on Kuaishou.
Low	FM6, M8, M10, FM11, M13, M16, FM21, M22, FM26	Can view videos in Kuaishou, explore WeChat Moments, and take pictures with their phone.
Average	M15, M19, M23, M28, FM33	Can pay with WeChat, find the videos you need on Kuaishou, and use videos to learn how to cook, clean, and do other things.
High	FM5, M9, FM31, FM34	Can shop online, share content on WeChat Moments, upload works to short video sites, and use a few other entertainment apps.
Higher	FM12	Can use their smartphone to interact, make friends, watch videos, buy things, and pay their bills and pensions.

FM represents female, M represents male.

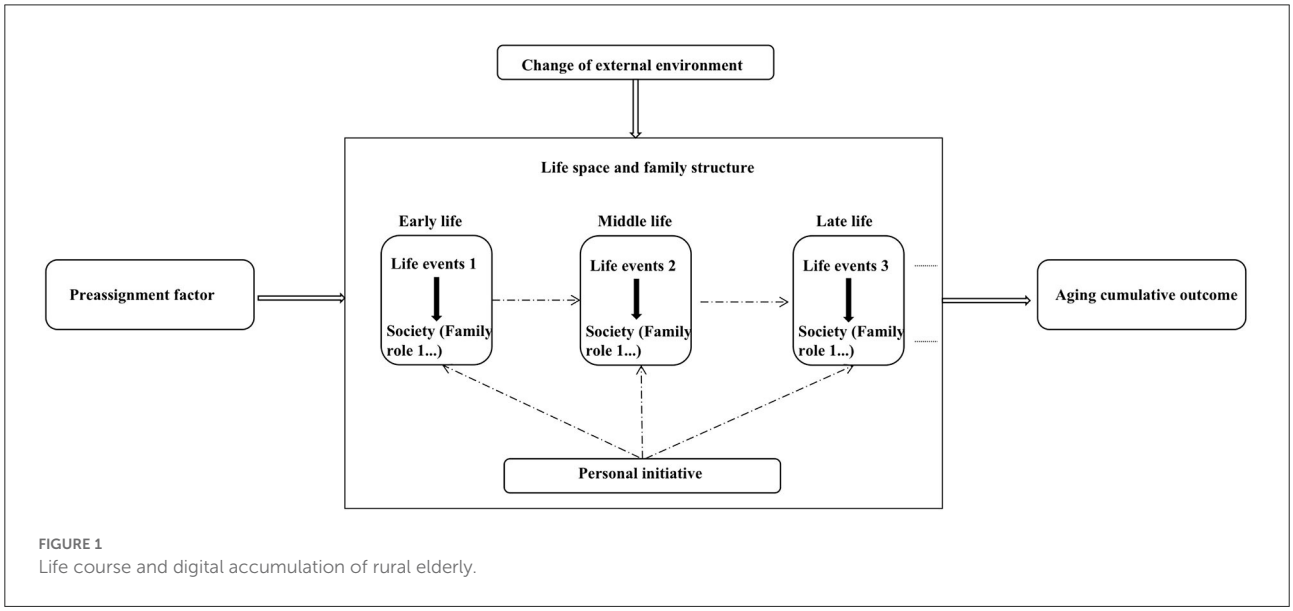

FIGURE 1
Life course and digital accumulation of rural elderly.

RQ2: What elements in the life courses of an individual inhibit the process of digital inclusion, and what elements promote it?

Research design

Life course: Introduction of a research perspective

In actuality, smartphone adoption is not binary (42), meaning that it does not refer to the option to use or not use. It is a cyclical process in which potential adopters continually seek out new knowledge about a technology, are affected by their peers and family, and adapt their behavior as their life circumstances change (43). Integration into the digital society is a cumulative result of subjective and objective factors, and this paper employs a life course research perspective to investigate the factors impacting smartphone use among rural seniors.

The notion of life Course is retaken from Elder (44), to whom studying the life tracks, involves analyzing the development of human life in its temporal extension and its sociohistorical contexts. The life course of an individual can be found in a set of specific trajectories corresponding to different fields or areas in which the person develops. Such paths may be more or less related, they are presented in a relatively orderly sequence, reflecting positions, transitions, or events experienced by the subject (45). Accumulation and turning points are two fundamental concepts in life course research. Accumulation refers to the positive and negative events, habits, and personalities that result from several early life stages. A turning point is a momentous occurrence that alters or redirects the course of a person's life (46).

As a theoretical and methodological paradigm, it ties age to cumulative strengths or weaknesses, focuses on assessing events and roles in the life course, and analyses a decision, action, or outcome within the context of a person's entire life span. It is frequently used to investigate the interplay between individual experiences and social institutions (47), to explain the diverse outcomes of individual development (48), and to show the elements that influence individual decisions and intentions (49).

In this particular study, social inclusion is a continuous process that unfolds gradually over the life course, and digital inclusion cannot be considered in isolation from the life course. The introduction of the life course perspective has to some extent broadened this type of research, so that the study of digital inclusion and social inclusion of older people is not confined to the description of the old age stage, but also encompasses their entire life history.

People exist initially in their families and then in societies, which determine their normative roles and expected life patterns and provide a framework for comprehending individual behavior and psychology. This study broadly divides the life course of rural elders into three stages: early life, middle life, and late life, to examine the major life events and corresponding social and family roles in each stage and to analyze the cumulative outcomes of the older stages in the context of individual-environment interactions.

This paper relates to the life course cumulative diagram suggested by Hu (48) and derives the simplified diagram below based on the actual findings of this investigation. Specifically, see (Figure 1). The significance of introducing the life course perspective is threefold: first, to provide a feasible way to understand the behavior, and psychology of the rural elderly; second, to account for the diversity of individuals within the elderly group; and third, to answer the complex reasons for the digital inclusion problem from the perspective of users, and to provide a basis for decision making to advance the digital China strategy.

Research object and method

The village is situated on a plain 36 km southeast of Tangshan City, Hebei Province. The study site was chosen using a convenience sample based on dialect similarity, geographic proximity, and demographic variables. The village has a total population of more than 800, and the villagers rely on farming as their main source of income. Due to the out-migration of the youthful people and their parents, the phenomena of aging is noticeable in the hamlet, with a large number of elderly and empty-nesters left behind. Due to their low barrier to entry and inexpensive cost, smartphones have become a common Internet access tool for senior citizens in the region. Consequently, this study focuses on smartphone usage and investigates the digital inclusion of rural seniors.

After visiting the area, the researcher recruited study volunteers through radio advertisements and street questions, then grew the study population through snowball sampling. As shown in Table 1, The age distribution of study participants ranged from 60 to 80 years. To investigate the differences within the group and to combine the actual age distribution of the study participants, we referred to the 60 to 66 as the younger-old group, which consisted of 14 individuals, and the 67–73 as the middle-old group, which consisted of 15 individuals, and the 74–80 as the senior-old group, which consisted of 5 individuals.

Participant observation and semi-structured interviews are the primary research methodologies utilized in this paper. From November 2020 to May 2021, the author observed the smartphone use of the study participants daily to understand their claims, habits, and preferences of using cell phones, including the contents received and disseminated through cell phones, to gain intuitive experiences and understanding, and recorded them. We also employed semi-structured interviews as a data collection technique. In July 2022, we conducted more interviews with four older individuals. At this stage, there were 34 participants, 17 of which were female and 17 of which were male. The retrospective life history study was used to conduct multiple interviews with each elderly individual, and due to the long-time gap, we cross-checked their recollections to present the past life history events, subjective feelings and perceptions, and the social background conditions of the time as objectively as possible.

Findings

Smartphone use among rural elderly

People in rural areas are not reliant on the Internet for their employment and daily lives, hence their adoption of the Internet is voluntary and unnecessary. The access order is mostly determined by family structure and economic cost. The village's brief history of the Internet and related equipment access reveals a generational progression of young children, middle-aged parents, and elderly grandparents. Since 2005, rural households have been gradually connected to broadband networks, with the majority of Internet access devices being home PCs and the majority of users being junior and senior high school students. After the development of smartphones, young children were still the first user in the family. After 2012, smartphone ownership began to increase among the middle-aged but had not yet reached the elderly. Only when economic expenses continue to decline will senior citizens have access to the Internet.

The elderly's access to devices is highly dependent on family support. First, the majority of the cell phones used by the elderly are low-end machines costing <1,000 yuan, which are primarily the old cell phones replaced by their children. In addition, most

seniors use home broadband, whose operational costs are paid for on a flat-rate basis by their children. And few old people decide to access smartphones on their own. Most are the result of a certain opportunity, coinciding with the replacement of cell phones by young people and operators' promotion in rural areas. And their children have a significant voice in this decision.

Adoption within the senior population reveals some age distinctions. There are five non-smartphone users among the 34 older adults examined in this study, four of whom belong to the senior-old group. Younger people use cell phones for a longer period than middle-olds and senior-olds. However, there is no necessary correlation between the level of usage and access duration. Despite having long access times, some elderly use only a limited number of cell phone features. The levels of literacy, aptitude for learning, and economic status eventually affect how they use Smartphones.

When people reveal their digital practices, it is comparable to unlocking Pandora's Box. Almost to the point of addiction, 17 out of the 29 seniors use smartphones for more than 10 h every day. Because they have more free time, older citizens use their phones more frequently than younger seniors who are still taking care of their grandchildren, or working in the fields.

This study first presents an overview of the actual smartphone usage of the rural elderly and then categorizes them into five categories based on the variation in their usage level to gain a clear picture of their digital inclusion. As (Table 2) shows, The two applications with the highest adoption rates were Kuaishou and WeChat. Of the respondents, 26 used Kuaishou, and 18 used WeChat. It's vital to remember that the levels of digital inclusion vary by age group, with younger and middle-aged groups having higher levels and senior-aged groups having lower levels. The following table displays the specifics.

In general, smartphone use among senior people in rural areas is characterized by slow device access, prolonged but shallow use, and a lack of media literacy. They have more psychological and practical impediments while engaging in digital practices. The elements affecting the older group's digital inclusion are continuous and cumulative, making it simple to find in the interviews that they may be linked to an earlier period in their life history. While some elders are fine with the status quo of superficial use, others are highly active users and explorers of smartphones. As will be covered in more detail later, this intra-group variance in use is partially caused by their upbringing and particular experiences.

Cumulative disadvantage and digital exclusion in the life course of rural elderly

Digital exclusion among older adults is a result of cumulative disadvantage over the life course. The cumulative disadvantage model created by Sampson and Laub (50) showed that breaking the law when you're young increases your chances of becoming delinquent later in life. Cumulative has two meanings in the context of this paper: first, it happens sequentially, affecting people's levels of digital inclusion in later life; and second, there is a chain reaction among them that, taken as a whole, has an effect on the result of digital inclusion.

Early in life: Education results initially and lasts a lifetime

The starting point of a person's life course is made up of the family's economic situation, parents' conceptual knowledge, and other variables, which first obviously affect their literacy level and then have an ongoing impact on them throughout their lives. Most residents of the village left school too soon to support their families. The elderly frequently described themselves as illiterate during the interviews.

M15 thought back to his adolescent years when he had to support his grandparents and look for his younger siblings.

> "*My father was waiting for me to join the production team so that I could earn work credits because my family was struggling and he wasn't feeling well. I was unaware of the future of education at the time, and only a small percentage of people could pass the exam.*" (M15)

M15 is 73 years old. He was a teenager during the foundation of New China when the country's economy was still comparatively backward and significantly worse in the rural. Many older individuals at his age had similar experiences. As the nation's economy develops, younger-older generations have less financial stress and require less family work while spending a disproportionately longer amount of time in school. However, many rural parents still force their children to leave school at home before completing junior high school because they have a poor understanding of education.

Women have considerably fewer educational possibilities in rural societies where patriarchy is pervasive.

> *"The family had a large number of kids at the time, and they were in poverty. I was told as a young girl that studying was unnecessary, so I took care of my sister at home and married young.*" (FM27)

When there is just one smartphone in the home and males are frequently the ones choosing what content to watch, gender discipline and inequity persist into old age.

In addition to restricting the accumulation of wealth and social contact in daily life, a low level of knowledge also prevents later-life resource acquisition and the growth of social networks. Even though older people can access smartphones, they frequently don't know how to utilize them or do so poorly. The digital gap is considered as a natural existence since older

people choose to seek young people to perform digital services for them rather than learning how to do so from them.

Access to and use of smartphones are influenced by economic capital and cultural capital. In contrast to M15, M9 has six brothers and a relatively abundant labor force in his family, and he is the youngest, therefore he is not responsible for supporting his family. After graduating from high school, he was assigned to an elementary school, where he taught for more than 30 years. Now that he is retired with a monthly income of almost 4,000 yuan, he purchased a smartphone for himself and his wife earlier. M9 will utilize more of the phone's features than other senior individuals.

Education is a crucial means of class advancement. In the short term, committing oneself to labor output improves the family's economic situation, but in the long run, it pushes them into the resource-poor middle and later life. When it comes to education, the elderly regret,

> *"If I had attended school and had a job, I would currently have a pension and could have purchased a cell phone if I so desired. It is inappropriate to request money from children."* (FM1).

Mid-life: The accumulation of role consciousness in rural life restricts personal initiative

In the 1970s and 1980s, along with the reform and opening up process, some daring young people were the first to leave the economically backward countryside and establish their roots in the cities. However, the majority of rural elderly have been in a relatively closed geographical and social environment for a long time, and their social networks are limited to relatives, and acquaintances in the same and neighboring villages. Some older individuals believe that residing in rural areas is the source of backwardness.

> *"My city-dwelling cousin had a smartphone approximately ten years ago. I've just been using cell phones for a couple of years, and I'm not even proficient."* (FM2)

The divide between urban and rural areas is a watershed for digital access. In urban areas, where the Internet was initially developed as an office tool, some people were compelled to become internet immigrants earlier, and the technology then gradually permeated people's daily lives. Farmers engage in manual labor and lack external motivation for digital inclusion. Among interpersonal interactions, villagers are accustomed to group chitchat, square dancing, card games, and other pastimes, forming an offline social way and less expanding social network relationships. Even after accessing the Internet, the number of their WeChat contacts is small, consisting primarily of family members, relatives, residents of the same village, and other acquaintances. In addition, due to their limited economic resources, rural families have developed media consumption habits that prioritize their children, so the brief history of Internet access reveals a sequence of children, parents, and older grandparents. Therefore, the elderly are typically the last members of the family to utilize smartphones.

As an external social structural force, traditional rural life also produces more closed dispositional tendencies, and personal initiative is constrained by the invisible constraints of identity and role. A close-knit society of acquaintances characterizes rural life, where people have a stronger sense of social roles and are easily influenced by the opinions of others.

> *"Dressing flamboyantly is imprudent, eating meat every day is a luxury, and we must be especially mindful of our behavior as daughters-in-law."* (FM1)

They will assume stereotypical roles in accordance with society's general perception. A role is a set of behavioral patterns that people in a particular social position must conform to in order to meet social expectations (51), and it is closely associated with the identity (52). Their professional identity as farmers requires timely field production. In family life, based on their gender identity, women are also expected to perform laborious housework, which affects their ability to accumulate capital in every way. As they grow older, the marginalization of status in the family structure causes a structural exclusion of smartphones.

In conclusion, social structure and personal initiative are intertwined, and the digital inclusion status of rural elders reflects both the limitations of personal initiative due to the role consciousness accumulated in traditional rural life and the behavioral choices made by individuals in the rural environment.

Later life: The behavioral discipline of the Familism concept and the absence of intergenerational feedback

Typically, retirement, an increase in leisure time, and the ability to explore new areas of life characterize the third age (53). These characteristics do not, however, apply to the elderly rural population in this study. In contrast, fathers continue to prioritize family interests over personal ones (54), shedding light on the life paths of rural elders. The elderly want to contribute more to the economic development of their families, but because they have no retirement income, many of them continue to perform manual labor even after reaching retirement age. This phenomenon is known as "intergenerational exploitation of the paternal generation by the offspring" (55). And in this regard, rural seniors have a delayed later life.

M26 is a mason, a less labor-intensive occupation that he can still perform at age 67:

> *"I earn 120 yuan per day, allowing me to support my son's family of four. When I can no longer do it, my grandchildren will have also grown up and I will be idle to play cards and smartphones."* (M26)

> FM34 further stated, *"I care for my grandchildren and cook for a large family during the day, so I simply do not have time to play on the phone. I only have some free time after 8 p.m to brush kuaishou, WeChat Moments, and Pingduoduo(a discount shopping application)."* (FM34)

At age 70, the rural elderly's life tasks are largely accomplished, and they retire from earning a living and caring for their offspring to enter what Laslett (56) refers to as the "third life" stage, in which they are free to pursue leisure activities without having to worry about household chores and endless caregiving responsibilities. After that, playing mahjong, visiting doors, and using their smartphones become daily activities, and the elderly, who rely on their children for support, make as few financial demands as possible.

In the observed rural families, the process of digital inclusion was not smooth, and feedback between generations was severely lacking. In addition to the objective factor of children leaving home to work or study and not living together for an extended period of time, there are also subjective causes. As the authority established by the traditional power of generation and gender in blood relatives is eroded, older people, particularly men, are inevitably lost, and grandparents do not wish to trouble or burden their children or grandchildren.

> *"Who would like to instruct an elderly woman like myself? "* (FM2) *"I have not made many requests of the children, and they are too busy to instruct me. Moreover, because I am a slow learner, they dislike teaching me."* (M24)

In addition, the young group has an authoritative role in the digital practice process of the elderly group due to their technological advantages. The young continue to discipline the elderly with words of caution, causing them to view smartphones as a dangerous "black hole" and to refrain from exploring new mobile phone functions.

Current research on digital inclusion focuses on the physiological learning ability of older adults while ignoring their psychological openness to new experiences. Older people will always be mindful of their words and deeds because they have been disciplined by their culture. Even when they have an Internet connection. According to them, the elderly should maintain a certain distance from the Internet, and overactivity is an "anomie" behavior that not only leads to gossip about themselves but also harms their children's reputations.

> *"There is an old lady in the village who sings and dances on TikTok, and people laugh at her behind her back."* (FM1)

Traditional experience will create psychological inertia, resulting in the elderly's digital inclusion being encumbered. The Internet has not entirely broadened the perspectives of the elderly. The majority of elderly individuals view mobile phones as a window to observe society, but not as a means to participate in society.

There are also elderly individuals who have always maintained traditional practices, resisted digital inclusion, and developed a stable system of self-interpretation.

> "*The absence of cell phone use has no effect on my life*" (FM4). "*I don't want to learn, it's pointless to learn, and the phone has nothing of value*" (FM3).

Smartphones and the elderly are mutually exclusive, to put it another way. The elderly have not yet broken away from old traditions when confronted with new experiences, forming a social-self, technology-psychological cycle.

When older individuals have Internet access, their decision-making is divided into distinct levels of inclusion in terms of outcomes. The first type, which can be termed the "exclusion type," consists of senior-aged individuals who have a lower reading level and are more constrained by traditional culture; the second type, which can be termed the "marginal type," consists of smartphone users who are content with superficial use. The third type, known as the "expectant type," is eager to engage in additional tasks in order to continuously improve themselves. They are predominantly young-old, have a relatively high reading level, are exposed to more novel experiences, and are more tolerant. In other words, there are age differences among rural elderly smartphone users. The older a person is, the lower their early education level, the less eager they are to learn, and the more likely they are to cling to old habits. In addition to the general cumulative disadvantage, there are factors that stimulate their motivation to access and utilize smartphones, resulting in disparities in the degree of digital inclusion.

Promotion factors and digital inclusion in the life course of rural elderly

Personality, role adaptation, and unique experiences stimulate personal initiative to varying degrees and, in conjunction with social-technical conditions, contribute to

the digital inclusion of the elderly. However, it should be noted that individual agency refers not only to the intentions people have when they act but also to their ability to act in the first place (57). The agency has played a positive role in encouraging the elderly to use digital devices, but it also reveals individual differences in usage. After gaining access to devices, it is still difficult for the elderly to bridge the digital divide due to their cumulative economic and cultural disadvantages.

Emotional requirements caused by role transformation

Individual behaviors are not entirely autonomous but are embedded in particular social relationships. In close-knit social networks, the life paths of individuals interact. The analysis of individual behaviors should also consider the people with whom they interact. There are numerous elderly and empty-nesters living in rural areas. After being liberated from their laborious family livelihood and farm work, they felt lost due to life changes and the loss of roles. Some seniors began using smartphones out of boredom and to kill time.

> *"Because my children are not at home, they no longer need me, which makes me feel lonely. however, when I play with my phone, time seems to pass quickly, and my loneliness is diminished."* (FM6) *"After my wife passed away, there is no one talk to, sometimes I can't sleep, I keep playing with my mobile phone, otherwise what can I do."* (FM7)

The two primary functions of mobile phones, according to Morley (58), are overcoming geographical distance barriers and maintaining social ties. For the elderly, mobile phones offer a new space for communication and emotional compensation, mitigating their sense of age-related alienation and marginalization. The use of smartphones also reflects the adaptation and imagination of elderly people to aging and death,

> *"At our age, the more we have to cherish, if we don't contact them now, maybe one day they will die."* (M16) *"The older I get the more I like to recall, I always want to leave some traces for my children to remember later."* (M9)

Although many old customs and traditions persist, the desire of the elderly to express themselves through mobile phones is still evident.

In addition, compared to their male counterparts, female seniors are more eager to satisfy emotional needs *via* smartphones. According to the outcomes of digital inclusion, although women have lower levels of literacy, their enthusiasm for playing mobile phone games is significantly greater than that of older men. Zhou's study on WeChat adoption found similar results (8).

The preservation of personality with age

Personality has a significant impact on older adults' digital inclusion. People who are socially active in their youth will be more active in their later years, whereas introverted people will be less active in their later years, which is a form of cumulative continuity, according to continuity theory. FM12 is a sociable individual who embraces new digital technologies. She spends more than 10 hours per day online, not only perusing online content but also documenting her life on WeChat moments and Kuaishou. The smartphone affords FM12 the opportunity to interact with the outside world, establish a sense of modernity, and achieve psychological inclusion. As the husband of FM12, M19 complains about his wife's conduct,

> "*Internet content is accessible to the general public. You should not expose yourself too much. If you live a poor life, you will be ridiculed, while if you live a good life, you will be envious of others.*" (M19)

Although M19 and his wife worked in a large city, he is so introverted that he uses his mobile phone far less than his wife. When FM12 is on a video call with family or children, he simply observes from the sidelines.

While actual society restricts the behavior of the elderly, cyberspace provides a platform for self-expression. Some individuals who are not accustomed to expressing their emotions in person are eager to do so on the Internet. FM5 is one such example.

> *"I go out infrequently and do not play mahjong as others do. I enjoy capturing videos of my two cats and uploading them to Kuaishou. I also post photographs of myself with added effects and music. It is a significant record of life."* (FM5)

From the short videos uploaded by the elderly, it is clear that they are attempting to make themselves appear younger than they actually are. It is not only a reflection of one's life but also a reflection of one's self-worth. According to them, it is worthwhile to record and share these videos, and the likes and comments they receive give them a sense of self.

> *"I uploaded my class group photo from my school days on Kuaishou, and I expected others to give me likes and comments, and it was fun.*" (M15, 73 years old)

Although there is an insurmountable gap between the Internet use performance of the elderly and that of the young, the self-presentation of the elderly in the media is a subjective effort to overcome age and role constraints.

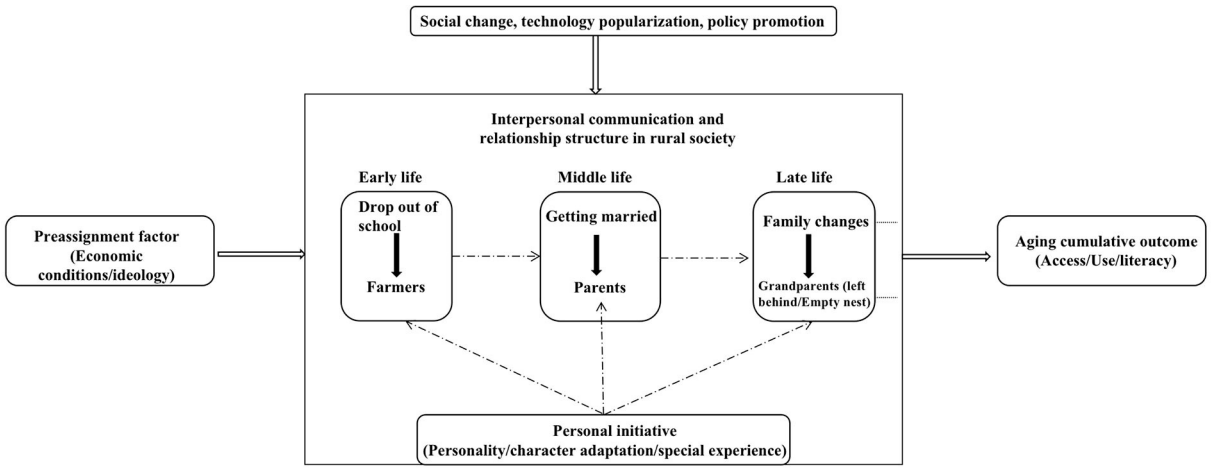

FIGURE 2
Association between life course and digital inclusion outcomes of rural elderly.

Unique life events encourage smartphone use

The impact of Turning point on digital inclusion has two sides. For instance, there was a pivotal moment in the lives of the couple FM12 and M19. In the 1980s and 1990s, rapid urbanization occurred in China as a result of reform and opening up. They felt uneasy about the village's poverty and backwardness, so they moved to Beijing and opened a pork shop in a supermarket. In 2007, they returned to their hometown because their children were ineligible to take the college entrance exam in Beijing. After living in a large city, FM12 is extremely open to new experiences. She is adept at utilizing mobile phone features such as instant messaging, moments, watching the news, shopping, and reading novels. According to her own words, she has a strong sense of social progression. Around the age of 40, M8 began a successful career in the animal feed retail industry. The business was thriving. The 2008 melamine incident altered his life trajectory and influenced the evolution of the village's dairy farming methods. For centralized management, the original free-range dairy cows were brought to the cattle farm. As a result, the cattle farm entered into a partnership with a large feed supplier and retailer, and his business suddenly declined. At the age of 60, following a cerebral thrombosis, he became a complete slacker. The enormous psychological gap made him reluctant to leave the house and compelled him to isolate himself. The mobile phone has become an additional means of communication with society.

> *"I use my mobile phone to listen to novels and read a wide range of Kuaishou videos. When I do not know how to operate it, my wife will help me."* (M8)

Certain events can serve as a turning point in an individual's life course. People can make decisions of their own accord the majority of the time, but they are sometimes compelled to act. In a mediated society, it is a practical necessity for some elderly individuals who wish to disconnect to learn how to use digital devices. During the COVID-19 pandemic, numerous senior citizens were required to use smartphones.

> *"My grandson was at home during this time for online classes, and it was my responsibility to take pictures of his completed homework assignments, upload them, and sign in on time using my smartphone and tablet. I was the only adult in the home, so I had to learn how to use my phone."* (FM14)

Similar circumstances convince the elderly who had no intention of adopting the Internet to do so. In some rural households, smartphones are also used as playthings by children. The elderly have learned to show their grandchildren cartoons and short videos on their mobile phones, which has relieved them of the burden of creating games and telling stories.

Personal initiative and life trajectory are intertwined, which encourages smartphone use in later life. The affordances of smartphones provide a remedy for anxiety, and the elderly are reestablishing new ways of life and meaning. As an extension of the body, smartphones create a new spiritual space for the elderly from the standpoints of utility and satisfaction. Some elderly people have gradually developed a positive aging mindset through exposure to the world and interaction with society. The positive experience of media use results in continued use, which assists the elderly in completing the transformation of their social and family roles.

Conclusion and discussion

The older groups of interest in this study have essentially consistent life paths, and as a result, their digital behaviors share traits like late access, skimpy use, and low literacy. Older rural residents who have worked in agriculture for a long period participate in a small number of social activities. The Internet and contemporary media were not a part of their previous lives. Once they reach senior status, they can just use smartphones. In the tension of life stage transition, factors such as their own personality, life encounters, and spiritual needs stimulate personal initiative to varying degrees. As a result, the willingness and degree of digital inclusion among the elderly vary by exclusion type, marginal type, and expectant type.

The digital use of rural seniors is not only influenced by the external social environment but also constrained by their subjective life experiences. The life course provides a framework for comprehending individual behavior and psychology by defining the normative roles and expected life patterns of the individual. Digital inclusion or exclusion is the choice of the elderly, which is determined by their experience, concept, mentality, and understanding of life stage, demonstrating a process of accumulation and differentiation. Under the social and cultural norms of rural areas, which are constrained by factors such as knowledge level, economic ability, social interaction, and family structure, the elderly have fallen behind in the use of smartphones, and individual initiative has also promoted their digital practice. The formation procedure is depicted in Figure 2.

The specific elaboration is as follows.

First, ascribed factors (such as economic status, ideology, etc.) brought by the family of origin act on educational opportunities, and then affect the accumulation of other forms of social capital, all of which have an impact on the life course outcome of an individual.

Second, the role consciousness generated by interpersonal communication and relationship structure in rural society affects the elderly's willingness and the degree to accept new things, such as using smartphones.

Thirdly, the accumulation and transition in later life (using or not using smartphones, duration, and degree of usage) is a result of the interaction between people and their environment in a particular time and place and reflects clear individual differences.

Moreover, changes in life stages (social roles and identities) and family situations (member separation, family disintegration, etc.) have a significant impact on behavior and psychology in old age, inhibiting or encouraging the release of personal initiative.

Lastly, specific life experiences (higher social mobility, physical and mental shocks, etc.) can influence personal initiative, ultimately, their willingness and level of digital inclusion.

In addition to the technical divide, the cultural divide stands out among the cumulative factors affecting the digital inclusion of the elderly in rural areas. It is difficult for elderly people in rural areas to escape the shackles of traditional culture and social relations, and they are unable to construct and express themselves freely in cyberspace. In addition, the collision between the inherent experience of the elderly and the modern mindset of the digital society has created a cognitive conflict for them, which is the greatest barrier to the elderly's digital inclusion. In other words, for rural seniors, digital inclusion involves not only technology but also culture. In order to strengthen the digital inclusion of the elderly, we must take care of their inner world and prioritize cultural assistance for the rural elderly, in addition to promoting aging-appropriate transformation and skills training.

In conclusion, when considering how to promote the digital inclusion of rural seniors, it is impossible to ignore the long-term influences on their life course. Instead of viewing old age as a decline in life, it should be viewed as a continuous stage of self-development rather than a hierarchical one (59). In addition, it should be noted that the life course of an individual is embedded in a macroscopic social force and social structure, and this paper examines the digital inclusion of the rural elderly by focusing only on the relevant life course factors and rarely on the social process. This is because the social engagement and interaction of the majority of rural elderly are minimal, and there is little correlation between individual life courses and social historical processes and the use of smartphones. This study has limitations due to its reliance on the elderly of a single village as its research subject, and its conclusions only reflect the reality of certain rural locations in northern China, which may differ from economically developed coastal villages in the southeast. Furthermore, this paper is a retrospective of the past based on the present, and the primary source of content is the self-reports of the elderly respondents, which results in an insufficient presentation of their rich and diverse developmental experiences due to their limited expressibility.

Data availability statement

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

Author contributions

HZ: study design, data collection, data analysis, and paper writing. RH: paper writing and manuscript review. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Gastrointestinal problem among Indian adults: Evidence from longitudinal aging study in India 2017–18

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Introduction: Diseases and illnesses of the gastrointestinal system (GIS) have grown in the last decade due to considerable lifestyle changes. People with gastrointestinal (GI) diseases have a high prevalence of depression, stress, anxiety, and impaired central nervous system functioning. Therefore, this study aims to explore the factors associated with the self-reported gastrointestinal problems among the Indian elderly and to explore the relationship between non-communicable diseases (NCDs), such as hypertension, heart diseases, diabetes, and neurological or psychiatric and gastrointestinal disorder.

Methods: This study uses data from the Longitudinal Aging Study in India (LASI), a population-based national survey, conducted during 2017–2018 with a representative sample of 72,250 individuals. Descriptive statistics were used to provide the frequency distribution of sociodemographic and economic profiles of adults. Bivariate analysis was used to understand the percentage distribution of adults suffering from gastrointestinal problems by their background characteristics. Binary logistic regression was used to determine the factors associated with gastrointestinal problems. In the binary logistic regression analysis, a systematic model building procedure was adopted.

Results: The overall prevalence of self-reported gastrointestinal problems was 18%, with significant variations among regions, and it substantially increased with the increasing age of men. Hypertension and neurological problems have significant individual effects on gastrointestinal problems. Prevalence was higher in those who suffered from neurological or psychiatric problems (27%) than in those who suffered from hypertension (22%) and heart disease (23%). Adults from the age group 45–54 (1.11, $p < 0.01$) and 55–64 (1.09, $p < 0.01$) years were significantly more likely to have gastrointestinal problems compared with the <44 years age group. Former and current smokers and adults with the habits of chewing tobacco were significantly more likely to report gastrointestinal problems than their counterparts. Moreover, the increasing economic status significantly and positively increased the likelihood of having self-reported gastrointestinal problems among adults.

Conclusion: Aging-related gastrointestinal problems are physiological or pathological and more prevalent in the elderly population aged 64 years and above. Hence, policies and interventions have to be made age-specific.

Gastrointestinal problems among older adults are acquiring greater importance in clinical practices to plan effective treatment, administration of gastrointestinal drugs, the early screening of gastrointestinal diseases. Given the policy focus through Health and Wellness centers for accessible NCD care, it is important that gastro-intestinal illnesses receive more focus and systemic support.

KEYWORDS

gastrointestinal problems, adults, longitudinal aging study in India-2017–18, India, aging

Introduction

Aging is characterized by a steady loss of physiological integrity, which results in reduced function and an increased risk of mortality. This degradation is a key risk factor for the majority of human illnesses, such as cancer, diabetes, cardiovascular disease, and neurological diseases (1, 2). All functions of the gastrointestinal system (GIS) are affected by aging, such as motility, enzyme and hormone release, digesting, and absorption. In addition, the GIS is involved in the absorption and metabolism of medications, and it is frequently impacted by adverse effects (2). In the absence of organic illness, functional gastrointestinal disorders (FGIDs) are diseases with chronic or recurrent symptoms related to the gastrointestinal (GI) tract that can be diagnosed by standard examinations (3). FGIDs do not lead to an increase in mortality, but they do cause considerable morbidity in the terms of lowering the quality of life and increasing healthcare utilization (4–8).

A number of population-based studies documented that FGIDs were more prevalent among women than men and were associated with lower quality of life and more frequent visits to the doctor (9, 10). A large-scale multinational study based on internet surveys has shown that >40% of people worldwide suffer from gastrointestinal complications, such as diarrhea, constipation, or irritable bowel syndrome (IBS), with a prevalence of 4.7, 11.7, and 4.1%, respectively (9). Increasing age, on the other hand, is linked to an increase in gastrointestinal motility problems in both men and women, such as constipation, diarrhea, or incontinence (11).

Due to considerable lifestyle changes, diseases and illnesses of the gastrointestinal system have grown in the last decade. Various studies have shown that people with gastrointestinal diseases have a high prevalence of depression, stress, anxiety, and impaired central nervous system functioning (9, 12–14).

Limited studies have been conducted to investigate the determinants associated with gastrointestinal disorders among older adults in India. The study aims to explore the factors associated with self-reported gastrointestinal problems among the Indian elderly using the recently released Longitudinal Aging Study in India (LASI, 2017–18). Moreover, the study explores the relationship between non-communicable diseases (NCDs), such as hypertension, heart diseases, diabetes, and neurological or psychiatric and gastrointestinal disorders.

Materials and methods

Data source and study population

We used unit data from large-scale population-based surveys, namely, the Longitudinal Aging Study in India (LASI), wave 1, conducted during 2017–18. A brief description of the data structure of the surveys is given below.

The LASI is a nationally representative study on the health, economic, and social wellbeing of older adults (45+ years) and their spouses in India, covering extensive biomarkers and self-reported health measures. It is a collaborative study of the International Institute for Population Sciences (IIPS), Mumbai, India, the Harvard T.H. Chan School of Public Health, and the University of Southern California, the United States. It has the distinction of being the largest-ever study, worldwide, with a representative sample of 72,250 individuals and 42,949 age-eligible households across all states and union territories of India except Sikkim. The age-eligible households included those households who had at least one member aged 45+ years. The LASI used a multistage stratified area probability cluster sampling design in the selection of the sample households. It provided comprehensive information on household economic wellbeing, work and employment, retirement and pension, chronic health conditions, functional health, mental health, extensive biomarkers, healthcare utilization, and health insurance of older adults in India.

Dependent variable

The dependent variable for this study is the self-reported gastrointestinal problems among the elderly (45+ years), coded

as "0" for no and "1" for yes. In LASI, gastrointestinal problems include gastroesophageal reflux disease, constipation, indigestion, piles, and peptic ulcer.

Independent variable

A number of independent variables have been used in this study. Individual factors, such as the age groups (<44, 45–54, 55–64, 65–74, and 75+ years), education level (no education, primary, secondary, and higher), currently working (never worked, currently working, and not currently working), marital status (currently married, divorced/others, and widowed), the presence of non-communicable diseases, such as diabetes (yes, no), stroke (yes, no), arthritis (yes, no), hypertension (yes, no), heart diseases (yes, no), neurological (yes, no) or psychiatric (yes, no), difficulty in Activities of Daily Living (ADL) (yes, no), and difficulty in Instrumental Activities of Daily Living (IADL) (yes, no) were included in the analysis. In addition, lifestyle factors, such as moderate activities (inactive, active), vigorous activities (inactive, active), smoking status (yes, no), chewing status (yes, no), and drinking status (yes, no) were included in the analysis. LASI collected information from households about the last 7 days of their spending on food (a reference period of 7 days) and non-food items (reference periods of 30 and 365 days). After standardizing the food and non-food expenditure to a 30-day reference period, the monthly per capita consumption expenditure (MPCE) was computed and used as the summary measure of consumption: poorest, poorer, middle, richer, and richest. Apart from these independent variables, the study also included the household factors, such as religion (Hindu, Muslim, Christian, and Others), castes [Scheduled castes (SCs), Scheduled Tribes (STs), Other Backward Classes (OBCs), and Others], place of residence (rural or urban), and region (north, central, east, northeast, west, and central) have been included in the analysis.

Methods

Descriptive, bivariate, and multivariable statistical techniques have been used in this study. Descriptive statistics were used to provide the frequency distribution of sociodemographic and economic profiles of adults in India. A bivariate analysis was used to understand the percentage distribution of adults suffering from gastrointestinal problems by their background characteristics in India.

A binary logistic regression was used to determine the factors associated with gastrointestinal problems. The basic form of the logistic regression model, which yields the probability of occurring of an event, can be depicted as:

$$log_e[P(Y_i = 1|X_i)/1 - P(Y_i = 1|X_i)] = log e\ [\pi|1 - \pi] = \alpha + \beta_1 X_{i1}, \ldots\ldots\ldots \beta_k X_{ik} \quad (1)$$

Where *Yi* is the binary response variable and X_i is the set of explanatory variables. The socio-demographic variables (Xi) used are age, sex, education, place of residence, caste, household size, and states. β_1, $\beta_{2,\ldots\ldots}$ $\beta_k$are the coefficients of the X_i variables.

In the binary logistic regression analysis, a systematic model-building procedure was adopted. Altogether, two models were estimated. Model 1 included the individual factors, lifestyle factors, and household factors along with non-communicable diseases, whereas model 2 included the interaction of hypertension and neurological disorder in addition to the variables included in model 1 to understand the independent effect of the interaction of hypertension and neurological problems on gastrointestinal disorders after controlling the potential confounding variables.

Results

Table 1 presents the socio-demographic and economic profile of adults in India. The majority of the adults (32%) reported their age as 45–54 years. A substantial proportion (10%) of adults belonged to the age group of 75 years and above and only 9% of them belonged to the age group of 44 years or less. In India, the prevalence of gastrointestinal problems was 18%. Approximately half of the adults (50%) were not educated and 23% of them received primary education only. About 17% of adults had attained the secondary level of education, whereas only 10% of the adults attained a higher level of education. Nearly half (46%) of the adults were currently working, however, 26% of the adults were not currently working and the remaining 28% had never worked. In the sample, 78% of the adults were currently married and a substantial proportion (22%) of the respondents were widowed. Wealth Index analysis portrays that an almost equal sample comprised of at each level of MPCE quintile varies from 21% in poorest, poorer, and middle to 18% in richest. The majority of the respondents belonged to the Hindu religion (82%), followed by Muslims (12%), and the remaining were Christians (3%) and other religions [Sikh, Buddhist, etc. (3%)]. A significant proportion of the respondent comprised Other Backward Classes (OBCs) 46%, while Schedule Castes (SCs) constituted 19% and Schedule Tribes (STs) 9% of the proportions of the sample. Findings depict that 68% of adults belonged to rural areas. In addition, regional variation was noticed in the sample of adults. A majority of women belonged to the Southern (24%), followed by Eastern (23%), Central (20%), Western (17%), Northern (12.0%), and North-eastern (4%) part of the country.

Table 2 presents the percentage of adults suffering from gastrointestinal problems by their background characteristics in India. The overall prevalence of self-reported gastrointestinal problems was 18%. However, the prevalence of self-reported

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TABLE 1 Socio-demographic and economic profile of adults in India, LASI-2017–18.

Background characteristics	%	Sample
Age groups		
<44	6,688	8.69
45–54	24,094	31.91
55–64	20,136	27.25
65–74	14,583	21.72
75+	6,749	10.43
Education level		
No education	33,211	49.50
Primary	17,736	23.21
Secondary	13,949	16.91
Higher	7,354	10.38
Currently working		
Never worked	21,289	27.57
Currently working	32,990	46.28
Not currently working	17,951	26.14
Marital status		
Currently married	55,396	75.60
Widowed	14,593	21.66
D/S/D/Others[a]	2,257	2.73
MPCE quintile		
Poorest	14,158	20.70
Poorer	14,530	21.22
Middle	14,537	20.47
Richer	14,686	19.59
Richest	14,339	18.03
Religion		
Hindu	52,973	81.92
Muslim	8,667	11.67
Christian	7,215	2.97
Others[$]	3,390	3.44
Caste		
Scheduled caste	12,046	19.15
Scheduled tribe	12,509	8.53
OBC[#]	27,184	45.50
Others	20,511	26.82
Place of residence		
Rural	46,534	68.20
Urban	25,716	31.80
Region		
North	12,970	12.01
Central	9,536	20.10
East	12,834	23.40
Northeast	9,676	3.64
West	9,822	16.48
South	17,412	24.38
Total	72,250	100

[a]Divorced, separated, and deserted; [$]Includes Sikh, Buddhist/neo-Buddhist, Jain, Parsi/Zoroastrian and others; [#]Other Backward Classes.

gastrointestinal problems was 1% higher among men (18%) than women (17%). The prevalence of self-reported gastrointestinal problems has substantially increased with the increasing age of men; however, men (20%) and women (20%) of 75+ years of age are at a high risk of suffering gastrointestinal problems. The prevalence of reported gastrointestinal problems was relatively lesser among those who had a higher level of schooling for both men (16%) and women (10%). An almost equal proportion of never worked and not currently working adults (19%) had reported gastrointestinal problems. Self-reported gastrointestinal problems were comparatively lesser among D/S/D/Others adults (12%) than currently married (18%) and widowed adults (18%). It was observed that the prevalence of self-reported gastrointestinal problems was higher among adults who had stroke (23% yes vs. 17% no), arthritis (23% yes vs. 17% no), difficulty in ADL (23 vs. 17%), and difficulty in IADL (21 vs. 17%).

By considering the lifestyle factors, it was found that adults who were active in moderate activities were more likely (18%) to report gastrointestinal problems than those who were inactive (17%). Among adults who were inactive in vigorous activities, the self-reported prevalence of gastrointestinal problems was a little higher than those who were active. Light and moderate exercises are well-tolerated and can benefit patients with inflammatory bowel disease and liver disease but severe exhaustive exercises, however, inhibits gastric emptying, interferes with gastrointestinal absorption, and causes many gastrointestinal symptoms, most notably gastrointestinal bleeding (15). The self-reported gastrointestinal problem was higher among those adults who were formerly involved in smoking and chewing tobacco than those who were currently involved and never involved in smoking and chewing tobacco. However, the prevalence of self-reported gastrointestinal problems was higher among women than men who were former and currently involved in smoking and chewing tobacco. Adults who were drinking reported more gastrointestinal problems (20%) than those who were not drinking (18%). While observing separately among men and women, it was found that the self-reported gastrointestinal problem was higher among men who were drinking (20% yes vs. 18% no), however, in the case of women it was higher among those who were not drinking (16% yes vs. 18% no).

There are no consistent changes in the prevalence of self-reported gastrointestinal problems among adults that have been observed with the increasing MPCE quintile. Additionally, men and women from the richer and richest wealth quintile were at a higher risk of gastrointestinal problems than their other counterparts. Furthermore, the prevalence of self-reported gastrointestinal problems was a little higher among women and men who belong to the other social group (21%), rather than the Scheduled Tribes (STs, 16% men and 14% women), Scheduled Castes (SCs, 20% men and 18% women), and Other Backward Classes (OBCs, 17% men and 16% women). The prevalence of

TABLE 2 Percentage of adults suffering from GI by their background characteristics in India, LASI 2017–18.

	Self-reported gastrointestinal problem					
Background characteristics	**Overall ($n = 72,037$)**	***p*-value**	**Men ($n = 30,460$)**	***p*-value**	**Women ($n = 41,577$)**	***p*-value**
Individual factors	**%**		**%**		**%**	
Age groups						
<44	15.3	$p = 0.000$	9.37	$p = 0.063$	15.33	$p = 0.000$
45-54	16.73		17.02		16.50	
55-64	18.62		18.46		18.75	
65-74	18.40		19.25		17.63	
75+	20.06		20.46		19.69	
Education level						
No education	17.70	$p = 0.000$	17.31	$p = 0.000$	17.86	$p = 0.000$
Primary	19.41		19.90		18.90	
Secondary	18.78		19.86		17.37	
Higher	13.36		15.79		9.56	
Currently working						
Never worked	18.82	$p = 0.000$	15.37	$p = 0.00$	18.99	$p = 0.000$
Currently working	16.67		17.86		14.96	
Not currently working	18.83		19.79		17.84	
Marital status						
Currently married	18.15	$p = 0.000$	18.54	$p = 0.000$	17.79	$p = 0.007$
Widowed	17.45		19.04		17.06	
D/S/D/Others[a]	11.88		11.48		12.18	
Morbidities						
Diabetes						
No	17.78	$p = 0.000$	18.32	$p = 0.009$	17.40	$p = 0.000$
Yes	18.18		18.88		17.61	
Stroke						
No	17.73	$p = 0.000$	18.24	$p = 0.001$	17.37	$p = 0.021$
Yes	23.06		24.14		21.54	
Arthritis						
No	17.35	$p = 0.000$	17.83	$p = 0.000$	17.00	$p = 0.000$
Yes	22.68		25.52		21.20	
Difficulty in ADL[b]						
No	16.81	$p = 0.000$	17.62	$p = 0.000$	16.21	$p = 0.000$
Yes	23.12		22.55		23.48	
Difficulty in IADL[c]						
No	16.27	$p = 0.000$	16.90	$p = 0.000$	15.72	$p = 0.000$
Yes	20.52		21.95		19.82	
Lifestyle factors						
Moderate activities						
Inactive	16.83	$p = 0.000$	17.20	$p = 0.000$	16.37	$p = 0.000$
Active	18.40		19.43		17.85	
Vigorous activities						
Inactive	18.2	$p = 0.000$	18.2	$p = 0.432$	18.20	$p = 0.000$
Active	17.06		18.64		15.18	
Smoking status						
Never	17.31	$p = 0.000$	17.51	$p = 0.000$	17.21	$p = 0.000$

(Continued)

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TABLE 2 (Continued)

Background characteristics	Overall ($n = 72,037$)	*p*-value	Men ($n = 30,460$)	*p*-value	Women ($n = 41,577$)	*p*-value
	Self-reported gastrointestinal problem					
Individual factors	%		%		%	
Former	25.00		24.20		30.44	
Current	19.38		18.96		22.60	
Chewing tobacco						
Never	16.51	$p = 0.000$	16.64	$p = 0.000$	16.43	$p = 0.000$
Former	24.74		23.21		27.51	
Current	22.23		22.01		22.54	
Drinking status						
No	17.55	$p = 0.001$	17.69	$p = 0.000$	17.48	$p = 0.045$
Yes	19.56		20.00		15.76	
Household factors						
MPCE quintile						
Poorest	15.63	$p = 0.000$	16.59	$p = 0.000$	14.95	$p = 0.000$
Poorer	18.21		18.73		17.83	
Middle	17.84		18.30		17.51	
Richer	19.21		19.79		18.80	
Richest	18.38		18.62		18.20	
Religion						
Hindu	17.60	$p = 0.000$	18.17	$p = 0.00$	17.18	$p = 0.000$
Muslim	19.37		19.60		19.21	
Christian	17.35		18.50		16.67	
Others[$]	18.55		19.67		17.69	
Caste						
Scheduled caste	18.98	$p = 0.000$	20.15	$p = 0.000$	18.16	$p = 0.000$
Scheduled tribe	14.82		16.32		13.75	
OBC[#]	15.95		16.61		15.46	
Others	21.08		20.87		21.24	
Place of residence						
Rural	19.38	$p = 0.000$	19.98	$p = 0.000$	18.93	$p = 0.000$
Urban	14.48		14.69		14.33	
Region						
North	22.74	$p = 0.000$	20.85	$p = 0.000$	24.13	$p = 0.000$
Central	16.91		17.30		16.58	
East	26.29		25.88		26.59	
Northeast	23.11		21.82		24.00	
West	12.57		14.79		11.06	
South	10.73		12.16		9.83	
NCD						
Hypertension	22.11	$p = 0.000$	21.82	$p = 0.000$	22.28	$p = 0.000$
Heart disease	22.57	$p = 0.000$	22.02	$p = 0.000$	23.09	$p = 0.000$
Neurological or psychiatric problems	26.99	$p = 0.000$	25.17	$p = 0.000$	28.37	$p = 0.000$
Total	17.83		18.38		17.42	

[a]Divorced, separated, and deserted.
[b]Activities of daily living includes dressing, walking across a room, bathing, eating difficulties, getting in or out of bed and toilet use (any one or more).
[c]Instrumental Activities of Daily Living (IADL) includes preparing a hot meal, shopping for groceries, making telephone calls, taking medications, doing work around the house or garden, managing money and getting around or finding address in unfamiliar place (any one or more).
[#]Other Backward Classes.
[$]Includes Sikh, Buddhist/neo-Buddhist, Jain, Parsi/Zoroastrian and others.

self-reported gastrointestinal problems was higher among men and women from rural areas (20% men and 19% women) than urban area (15% men and 14% women). The regional variation in the prevalence of self-reported gastrointestinal problems was also noticeable. The eastern region shows the highest prevalence of gastrointestinal problems among adults (26%) followed by the northeast (23%) and northern (23%) regions in India, where women were found to possess a higher burden of gastrointestinal problems, compared with men. Differences in access to healthcare and cultural factors, such as help-seeking behavior, may contribute to differences in the prevalence of men and women (16). Women have been shown to be more sensitive to pressure from an inflated balloon placed in the esophagus (swallowing tube between the mouth and the stomach), small intestine, colon or large intestine, and rectum than men. Among adults who have suffered from neurological or psychiatric problems (27%), the prevalence of self-reported gastrointestinal problems was higher than those who suffered from hypertension (22%) and heart disease (23%), however, the burden was higher among women (28%) than among men (25%).

Table 3 presents the adjusted odds ratio (*AOR*) estimates for self-reported gastrointestinal problems among adults by their background characteristics in India. Two models are presented in Table 3, model 1 analyses the individual factors, lifestyle factors, and household factors, whereas model 2 analyses the interaction between two NCDs, which strongly affect gastrointestinal problems along with the factors, which analyzed in model 1. Results from model 1 reveal that adults from the age groups of 45–54 (1.11, $p < 0.01$) and 55–64 (1.09, $p < 0.01$) years were significantly more likely to have gastrointestinal problems compared with the <44 years age group. Women were 1.15 ($p < 0.01$) times significantly more likely to report gastrointestinal problems than men. The education of the respondents was found to be significant and was negatively associated with the self-reported gastrointestinal problem in India. As the education level of the respondents increases, the odds of having gastrointestinal problems decrease simultaneously.

The likelihood of being affected by gastrointestinal problems was found to be lower among adults who were widowed (*AOR* = 0.92, $p < 0.01$) and D/S/D/Others (*AOR* = 0.77, $p < 0.01$) as compared with the adults who were currently married. Furthermore, considering the association between morbidities and gastrointestinal problems, it was found that adults who suffered from diabetes (*AOR* = 1.07, $p < 0.01$), arthritis (*AOR* = 1.32, $p < 0.01$), difficulty in ADL (*AOR* = 1.29, $p < 0.01$), and difficulty in IADL (*AOR* = 1.24, $p < 0.01$) were significantly more likely to report gastrointestinal problems than their counterparts. Regarding the lifestyle factors, results reveal that adults who were active in moderate activities were significantly more likely (*AOR* = 1.18, $p < 0.01$) to report gastrointestinal problems than those who were inactive. In contrast, adults who were active in vigorous activities were significantly less likely (*AOR* = 0.92, $p < 0.01$) to report gastrointestinal problems than those who were inactive. Additionally, Table 3 reveals the effect of behavioral habits, such as smoking, chewing tobacco, and alcohol use, on the self-reported gastrointestinal problems. Furthermore, adults who were formerly and currently smoking and chewing tobacco were significantly more likely to report gastrointestinal problems than their counterparts. Moreover, the increasing economic status significantly and positively increased the likelihood of having self-reported gastrointestinal problems among adults. On the other hand, the risk of gastrointestinal problems was found to be significantly lower among adults who belong to the Scheduled Tribes (STs) (*AOR* = 0.71, $p < 0.01$) and Other Backward Classes (OBCs) (*AOR* = 0.93, $p < 0.01$) category of the social group. The regional variation in the prevalence of gastrointestinal problems is also noticeable. Except for the eastern region, all other regions were significantly less likely to report gastrointestinal problems than the northern region.

The likelihood of being affected by gastrointestinal problems was found to be higher among adults who were affected by NCDs, namely, heart disease, hypertension, and neurological or psychiatric problems. The odds of individual factors, lifestyle factors, and household factors were unchanged in model 2, whereas the association among being affected with hypertension, neurological problems, and self-reported gastrointestinal problems was less likely and insignificant. The insignificant interaction term clearly shows that hypertension and neurological problem have significant individuals effect on gastrointestinal problems.

Discussion

In this study, we investigated the self-reported prevalence of gastrointestinal problems and the associated risk factors with an emphasis on non-communicable diseases, namely, heart disease, hypertension, and neurological disorders. The prevalence of self-reported gastrointestinal disorders was found to be ∼18% in India. Whereas, the prevalence of gastroesophageal reflux disease (GERD) ranges from 2.5% to 7.1% in most population-based studies in Asia. No significant difference was found among both genders with respect to gastrointestinal problems. Respondent's age, educational status, work status, marital status, and morbidities, such as diabetes, stroke, and arthritis, were found to be the significant predictors of GI in our population. Moreover, difficulty in ADL, IADL, and other lifestyle factors, such as moderate and vigorous physical activity, smoking alcohol and consuming tobacco, and other household factors, such as wealth status, religion, caste, place of residence, and having non-communicable diseases, such as hypertension, heart disease, and neurological disorders were also found to be significantly associated with GI symptoms in Indian adults.

TABLE 3 Adjusted odds ratio estimates for GI among adults by their background characteristics in India.

Background characteristics	Model-1 (Full model)	Model-2 (Full model with interaction between two NCD which strongly affect GI)
	AOR 95% CI	AOR 95% CI
Age groups		
<44		
45–54	1.109*** (1.03, 1.20)	1.109*** (1.03, 1.20)
55–64	1.089** (1.00, 1.18)	1.088** (1.00, 1.18)
65–74	0.988 (0.9, 1.08)	0.988 (0.9, 1.08)
75+	0.939 (0.84, 1.05)	0.938 (0.84, 1.04)
Sex		
Male		
Female	1.151*** (1.08, 1.22)	1.151*** (1.08, 1.22)
Education level		
No education		
Primary	1.173*** (1.11, 1.23)	1.173*** (1.11, 1.23)
Secondary	1.116*** (1.05, 1.19)	1.116*** (1.05, 1.19)
Higher	0.902** (0.83, 0.98)	0.902** (0.83, 0.98)
Currently working		
Never worked		
Currently working	0.984 (0.93, 1.04)	0.984 (0.93, 1.04)
Not currently working	1.045 (0.99, 1.11)	1.045 (0.99, 1.11)
Marital status		
Currently married		
Widowed	0.923*** (0.87, 0.98)	0.923*** (0.87, 0.98)
D/S/D/Others[a]	0.768*** (0.68, 0.87)	0.768*** (0.68, 0.87)
Morbidities		
Diabetes		
No		
Yes		
Stroke	1.065** (1.001, 1.13)	1.065** (1, 1.13)
No		
Yes	0.955 (0.83, 1.10)	0.957 (0.83, 1.10)
Arthritis		
No		
Yes	1.319*** (1.23, 1.41)	1.319*** (1.23, 1.41)
Difficulty in ADL[b]		
No		
Yes	1.294*** (1.22, 1.37)	1.294*** (1.22, 1.37)
Difficulty in IADL[c]		
No		
Yes	1.24*** (1.18, 1.30)	1.24*** (1.18, 1.3)
Lifestyle factors		
Moderate activities		
Inactive		
Active	1.188*** (1.14, 1.24)	1.188*** (1.14, 1.24)
Vigorous activities		
Inactive		
Active	0.917*** (0.87, 0.96)	0.917*** (0.87, 0.96)
Smoking status		
Never		
Former	1.448*** (1.32, 1.59)	1.448*** (1.32, 1.59)
Current	1.253*** (1.17, 1.34)	1.253*** (1.17, 1.34)
Chewing tobacco		
Never		
Former	1.572*** (1.40, 1.77)	1.572*** (1.4, 1.77)
Current	1.472*** (1.40, 1.55)	1.472*** (1.4, 1.55)
Drinking status		
No		
Yes	1.054* (0.99, 1.12)	1.054* (0.99, 1.12)
Household factors		
MPCE quintile		
Poorest		
Poorer	1.203*** (1.13, 1.28)	1.203*** (1.13, 1.28)
Middle	1.219*** (1.14, 1.30)	1.218*** (1.14, 1.30)
Richer	1.358*** (1.27, 1.45)	1.358*** (1.27, 1.45)
Richest	1.347*** (1.26, 1.44)	1.347*** (1.26, 1.44)
Religion		
Hindu		
Muslim	0.971 (0.91, 1.03)	0.971 (0.91, 1.03)
Christian	1.05 (0.96, 1.14)	1.05 (0.96, 1.14)
Others[$]	0.894** (0.81, 0.98)	0.894** (0.81, 0.98)
Caste		
Scheduled caste		
Scheduled tribe	0.712*** (0.66, 0.77)	0.712*** (0.66, 0.77)
OBC[#]	0.929** (0.88, 0.98)	0.928** (0.88, 0.98)
Others	0.969 (0.91, 1.03)	0.969 (0.91, 1.03)
Place of residence		
Rural		
Urban	0.962* (0.92, 1.01)	0.962* (0.92, 1.01)
Region		
North		
Central	0.756*** (0.7, 0.81)	0.756*** (0.7, 0.81)
East	1.169*** (1.1, 1.25)	1.169*** (1.1, 1.25)
Northeast	0.846*** (0.78, 0.92)	0.847*** (0.78, 0.92)
West	0.463*** (0.43, 0.50)	0.463*** (0.43, 0.50)
South	0.539*** (0.5, 0.58)	0.539*** (0.5, 0.58)

(Continued)

TABLE 3 (Continued)

Background characteristics	Model-1 (Full model)	Model-2 (Full model with interaction between two NCD which strongly affect GI)
	AOR 95% CI	AOR 95% CI
NCD	1.168*** (1.06, 1.29)	1.169*** (1.06, 1.29)
Heart disease		
Hypertension	1.476*** (1.41, 1.54)	1.481*** (1.42, 1.55)
Neurological or psychiatric problems	1.344*** (1.19, 1.52)	1.424*** (1.21, 1.68)
Hypertension[#] neurological		
Yes[#] Yes		0.883 (0.70, 1.12)
Constant	0.135 (0.12, 0.15)	0.135 (0.12, 0.15)
Log likelihood	−32,651.132	−32,650.607

[#]Other Backward Classes.
[$]Includes Sikh, Buddhist/neo-Buddhist, Jain, Parsi/Zoroastrian and others.
[a]Divorced, separated, and deserted.
[b]Activities of daily living includes dressing, walking across a room, bathing, eating difficulties, getting in or out of bed and toilet use (any one or more).
[c]Instrumental Activities of Daily Living (IADL) includes preparing a hot meal, shopping for groceries, making telephone calls, taking medications, doing work around the house or garden, managing money and getting around or finding address in unfamiliar place (any one or more).
*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Globally, studies have reported varying rates of gastrointestinal problems, ranging from 14% in Iran to 54% in some western countries. Compare with other studies, GI prevalence is higher than in many neighboring nations and lower than that in many industrialized nations, such as the United States and Russia (17, 18). Many studies across the world have yielded different results about the prevalence of gastrointestinal problems and it has been reported to range from 14% in Iran to 54% in some western countries. The estimates obtained in our population are lower than the estimates reported in Sikkim and Darjeeling where 60% and 70% of people, respectively, reported complaining of gastrointestinal disease (15). The high prevalence of GI in some parts of the country may be due to the diet and cultural behaviors of the people (19). Moreover, these differences are also due to different study populations, lifestyles, and different diagnostic criteria used to estimate the prevalence.

Results from logistic regression analysis indicated that with the increase in age up to 64 years, the risk of having gastrointestinal problems increased significantly. However, this pattern was not significant at higher ages. Similar pieces of evidence have been found in a study conducted in India (19, 20).

In line with several western countries and some Indian studies, our findings showed that women were at a higher risk of gastrointestinal problems (20–22). Though the reasons are largely unknown, differences in access to healthcare and cultural factors, such as health-seeking behavior, may contribute to prevalence differences as well. However, a number of Indian studies have observed no significant gender differences in the risk of having gastrointestinal problems (23, 24). Further, higher education in adults was associated with a lower risk of gastrointestinal problems as found in a number of other studies worldwide. The increased awareness toward a healthy diet might be the possible explanation for the observed variation. The results on socio-economic status, wealth, and education are in line with findings across the world (25, 26).

Our findings indicated a strong association between having diabetes, arthritis, and difficulty in ADL and IADL activities and GI problems. Previous studies have documented the association between GI symptoms in patients with diabetes mellitus (27). We observed a high prevalence of gastrointestinal problems among those with psychiatric or neurological problems, which supported the other studies where psychological distress was found to be positively related to gastrointestinal problems (28). However, an in-depth examination of psychological distress and gastrointestinal problems shows that there exists a bidirectional relationship between stress and inflammatory bowel disease (IBD) symptoms. Moreover, patients with chronic health conditions, such as IBD, have a higher level of stress which impacts IBD (29, 30). Multiple lifestyle-related factors were shown to be related to inflammatory bowel syndrome, such as poor socioeconomic status, smoking, alcohol, and difficulty in ADL and IADL activities. In line with the already existing association, we found that vigorous activity significantly reduced the risk of having gastrointestinal problems (31, 32).

Additionally, smoking has been documented to be associated with an increased risk of inflammatory bowel disease (33). This study observed that individuals who quit smoking were more likely to have gastrointestinal problems, which is similar to the findings obtained by Cosnes and colleagues (34). According to our findings, despite the fact that this study suggests that alcohol users are more likely to experience gastrointestinal issues, alcohol has not consistently been linked to an increased risk of IBD development in other studies (35).

The rural-urban variation in the prevalence of this disease may be due to environmental and socio-demographic factors. Moreover, the sufficient intake of fruits and vegetables in their diet might be the possible reason behind the reduced risk of urbanites having gastrointestinal problems. The effect of dietary patterns on functional gastrointestinal disease has been well-established (28, 36). The regional variation in the prevalence of gastrointestinal problems can be attributable to cultural differences, ethnic diversity, genetics, and dietary habits. Current research uses data from the nationally representative study to show the importance of age, level of

education, the influence of other illnesses, and substance abuse on gastrointestinal problems. Aging-related gastrointestinal problems are physiological or pathological and more prevalent in the population aged 64 years and above. The gastrointestinal system plays an essential role in medication absorption and metabolism. The GI system is frequently impacted by medication side effects and plays a crucial role in both drug absorption and metabolism. The management of GI disease among older adults, including prompt diagnostic and therapeutic methods, is complicated by the existence of complex comorbidities, lengthy drug intake, and other factors. GI problems among older adults are acquiring greater importance in clinical practices to plan effective treatment, administration of gastrointestinal drugs early screening, and management of GI diseases. Given the policy focus through Health and Wellness centers for accessible NCD care, it is important that gastrointestinal illnesses receive more focus and systemic support. In the present study, the disease states under the survey are self-reported, with a potential for several recall/social-desirability biases, which might lead to gross under-reporting due to stigma or other forms of respondent behaviors. Moreover, the LASI survey only captures the self-reported prevalence of diagnosed gastrointestinal diseases. Additionally, there is no comprehensive report of the burden of GI diseases in India. To improve the quality of life of the older population, more population-level research is required to understand the types of GI diseases, as well as lifestyle, behavioral, and dietary factors that contribute to GI disorders.

Data availability statement

The study used secondary datasets available in the public domain. These can be accessed upon reasonable request via https://www.iipsindia.ac.in/content/lasi-wave-i.

Ethics statement

The studies involving human participants were reviewed and approved by the Indian Council of Medical Research (ICMR) extended the necessary guidelines and ethics approval for undertaking the LASI survey. The patients/participants provided their written informed consent to participate in this study.

Author contributions

SD, PD, and ID conceived and designed the research paper and contributed agents, materials, and analysis tools. PD and SD analyzed the data and wrote the manuscript. ID refined the manuscript. All authors read, reviewed, and approved the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Cost-effectiveness analysis of a community-based colorectal cancer screening program in Shanghai, China

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Background: Since 2011, through the Community-Based Colorectal Cancer Screening Program in Shanghai, China (SHcsp), residents aged >50 years were offered initial colorectal cancer screening using the fecal immunochemical test (FIT) and risk assessment questionnaire (RAQ) for free. Colonoscopy was then recommended for positive results.

Objective: To evaluate the cost-effectiveness of the Community-Based Colorectal Cancer Screening Program in Shanghai, China from the payer perspective.

Methods: This analysis estimated the long-term cost and effectiveness of the 2014–2016 SHcsp based on real-world follow-up data from the SHcsp database, Shanghai Cancer Registry System, vital statistics from Shanghai Municipal Center for Disease Control and Prevention and inpatient CRC expense data from hospitals. A decision-tree model and Markov model were constructed to simulate the 25-year health outcomes. The screening branch was the cohort with a definite diagnosis of adenoma, advanced adenoma, and CRC. The other branch was residents who were neither screened nor treated until CRC symptoms appeared. A payer prospective was adopted to measure direct costs and effectiveness by life years (LYs) and quality-adjusted life years (QALYs) gained, and were discounted by 3%. Stimulation robustness was tested by one-way sensitivity analysis.

Results: Of 1,097,656 residents, 13,250 were diagnosed with adenoma, advanced adenoma, or CRC. Assuming those had not been found through screening, SHcsp resulted in 1,570.1 LYs and 13,984.3 QALYs gained at an extra cost of USD9.96 million. The incremental cost-effectiveness ratio (ICER) was USD6,342.02 per LY and USD712.08 per QALY obtained, far below the threshold of USD59,598 of three-time GDP per capita in Shanghai.

Conclusion: The SHcsp was cost-effective than no screening strategy. The results were generalisable to the Chinese population for mass CRC screening.

KEYWORDS

cost-effectiveness, colorectal cancer, mass screening, community screening, China

Introduction

Colorectal cancer (CRC) is the fourth most common cancer in China; 4.29 million new cases were diagnosed in 2018, accounting for 1/4 of new cases worldwide. It is also the second most common cause of cancer-related deaths in China, with 2.81 million CRC-related deaths in 2018, with a rapid growth rate (1). Accumulated evidence from global CRC screening programs strongly suggests that CRC screening increases the proportion of early detection and reduces CRC incidence and mortality (2–5). Epidemiological studies have shown that annual mortality of CRC in the United States fell by 3.9% every year from 2002 to 2009, and 53% of the reduction was attributed to screening (6). Due to the lack of CRC screening in China, only 12% of the newly diagnosed cases per year were in the early stages in 2012 (7), compared with 39% of US cases in the same period (8).

Colorectal cancer screening programs have been conducted worldwide. Over half of European countries, such as Germany, France, the United Kingdom, Denmark, and the Netherlands, have implemented CRC screening programs, and several countries have established the guidelines for CRC screening (9–13). These programs mostly targeted the natural population over 50 years old instead of the high-risk population, used the fecal immunochemical test (FIT) as initial screening and colonoscopy as diagnostic tests, and operated regularly and periodically. South Korea, Croatia, and some developing countries have also explored the feasibility of CRC screening (14, 15). In the 1970s, some small cities in China carried out a few pilot screening programs for CRC among local residents, such as Haining and Jiashan in Zhejiang Province (16, 17). Recently, metropolitan areas in mainland China, including Shanghai, Tianjin, and Guangzhou, have promoted screening programs for CRC on a larger scale (18–20). In addition, health economics research has shown CRC screening programs to be cost-effective in France, England, and Belgium (4, 9, 21, 22). However, the long-term outcomes and economic evidence for mass CRC screening programs are unknown, apart from cohort simulations in China and other developing countries (23).

As one of the most developed cities in China, Shanghai faces the threat of a dramatically increased incidence and mortality of CRC, which are second and fourth highest among all cancers, respectively (24). As an aging megalopolis in China, Shanghai is the pioneer of mass CRC screening for community residents with the most extensive participation. After a pilot CRC screening program in the Qibao community, the Community-Based Colorectal Cancer Screening Program in Shanghai (SHcsp) was officially launched in 2011 to provide free colorectal cancer screening for community residents over 50 years old every 3 years (18). Approximately 4 million community residents were estimated to be eligible, and ∼1 million were planned to be included every 3 years. During 2011–2013, SHcsp made significant achievements (18), and during 2014–2016 provided 1,097,656 initial screenings.

The entire process can be divided into four steps (shown in Figure 1): (1) Sponsored by the local government and organized by the community health centers, the initial screening was free for residents after registration and completion of FIT and risk assessment questionnaire (RAQ). (2) Community physicians informed participants of their initial screening results and recorded them in the SHcsp database. (3) Participants with positive screening results based on either FIT or RAQ results were suggested by doctors in community health centers to undergo colonoscopy in hospitals, which was covered by the local basic health insurance schemes. As a diagnostic test, colonoscopy results confirmed the patients' health status. (4) Patients diagnosed with adenoma, advanced adenoma, or CRC were treated differently. Almost all adenomas and advanced adenomas were surgically removed during colonoscopy in outpatient settings. Only a few advanced adenoma and CRC patients required hospitalization for further treatment, and CRC patients were reported to the Shanghai Cancer Registry System (SCRS). Patients were followed up by doctors in community health centers for one year after their initial screenings, which were updated in the SHcsp database.

SHcsp is rare in community-based populations and extensive participation. It is essential to evaluate not only the short-term results of the implementation, but also the long-term health effectiveness (18). Other CRC screening programs in China were limited to evaluate the health value of community-based CRC screening programs because of the small sample size, short-term implementation, or lack of detailed follow-up data on diagnosis, treatment, and survival results. The cohort of one million people, strict procedures, and accessible data of SHcsp are suitable for analyzing the cost-effectiveness of mass CRC screening programs and providing real-world economic evidence in China.

This study, based on real-world data collected from the SHcsp database, Shanghai Cancer Registry System managed by Shanghai Municipal Center for Disease Control and Prevention (SCDC), vital statistics from SCDC and inpatient information from hospitals, constructed a decision tree model and a Markov model to stimulate the cost and effectiveness over 25 years from the payer perspective. The incremental cost-effectiveness ratio (ICER) was reported to show the results, and a sensitivity analysis was performed to confirm the validity of this study.

Materials and methods

Model overview

Of 1,097,656 SHcsp participants, positive initial screening results were detected in 284,287 and 82,729 of them underwent colonoscopy. Finally, 13,250 patients were diagnosed: 10,653 had adenoma, 745 had advanced adenoma, and 1,852 were CRC patients without obvious symptoms. Because SHcsp prevented

FIGURE 1
Process of 2014–2016 SHcsp.

disease progression in the 13,250 patients who were finally diagnosed and treated, our study focused on the long-term effectiveness of these patients. Their improved health condition directly and accurately reflected the real screening performance, rather than simulating a hypothetical cohort based on CRC prevalence rate, sensitivity and specificity of FIT and RAQ, detection rates, and adherence to colonoscopy (shown in Figure 1).

The target population can be divided into two groups: the screening group, with 13,250 residents diagnosed positive; and the comparison group, as counterfactual reference, residents who did not participate in the screening and whose diseases progressed naturally until their clinical symptoms of CRC emerged and they sought medical care.

The essential difference between the two groups was that in the screening group, adenoma, advanced adenoma, and more early stage CRC patients were diagnosed and treated, which greatly prevented or slowed down the disease progression. However, in the comparison group of natural disease processes, these patients could hardly be detected because they were normally asymptomatic.

Model structure

To represent the screening results and further progress of CRC, a model combining a decision tree and a Markov model was constructed (9, 21, 22, 25, 26). The screening program only changed the initial health state distribution of residents shown by the decision tree, but did not influence the further transition probabilities between health states in the Markov model. The Treeage Pro 2018 was used to generate the cost-effectiveness estimates.

According to the Tumor-Node-Metastasis (TNM) stages recommended by American Joint Committee on Cancer (AJCC) (27), a decision tree was constructed to determine the initial distribution in the Markov model (21). Based on the diagnostic results of colonoscopy for 13,250 residents, the initial distribution of the screening group and the comparison group was divided into 12 initial states (shown in Figure 2).

We classified the 15 possible health states of the two groups in the Markov model (shown in Figure 3): normal (no adenomas or cancer), adenoma (low-risk adenoma with a diameter <10 mm), advanced adenoma (high-risk adenoma with a diameter bigger than 10 mm), adenoma follow-up (5 years after adenoma polypectomy), advanced adenoma follow-up (5 years after advanced adenoma polypectomy), undiagnosed CRC Stage I, Stage II, Stage III, and Stage IV; CRC follow-up Stage I, Stage II, Stage III, and Stage IV; death from CRC, and death from other causes. Transitions occur once in each annual cycle over 25 years, considering the starting age for screening and life expectancy of Shanghai residents (25, 26).

The assumptions to simplify our model are as follows:

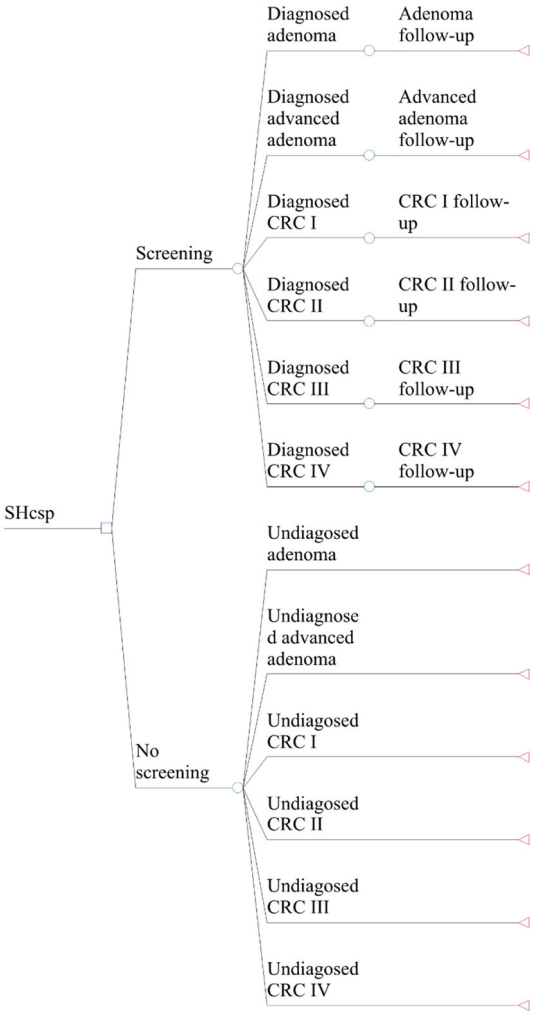

FIGURE 2
Structure of decision tree model.

(1) During 2014–2016, only unscreened natural residents were included in the SHcsp. Neither repeat screening nor complications of initial screening were considered, due to the low incidence.
(2) In the screening group, residents diagnosed with adenoma or advanced adenoma underwent immediate polypectomy during colonoscopy and returned to the normal state after a 5-year follow-up. In the comparison group, adenoma or advanced adenoma patients could not be detected or treated, and no death occurred.
(3) In the screening group, patients diagnosed with CRC were assumed to undergo radical surgery and transition to the corresponding follow-up states with no recurrence. In the comparison group, only a small number of undiagnosed patients were diagnosed and treated due to clinical symptoms and timely consultations.

Model parameters

The model was built as much as possible with real-world follow-up data from the SHcsp database, Shanghai Cancer Registry System, and inpatient CRC expense data from hospitals, supplemented by the literature where necessary. The half-cycle correction was applied, and the annual discount rate was assumed to be 3% (2, 3, 23, 28, 29). The parameters of the model are listed in Table 1.

Clinical data

The initial distribution was calculated based on the follow-up results from the SHcsp database. The 13,250 diagnosed patients were divided into six states by the decision tree: adenoma follow-up, advanced adenoma follow-up, Stage I CRC follow-up, Stage II CRC follow-up, Stage III CRC follow-up, and Stage IV CRC follow-up. These patients were treated immediately after diagnosis and returned to the corresponding follow-up status.

The crude mortality of residents was reported by vital statistics from SCDC. The CRC mortalities of the four CRC stages were calculated, respectively, as 5-year survival rates derived from the SCRS in the same period. The 5-year survival rates of the four stages were converted to annual survival rates. The CRC mortality rates of the four CRC stages were then determined and are shown in Table 2 using the following formula: Other transition probabilities between underlying disease states were mainly based on previously validated studies.

$$SurvivalRate_{annually} = SurvivalRate_{5-year}{}^{\frac{1}{5}}$$
$$Mortality = 1 - SurvivalRate_{annually}$$

Costs

From the payer perspective, direct costs of SHcsp during 2014–2016 were collected, including initial screening costs, colonoscopy costs, and treatment costs for advanced adenoma and CRC patients. There were different numbers of participants at each step of the whole screening process and treatments afterwards, as shown in Figure 1 and Table 3. The mean exchange rate of US dollar to Renminbi during 2014 to 2016 was used, where USD1 equals RMB6.3743.

During 2014–2016, initial screening costs for 1,097,656 participants included costs of purchasing materials, organizing programs, publicizing, communicating with residents, and manpower inputs. The costs of materials, organization, and publicity, which were sponsored by the municipal and district governments, were the actual expenses of SHcsp and were collected from organizers such as community health centers and SCDC. To calculate other costs, our staff designed a questionnaire and interviewed health care

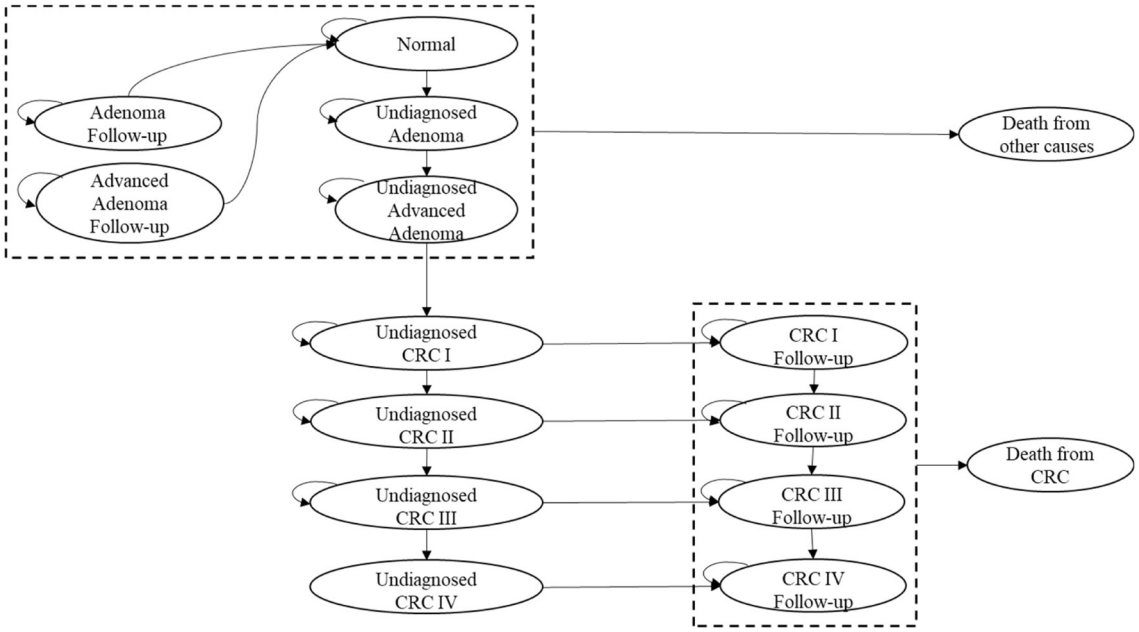

FIGURE 3
Structure of the Markov model.

providers and administrators from community health service centers and SCDC, who implemented SHcsp in practice. We collected information on staff man-hours spent on SHcsp and their monthly salaries. The total cost for initial screening was USD16,852,628.

Colonoscopy costs for 82,729 participants were calculated by multiplying the number of patients with the costs per patient. According to the guidelines and clinical practice in Shanghai, the average costs included the costs of colonoscopy and preoperative tests, including chest radiography, electrocardiogram, and liver function tests. The flat fees for these tests were summed up based on the official prices in Shanghai. The cost for colonoscopy was USD158.73 per capita.

As mentioned before, 13,250 residents who were detected were entered in the model, so that the costs of initial screening and colonoscopy were converted into average costs of screening for every 13,250 residents as model inputs. The input cost for initial screening and colonoscopy was USD1,271.90 in total.

The treatment costs for 10,653 adenoma patients were included in the colonoscopy costs. The vast majority of adenoma polypectomies were completed during the colonoscopy procedure in an outpatient setting with limited extra cost, as suggested by health care providers.

Treatment costs for 745 advanced adenoma and 1,852 CRC patients were calculated by multiplying the number of patients with the median treatment costs for each status. Patients' health expenses were collected from local hospitals by matching the unique IDs of registered residents in SHcsp. The treatment costs were defined as the total hospitalization expenses of each diagnosed patient who underwent operations and other treatments in hospitals within 1 year after screening. After data cleansing, we deleted outliers and used median treatment costs due to the partial distribution. The median treatment costs for advanced adenoma and four stages of CRC were USD1,109, USD8,567, USD10,555, USD13,396, and USD11,178 per patient, respectively.

Effectiveness

As for effectiveness in our analysis, health outcomes were valued in terms of life years (LYs) gained as the main results, and utilities of possible health states of Chinese residents and patients were obtained from the literature. We estimated cumulative life years and quality-adjusted life years over 25 years using the model to reflect the survival condition of the population.

As recommended by the World Health Organization (36), three times the local gross domestic product (GDP) per capita was used as the threshold to estimate whether SHcsp was cost-effective. In 2017, the GDP per capita in Shanghai was USD19,866 per capita.

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TABLE 1 Parameters of the Markov model for SHcsp.

Parameters	Base-case	Reference
Distribution of screening group		
Adenoma follow-up	0.8040	SHcsp follow-up data
Advanced adenoma follow-up	0.0562	SHcsp follow-up data
CRC I follow-up	0.0578	SHcsp follow-up data
CRC II follow-up	0.0361	SHcsp follow-up data
CRC III follow-up	0.0371	SHcsp follow-up data
CRC IV follow-up	0.0088	SHcsp follow-up data
Distribution of assumed no-screening group		
Adenoma	0.8040	SHcsp follow-up data
Advanced adenoma	0.0562	SHcsp follow-up data
Undiagnosed CRC I	0.0578	SHcsp follow-up data
Undiagnosed CRC II	0.0361	SHcsp follow-up data
Undiagnosed CRC III	0.0371	SHcsp follow-up data
Undiagnosed CRC IV	0.0088	SHcsp follow-up data
Transition probability (per year)		
From normal to adenoma	0.0160	(30)
From adenoma to advanced adenoma	0.0200	(30)
From advanced adenoma to undiagnosed CRC I	0.0326	(31)
From undiagnosed CRC I to undiagnosed CRC II	0.2400	(32, 33)
From undiagnosed CRC I to CRC I follow-up	0.2000	(32)
From undiagnosed CRC II to undiagnosed CRC III	0.3600	(32, 34)
From undiagnosed CRC II to CRC II follow-up	0.2000	(32)
From undiagnosed CRC III to undiagnosed CRC IV	0.1750	(32, 34)
From undiagnosed CRC III to CRC III follow-up	0.6500	(32)
From undiagnosed CRC IV to CRC IV follow-up	1.0000	(32)
Death from other causes	0.0175	(35)
Death from CRC I follow-up	0.0218	Vital statistics and SHcsp follow-up data
Death from CRC II follow-up	0.0458	Vital statistics and SHcsp follow-up data
Death from CRC III follow-up	0.0994	Vital statistics and SHcsp follow-up data
Death from CRC IV follow-up	0.2028	Vital statistics and SHcsp follow-up data
Costs ($ per capita)*		
Cost for initial screening and colonoscopy	1,271.90	Questionnaire and official prices data
Treatments for advanced adenoma	1,108.82	Inpatient expense data
Treatments for CRC I	8,566.63	Inpatient expense data
Treatments for CRC II	10,554.70	Inpatient expense data
Treatments for CRC III	13,395.73	Inpatient expense data
Treatments for CRC IV	11,177.51	Inpatient expense data
Utility		
Normal	1.000	Assumption
Adenoma	0.871	(25)
Advanced adenoma	0.827	
Stage I CRC	0.829	
Stage II CRC	0.860	
Stage III CRC	0.814	
Stage IV CRC	0.738	
Discount rate		
Discount rate of costs	3%	(2, 3, 23, 28, 29)
Discount rate of life years gained	3%	(2, 3, 23, 28, 29)

*All costs converted into dollars using 2014–2016 mean exchange rate of USD $1 = RMB ¥ 6.3743.

Uncertainty

A one-way sensitivity analysis was performed on the model parameters: (1) Transition probabilities between health states: the transition probabilities from normal to adenoma, from adenoma to advanced adenoma, and between different CRC stages. (2) The costs for diagnosis and treatment: the costs of colonoscopy and treatment costs for the four CRC stages. (3) Discount rates. These explored the uncertainty of the model results due to important parameters, especially those not derived from program data. The substituted parameters used in the analysis were independently varied by ±25% from the base-case value. The results of the sensitivity analysis are reported in Table 5 and presented in a tornado diagram in Figure 4. A cost-effectiveness threshold was also used.

Results

Incremental cost-effectiveness

The estimates of cost and effectiveness of SHcsp are shown in Table 4. The total costs of the screening group and the no screening group were USD37.17 million and USD27.21 million respectively. The incremental costs for SHcsp were USD9.96 million.

After 25 years, a total of 187,377.7 LYs were cumulated in the screening group and 185,807.4 LYs were cumulated in the no screening group. Compared with no screening strategy, the SHcsp gained additional effectiveness of 1,570.1 LYs with extra costs of USD9.96 million. The ICER was $6,342.02 per LY gained.

Considering the health utility of patients, we also estimated the cost-utility of SHcsp. After 25 years, a total of 174,587.2 QALYs were cumulated in the screening group and 160,602.9 QALYs were cumulated in the no screening group. Compared with no screening, additional 13,984.3 QALYs were gained with same extra costs of USD9.96 million. Only USD712.08 was required for each QALY gained.

The Shanghai GDP in 2017 was US$ 19,866 per capita. The ICER of SHcsp was under Shanghai GDP per capita in 2017 and far below the threshold of three times the Shanghai GDP per capita (USD59,598). These results prove that SHcsp is highly cost-effective.

Sensitivity analysis

A one-way sensitivity analysis was performed on the relevant model parameters, as listed in Table 5. A tornado diagram graphically displays the results of one-way sensitivity analysis of the 14 parameters with their respective impacts on ICER (Figure 2).

TABLE 2 Survival rates and mortality of the four CRC stages.

	5-year survival rate	Annual survival rate	Mortality
CRC I	0.8957	0.9782	0.0218
CRC II	0.7912	0.9542	0.0458
CRC III	0.5924	0.9006	0.0994
CRC IV	0.3220	0.7972	0.2028

The one-way analysis demonstrates the robustness of the results of the cost-effectiveness analysis, indicating that our model was relatively insensitive to changes in parameter values. The most sensitive of the parameters was the discount rate, with a range of 0–5% leading to a change in ICER from USD1,360.84 to USD4,137.28 per LY gained. The costs for screening and treatment had relatively limited impacts on cost-effectiveness, such as the annual transition probabilities between health states. All the results were still under the threshold.

Discussion

This study demonstrates the notable cost-effectiveness of mass CRC screening for Chinese community residents. SHcsp brought benefits for 13,250 residents with more precancerous lesions, causing a higher detection rate of early stage CRC and providing the chance to prevent and treat CRC, which directly relieved the burden of disease for patients and society. In the long term, after the 25-year simulation, there was more health improvement and life years gained. The incremental cost-effectiveness ratio was USD6,342.02 per LY and USD712.08 per QALY gained, which was far below the threshold of USD59,598. The cost-effectiveness results of the base-case scenario were shown to be robust by sensitivity analysis.

China has only implemented CRC screening programs in a few cities. However, no economic evaluation of mass CRC screening has been performed. There are also limited studies that have evaluated completed programs globally (4, 9, 21). On the contrary, most of the economic evaluations of CRC screening have been based on simulative cohorts using parameters from the literature that are not appropriate for specific populations in other countries (3, 5, 23, 25, 26, 29, 31). Seizing the opportunity to analyse a long-term, large-scale, and well-finished program, our study aimed to analyse the cost-effectiveness of mass CRC screening programs in developing countries. Another advantage was the SHcsp data accessibility and integrity of other population health indicators in Shanghai, leading to more convincing results. Our study provides new evidence that mass CRC

TABLE 3 Costs for SHcsp and input costs in the Markov model.

	N	Total costs ($)	Per capita cost included in the model ($)
Costs for initial screening and colonoscopy allocated to the diagnosed patients	13,250	16,852,628	1,271.90
Initial screening	1,097,656	3,721,054	280.83
Colonoscopy	82,729	13,131,574	991.06
Treatments for advanced adenoma	745	826,071	1,108.82
Treatments for CRC I	766	4,814,446	8,566.63
Treatments for CRC II	478	3,704,700	10,554.7
Treatments for CRC III	492	4,835,859	13,395.73
Treatments for CRC IV	116	950,088	11,177.51

All costs converted into dollars using 2014–2016 mean exchange rate of USD $1 = RMB ¥ 6.3743.

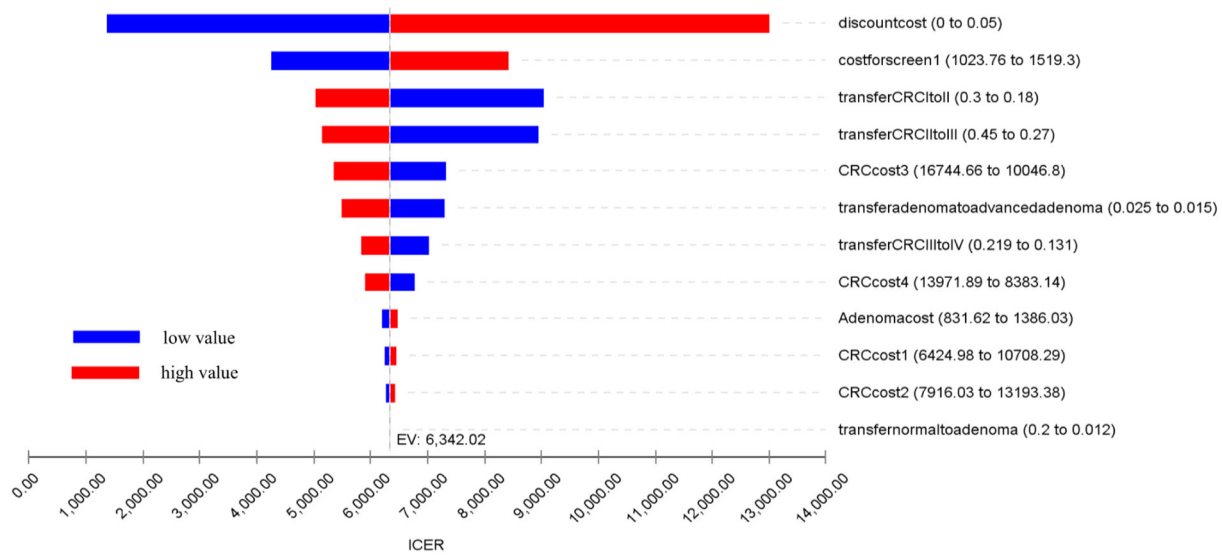

FIGURE 4
Tornado diagram of the results of the one-way sensitivity analysis.

screening has effective outcomes and economic influence in China.

Although there were false-positive results in practice, these residents' health conditions were not influenced by SHcsp, but all screening and colonoscopy expenses were included in the analysis. To directly and accurately reflect real-world effectiveness, our study focused on 13,250 diagnosed and treated patients. For the same reason, we did not make ideal model assumptions regarding such factors as the disease morbidity rate, colonoscopy compliance of patients with positive initial screening (2), or sensitivity and specificity of the screening tests (29), thereby reducing bias and distortion. Our model combined a decision tree, indicating the main results of the screening, with a Markov model of long-term health state transitions. The Markov model was established through careful consideration, and 15 health states might be closer to the natural disease progression of CRC (2, 3, 5, 23).

The transition probabilities between health states were calculated according to the actual incidence and mortality rates in Shanghai. These local and detailed information included data from the SHcsp follow-up database, the Shanghai Cancer Registry System of SCDC, vital statistics from SCDC, and clinical records from hospitals. The integrity of multiple local data resources, the initial distribution, and costs were more reliable and suitable than previous studies, which mainly used

simulative cohorts and data from other original studies (3, 5, 21, 23, 25, 26, 29, 31).

This study has several policy implications. Mass CRC screening programs are feasible, effective, and cost-effective for the Chinese population and in the current situation. The initial screening strategy combining FIT with RAQ proved to be scientific and suitable (18). These results should be generalisable to the Chinese population, because the clinical and cost parameters were mostly based on real-world data from the completed program (3, 25). Policymakers and healthcare providers in other regions should also use care when taking this local evidence into consideration (26, 29).

This study has a few limitations. First, like all model simulations, our model structures were simplified from the natural history of CRC. All treatments were regarded as radical treatment, so recurrences after treatment were not considered (21, 26, 31). Second, due to the limitations of available data, the probabilities of cancer progression were assumed to be equivalent in different ages and between the two groups, and the medians of treatment costs were used due to loss to follow-up of every treatment, leaving room for improvement (22). Last but not least, as other related studies have mentioned, it is difficult to determine transition probabilities without the basis of solid epidemic studies or pathological examination of colorectal adenoma and cancer, so some of the transition probabilities were derived from estimates in the literature (21, 31). For further research, basic epidemic studies, accurate follow-ups and registered data are required. In addition to direct costs, indirect costs should be measured to shed light on the comprehensive burden of CRC (5, 23, 25, 29), and investigations of patients' life condition and health-related utility should be conducted.

In conclusion, using real-world data from the completed program and a valid combined model, this study demonstrated that mass CRC screening, SHcsp during 2014–2016, was cost-effective compared to no screening, improving the general health state and relieving the disease burden. Mass CRC screening with a suitable strategy and optimized process is feasible, beneficial, and economical.

TABLE 4 Comparison of the cost effectiveness between SHcsp and no screening.

	SHcsp screening	No screening
Effectiveness		
Deaths from CRC	1,226	1,821
Deaths from other causes	4,067	3,831
Life years gained (LYs)	187,377.70	185,807.40
Quality-adjusted life years (QALYs)	174,587.20	160,602.90
Incremental life years (LYs)	1,570.1.10	–
Incremental quality-adjusted life years (QALYs)	13,984.30	–
Costs (million $)		
Total costs	37.17	27.21
Incremental costs	9.96	–
Incremental cost-effectiveness ratio		
Incremental costs/LY gained ($/LY)	6,342.02	–
Incremental costs/QALY gained ($/QALY)	712.08	–

TABLE 5 One-way analysis of the parameters in the Markov model.

Model parameters	Base-case	Sensitivity analysis		ICER($/LY)	
		Low value	High value	Low value	High value
Discount rate	3%	0%	5%	1,360.84	13,013.86
Costs for initial screening and colonoscopy per diagnosed patient					
Colonoscopy per diagnosed patient	158.73	119.05	198.41	4,251.19	8,432.84
Costs for treatments					
Advanced adenoma	1,108.82	831.62	1,386.03	6,210.49	6,473.55
CRC I	8,566.63	6,424.98	10,708.29	6,235.01	6,449.02
CRC II	10,554.70	7,916.03	13,193.38	6,262.05	6,421.98
CRC III	13,395.73	10,046.80	16,744.66	7,324.67	5,359.37
CRC IV	11,177.51	8,383.14	13,971.89	6,774.84	5,909.19
Transition probabilities (from – to)					
Normal-adenoma	0.016	0.012	0.020	6,342.02	6,342.02
Adenoma-advanced adenoma	0.02	0.015	0.025	7,306.69	5,478.46
Undiagnosed CRC I-undiagnosed CRC II	0.24	0.180	0.300	9,003.41	5,039.56
Undiagnosed CRC II-undiagnosed CRC III	0.36	0.270	0.450	8,958.52	5,145.85
Undiagnosed CRC III-undiagnosed CRC IV	0.175	0.131	0.219	7,025.71	5,837.66

Data availability statement

The original contributions generated for the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Author contributions

HJ and PZ contributed to the conception and design of the study under the supervision of WC and CF. KG, YG, and YS performed the data collection. PZ, KG, and DA conducted statistical analysis. PZ wrote the manuscript and revised as needed under the guidance of HJ and WC. WC and CF supervised the overall study and provided feedback throughout all stages. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Psychometric evaluation of the healthy aging activity engagement scale

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Objective: The aim of this study was to translate the Healthy Aging Activity Engagement Scale (HAAE) into Chinese and validate its psychometric properties in the middle-aged and elderly population.

Methods: A total of 424 middle-aged and elderly people were recruited from China's Jiangsu Province, Liaoning Province, Shandong Province, and Heilongjiang Province. Cronbach's α co-efficient, split-half reliability, and test-retest reliability were used to evaluate the reliability of the translated scale. Expert consultation was used to evaluate the content validity of the translated scale. Exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) were used to evaluate the structural validity of the scale.

Results: The Cronbach's α co-efficient of the Chinese version of HAAE was 0.965 and the Cronbach's α co-efficient of the dimensions ranged from 0.898 to 0.957. The split-half reliability was 0.807, and the test-retest reliability was 0.850. The content validity index of the scale (S-CVI) was 0.969. A total of three common factors were extracted from the EFA. The CFA validated the explored 3-factor structure, and the indicators were fitted well ($\chi^2/df = 1.393$, comparative fit index = 0.982, goodness- of- fit index = 0.911. Tucker-Lewis Index = 0.981 and root mean square error of approximation = 0.030).

Conclusion: The translated Chinese version of HAAE had suitable reliability and validity in the middle-aged and elderly population. The translated scale will be used to evaluate the level of healthy aging among middle-aged and elderly people in Chinese mainland. Furthermore, it also can provide some health advice for clinical patients.

KEYWORDS

aged, healthy lifestyle, disease prevention, healthy aging, factor analysis

Introduction

Aging of population is not only a problem in developed countries, but also in some developing countries. According to China's latest census, people aged 60 and above accounted for 18.7 % of the total population, of which 13.5% were aged 65 and above (1). With the increasing degree of population aging, Chronic diseases account for more prominent proportions of the elderly population. The occurrence of chronic diseases greatly affects their quality of life and increases the financial burden on the family. At the same time, studies have shown that older people are able to benefit from an

active lifestyle (2). Furthermore, psychological state has also become an important factor affecting health. Some scholars have pointed out that psychological stress has also become a contributing factor to the disease, and studies have shown that stress increases the incidence and severity of cardiovascular diseases, diabetes and obesity (3, 4). Combining a holistic lifestyle of healthy eating, regular exercise and stress reduction will improve quality of life and reduce cardiovascular and the occurrence of cancer (5, 6). Moreover, healthy lifestyle should not be vigorously promoted among older people, but should be promoted as early as possible. There are a number of other studies that have shown that obesity in the middle-aged population increases the incidence of cardiovascular disease as well as dementia (7, 8). The incidence of stroke and kidney disease in middle-aged people is also rising (9). Therefore, for middle-aged people, it is necessary to participate in a healthy aging lifestyle as soon as possible.

A healthy aging lifestyle are primarily about engaging in exercise, cognitive and social engagement, and reducing stress. Engaging in more physical activity can delay cognitive decline (10, 11). Physical capability and activities at older ages is not only an important aspect of a healthy life but also reduces the risk of pre-mature death (12). Moreover, broader social engagement can make older people feel more rewarded in their lives and it can reduce the risk of frailty of the elderly (12, 13). Meanwhile, the concept of healthy aging is affected by stress; stress increases the incidence of a range of chronic diseases later in life, such as CVD (14–17). Therefore, in the process of healthy aging, we must not only pay attention to physical exercise and reasonable diet structure, but also pay attention to some factors related to psychology (such as cognitive changes, stress, etc.).

Some questionnaires are able to assess the level of healthy behaviors in certain specific areas (such as stress, physical health, diet) (18). However, there is currently no scale that can comprehensively assess the level of individual participation in multidimensional healthy aging, especially among middle-aged and elderly people in China. Professor Maureen Schmitter-Edgecombe used traditional measurement analysis and Rasch modeling techniques to develop a Healthy Aging Activity Engagement scale (HAAE) and conducted validation in 2017 (19). In contrast to traditional scales, the HAAE scale is no longer a single assessment of a particular aspect of health behavior involvement; It comprehensively evaluates the healthy aging behavior of middle-aged and elderly people from multiple perspectives.

This study aimed to translate the HAAE into Chinese and validate its psychometric properties. To provide a tool for measuring the level of engagement in healthy aging among middle-aged and elderly Chinese population.

Methods

Study design and participants

The multicenter cross-sectional study was conducted in China from December 2021 to February 2022. A total of 424 participants were recruited using the convenient sampling method, which comes from China's Jiangsu Province, Liaoning Province, Shandong Province and Heilongjiang Province.Participants were selected from community. The sample size required at least three participants for each factor. If possible, it also can obtain larger sample sizes (18). In this study, to ensure the accuracy of exploratory factors analysis and confirmatory factor analysis, a minimum of 10 participants were required for each item. Included participants should meet the following criteria: (1) Age $\geq$ 45 years. (2) The length of time of residence in the local area$\geq$6 months. (3) Participants were able to understand the questionnaire and completed it independently. (4) People who gave informed consent and voluntarily participated in this study. People with severe physical and mental illnesses were excluded, such as impaired consciousness, severe physical activity disorder, advanced malignancy, and inability to take care of themselves.

Instruments

General demographic characteristics questionnaire

A questionnaire on general demographic characteristics was designed by reading the literature related to this study prior to conducting the survey. It mainly includes five items: age, gender, education level, occupational status, and self-assessment lifestyle health.

Healthy aging activity engagement scale

This study used the Healthy Aging Activity Engagement Scale developed by Professor Maureen and others in 2017 (19). The scale consists mainly of 32 items. Scoring was made using the Likert 5-level scoring method, with scores ranging from 1 to 5. The scoring criteria were as follows: 1 = Strongly disagree, 2 = disagree, 3 = Somewhat agree, 4 = agree, 5 = Strongly agree. The scale mainly evaluated the engagement of middle-aged and elderly people in healthy aging from three dimensions: biologic health, social and cognitive strategies and health safeguard behaviors. A higher score indicated a higher level of participation in healthy aging. Both the reliability and validity of the translated scale were within acceptable limits.

Procedures

Translation and cultural adaptation

With the consent of Professor Maureen, the scale was translated into a Chinese version and cultural adaptation was implemented. The original scale was translated using the Brislin double-translation model (20). First, two Master's Chinese students majoring in English translated the scale into Chinese. After negotiation, a Chinese version of the scale was finally formed. Then, two native English-speaking Chinese teachers reverse-translate the translated content without reading the original scale. Three nursing professors were invited to assess whether the translated items were in line with Chinese language expression habits. The researchers made modifications based on the results of the expert review. Finally, a scale suitable for measuring the level of participation in healthy aging activities among middle-aged and elderly people in China was formed. Twenty middle-aged and elderly people were selected for pre-survey to validate whether the items for the translated scale were easy to read and understand. The results showed that it took about 6 min to complete the scale and the content can be understood.

Data collection procedure

The researchers collected questionnaires from four provinces, respectively. A total of 450 middle-aged and elderly people were recruited in the community using the convenient sampling method. Four hundred and forty people volunteered to participate in, cross-sectional surveys were used on these populations. All questionnaires were completed anonymously. After excluding invalid questionnaires, 424 questionnaires were collected. The effective recovery rate of the questionnaires was 96.36%.

Data analysis procedure

Items analysis

In items analysis, divide the total score of the scale into two parts: the first 27%was high-score group and the last 27% was poor-score group. By comparing the relationship between the two to judge the reliability and discernment of the translated items. Using the critical ratio to judge whether the difference between the items was statistically significant. Cronbach's α co-efficient if item deleted was used to judge whether items for the translated scale needed to be deleted.

Reliability analysis

Reliability refers to the consistency or repeatability of a measurement (21). The internal consistency of the scale was evaluated using the Cronbach's α co-efficient and split-half reliability. Items were divided into equal groups according to the parity principle and calculate the relationship between the two to represent the split-half reliability. The time interval between two measurements in the elderly is 2 weeks (22). After 2 weeks, a total of 40 people were selected from the original population and measured again to reflect the test-retest reliability. It reflected the consistency of the two tests.

Validity analysis

The evaluation of the content validity was assessed by seven experts using the Delphi Expert Consultation method. Its evaluation results were expressed in terms of the content validity index of the items (I-CVI) and the content validity index of the scale (S-CVI). Each item was divided into 4 levels (from inappropriate to appropriate), which was scored separately by each expert. The value of I-CVI is equal to the number of experts scored 3 or 4 points divided by the total number of experts participating in the score. S-CVI is the average of the I-CVI value for each item.

The EFA and CFA were used to explore and verify the potential factor structure of the scale, respectively. The 424 participants were divided into two groups of the same number according to the principle of randomization. Each group of 212 people were tested by EFA and CFA, respectively. The scale is suitable for factor analysis only when the KMO > 0.6 and the Bartlett spherical test was statistically significant ($P < 0.05$). Amos (23.0) software was used to validate the consistency of the model structure with the explored factor structure. CMIN/DF, comparative fit index (CFI), goodness- of- fit index (GFI) and Tucker- Lewis Index (TLI) were used to represent the fit of the model. The closer the CMIN/DF value is to 0, the better fit of the model (23, 24). When the values of CFI, GFI, and TLI are ≥ 0.9, it means that the model fits well (23, 25). RMSEA is used to evaluate the degree of unfitting of a model, and the closer its value is to 0, the better its fit (23, 25).

Ethical approval

Each participant completed an informed consent form. The information in each questionnaire was protected. Moreover, This study was approved by the Ethics Committee of the Jinzhou Medical University and the process followed the code of ethics provided by the Ethics Committee.

Results

Demographic information

A total of 424 participants who met the criteria were included: 205 females (48.3%) and 219 males (51.7%). The

TABLE 1 General demography data ($n = 424$).

Items	Group	*n*	%
Age	45–50	50	11.8
	50–55	38	9.0
	55–60	70	16.5
	≥60	266	62.7
Sex	Male	219	51.7
	Female	205	48.3
Educational level	Primary school and below	145	34.2
	Junior high school	172	0.6
	High school and junior college	99	23.3
	University and above	8	1.9
Occupation	Work	114	26.9
	Retire	256	60.4
	Unemployment	54	12.7
Lifestyle	Poor	58	13.7
	Not bad	183	43.2
	Good	183	43.2

elderly group aged 60 and above accounted for 62.7%.Middle-aged population accounted for 37.3%. 60.4% of the population was in retirement. Only 13.7 percent rated themselves as having a poor lifestyle. The remaining demographic information can be found in Table 1.

Item analysis

The critical ratio was used to indicate the degree of differentiation of the item. When critical ratio ≥ 3, it means that the item is better distinguished. In this translated scale, the critical ratio of the 32 items were ranged from 8.354 to 15.468. It indicated that the differentiation of each item was within acceptable range. The Pearson Correlation Analysis method was used to analyze the relevance between the items and the total score. The relationship between the items and the scale was moderately correlated ($r = 0.547$–0.688, $P < 0.05$). After the items were deleted, the Cronbach's α value for each item ranged from 0.964–0.965. The value of each item was lower than the total Cronbach's α value of the scale (0.965). Therefore, each item can be accepted without deletion.

Reliability analysis

The total Cronbach's α co-efficient of the scale was 0.965. Cronbach's α co-efficient for each dimension ranged from 0.898 to 0.957. Moreover, the scale had a split-half reliability of 0.807. After 2 weeks, 40 people were randomly selected to obtain a test-retest reliability of 0.850. It can be concluded that the translated scale had a suitable reliability (Table 2).

Validity analysis

Content validity analysis

The content validity of the translated scale was evaluated by 7 experts. Each item was separately scored by each expert. The range of the I-CVI was 0.857–1.000 and the value of S-ICV was calculated to be 0.969. The translated scale had the suitable content reliability (Table 3).

Exploratory factor analysis

In this study, KMO = 0.960, Bartlett's spherical test was statistically significant ($\chi^2 = 4{,}819.743$; $P < 0.001$). This results indicated that the translated scale was suitable for factor structure analysis. A total of three factors with eigenvalues > 1 were extracted and a total of 63.448% of the data discrepancies were explained. Screen plot (Figure 1) further confirmed the existence of the 3-factor structure. Furthermore, the results of EFA showed that each factor load was > 0.4. Therefore, all items were retained. The specific results can be found in Table 4.

Confirmatory factor analysis

Confirmatory factor analysis was used to validate whether the relationship between each item and the factor is consistent with the hypothesis. In this study, the results of the validation showed that the fittings were good. The values of the indicators were: $\chi^2/df = 1.393$, CFI = 0.982, GFI = 0.911. TLI = 0.981, and RMSEA = 0.030. It showed that the translated scale factors correspond well to the corresponding items.

Discussion

Healthy behavior is an important aspect of healthy aging (24). There are indeed some scales that assess healthy behavior of older adults (26, 27), But they were limited to a specific aspect, such as exercise. There is currently no tool that can measure the level of participation of middle-aged and elderly populations in healthy aging from multiple angles. The HAAE scale applied not only to the elderly, but also to middle-aged people. The development of the disease is showing a trend of rejuvenation. Similarly, Middle-aged people are also at risk of aging, Participation in healthy aging is imminent. Furthermore, the application of the HAAE scale in middle-aged people can greatly promote the dissemination of healthy aging knowledge, let them know the importance of preventing the occurrence

TABLE 2 Reliability analysis for Chinese version of the HAAE.

The scale and its dimension	Cronbach's Alpha	Split-half reliability	Test-retest reliability
The HAAE	0.965	0.807	0.850
Biological health	0.957		
Social and cognitive strategies	0.954		
Health safeguard behaviors	0.898		

TABLE 3 Item-level CVI for the Chinese version of the HAAE.

HAAE items	Expert1	Expert2	Expert3	Expert4	Expert5	Expert6	Expert7	I-CVI
1	2	3	3	3	3	3	3	0.857
2	3	4	4	4	3	4	4	1.000
3	4	3	2	4	4	4	4	0.857
4	4	4	3	3	4	3	3	1.000
5	3	4	4	4	4	3	3	1.000
6	3	4	4	2	4	3	3	0.857
7	3	3	4	3	3	2	3	0.857
8	3	4	4	3	4	3	4	1.000
9	4	4	4	4	3	3	3	1.000
10	3	4	3	3	3	4	4	1.000
11	4	4	4	4	3	4	3	1.000
12	4	3	4	3	3	4	3	1.000
13	4	3	4	4	3	4	3	1.000
14	3	3	4	4	4	3	3	1.000
15	4	3	3	3	3	4	4	1.000
16	4	4	4	4	4	3	3	1.000
17	3	3	3	4	4	4	3	1.000
18	4	4	4	3	4	3	4	1.000
19	3	4	3	4	3	3	4	1.000
20	3	4	2	3	3	3	3	0.857
21	3	3	4	3	4	3	3	1.000
22	3	3	3	3	4	4	4	1.000
23	3	3	4	4	4	4	3	1.000
24	3	3	3	2	4	4	3	0.857
25	3	4	4	3	4	3	4	1.000
26	3	4	4	4	3	3	4	1.000
27	3	3	3	4	3	4	3	1.000
28	3	4	4	3	4	3	4	1.000
29	4	3	4	3	4	3	4	1.000
30	4	3	4	3	3	4	3	1.000
31	3	4	3	4	3	4	4	1.000
32	3	2	4	3	4	3	3	0.857

of diseases as soon as possible, and reduce the occurrence of diseases after they enter old age. Therefore, this is an important tool for both the elderly and middle-aged to measure their own health participation.

The translation of the scale followed the Brislin double-translation model (20). The process mainly consists of two parts: translation and reverse-translation. In order to ensure the translated statement was simple, clear and easy to understand, the "in the past seven days" in each item was adjusted in the description at the head of the table. In addition, the "4 servings (1½—1 cup per serving) of fruits and vegetables" mentioned in the original scale item 4, In order to localize its expression, it was

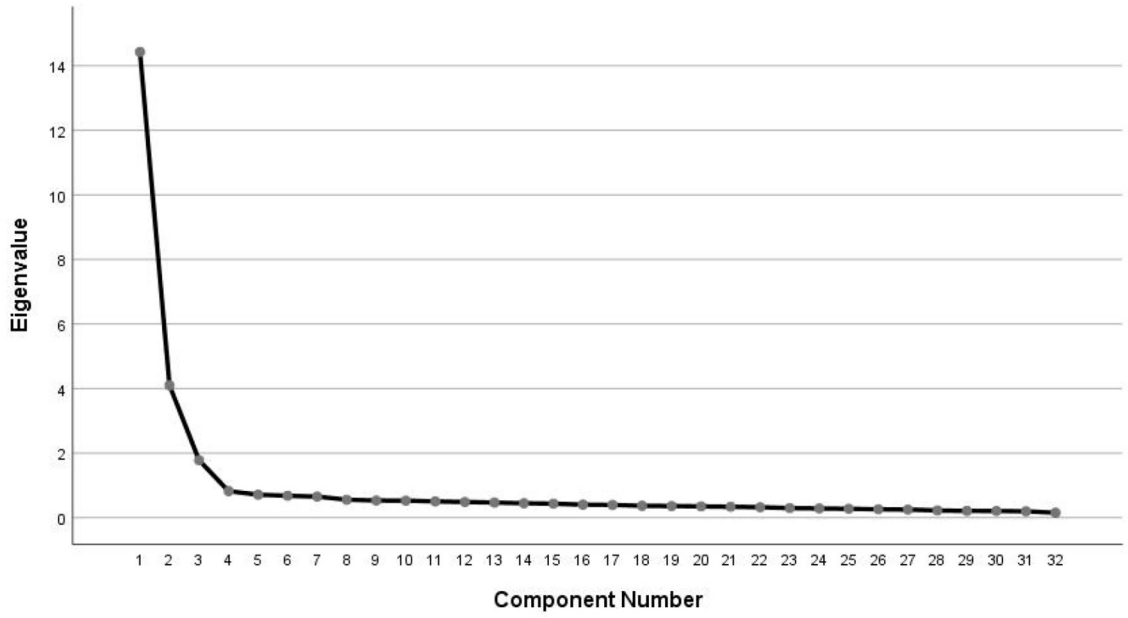

FIGURE 1
Screen plot of exploratory factor analysis for Chinese version of the HAAE.

finally changed to "400 g fruits and vegetables" through literature review and expert correspondence. Three nursing specialists were invited to review the items of the translated scale. Finally, the items in the Chinese version of the HAAE scale were concise and easy to understand. By comparing the change in reliability after the deletion of items, it was concluded that 32 items were acceptable.

In this study, the reliability and validity of the Chinese version of the HAAE scale were examined. The I-CVI and S-CVI of the translated scale were higher than reference value (28). The three-factor structure extracted by EFA was consistent with the original scale (18), which can explain 63.448% of the variation and each item factor load was > 0.4.

At the same time, the CFA validate the degree of fit of the scale, the correlation co-efficients between the latent variables were all within the acceptable range (<0.7), and the distinction between the dimensions was good. The translated scale had a Cronbach's α co-efficient of 0.965, which was higher than the original scale (18). In addition, both split-half reliability and test–retest reliability were acceptable (>0.8), and the translated scale had suitable stability.

Limitations

This study had the following limitations: Firstly, there was no distinction between middle-aged and elderly people. Because of the influencing factors of the level of engagement in healthy aging activities in the two populations were different. Secondly, because of only selecting people who meet the requirements of some areas. There is some bias in this study in population selection.

Conclusions

The translated HAAE scale had good reliability and validity. It was well used among middle-aged and elderly people in China after cultural adaption. Aging is the trend of Chinese population development. It can provide a measurement tool for the middle-aged and elderly population in China. The HAAE scale can be used to measure the extent to which they are involved in a healthy lifestyle. In addition, it can strengthen the health awareness of middle-aged and elderly people and promote the spread of healthy aging patterns.

Implications

Healthy lifestyle is particularly important in the middle-aged and elderly population, which are related to the incidence of future diseases and the quality of life in later years. Therefore, it is very meaningful to assess their level of

TABLE 4 Factor loadings of exploratory factor analysis for the healthy aging activity engagement scale.

Item	Factor1	Factor2	Factor3
1	0.781	–	–
2	0.735	–	–
3	0.698	–	–
4	0.732	–	–
5	0.729	–	–
6	0.701	–	–
7	0.744		–
8	0.771		–
9	0.774		–
10	0.727		–
11	0.758		–
12	0.744		–
13	0.658		
14	0.720		
15	0.699		
16	–	0.758	–
17	–	0.734	–
18	–	0.764	–
19	–	0.779	–
20	–	0.797	–
21	–	0.770	–
22	–	0.760	–
23	–	0.748	–
24	–	0.784	–
25	–	0.773	–
26	–	0.703	–
27	–	–	0.708
28	–	–	0.713
29	–	–	0.748
30	–	–	0.733
31	–	–	0.651
32	–	–	0.721

engagement in healthy aging. The translated HAAE scale will be used to assess the level of engagement in healthy aging in Chinese middle-aged and elderly population and make targeted recommendations.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

TL completed the writing of this article. HZ put forward important revision suggestions and made corresponding modifications for this article. LK played a key role in part of the data collection. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Effect and mechanism of reading habits on physical and mental health among the elderly: Evidence from China

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Responding to an aging society worldwide and ensuring the physical and mental health of the elderly are important problems that need to be addressed. Thus, this study aimed to improve the quality of providing the spiritual and cultural needs of the elderly and study the internal transmission of reading habits and its effect on the physical and mental health of the elderly. Using the data from China's comprehensive social survey in 2018, this study applied the Probit model and ordinary least squares method to comprehensively estimate the influence of reading habits of the elderly on their physical and mental health. Stepwise regression and bootstrap method were combined to explore the influencing mechanism, and an instrumental variable method was used to solve endogeneity problems. Results indicate that the reading habits of the elderly have a significantly positive effect on their own physical and mental health. Social activity is the positive conduction path, whereas social justice perception and learning willingness are the negative conduction path. Among low-income families, agricultural workers, and the elderly whose household registration is in rural areas, the benefits of reading to the body and mind are more significant. After dealing with endogeneity problems and a series of robustness tests, the conclusion of this paper still holds. Finally, reference policy suggestions are proposed for the follow-up active aging policy, such as promoting reading for all, organizing various social activities, formulating active pension policies for the elderly, and allocating more public resources for vulnerable elderly groups.

KEYWORDS

reading habits, elderly, physical and mental health, influencing mechanism, China

Introduction

With the growing elderly population worldwide, the health problems of the elderly have become the focus of many countries. Good health will not only improve the quality of life of the elderly, but also slow down the burden and pressure on families and countries and ensure the stable development of society. According to the World Health Organization, health not only refers to the absence of disease or weakness in a person's body, but also includes the integrity of an individual's ability in physiological,

psychological, and social adaptation. In existing literature on the physical and mental health of the elderly, scholars mostly discuss the physical and mental health of the elderly from the aspects of social security, physical exercise, and medical improvement (1–4). However, only a few discuss the improvement of the physical and mental health of the elderly from the perspective of cultural embedding. Reading, as a complex creative spiritual production activity, could maintain the physical and mental health of the elderly.

In China, the problem of an aging population is pronounced. Based on the data of the seventh census released by the China Bureau of Statistics, in 2020, the number of elderly people over 60 years old in China has reached 260 million, accounting for 18.7%, and the number of elderly people over 65 years old has reached 190 million, accounting for 13.5%. These figures have reached the United Nations Organization's demarcation standard for population aging (5). In addition, the education level and cultural accomplishment of the elderly are constantly improving. Based on the data of the seventh census, among the elderly over 60 years old, 36.69 million have high school education or above. This group has increased by 131.6% compared with the statistics 10 years ago. The significant improvement of the education level indicates the significant improvement of spiritual and cultural needs of the elderly. In this context, China has actively echoed the concept of "active aging" proposed by the WHO and the strategy of "Healthy China" (6). In the strategic action, the needs of the aging population must be met while promoting economic and social development from the perspective of cultural construction and social governance and actively responding to population aging with Chinese characteristics. In the concept of "productive aging," Robert advocates that the aging group should not be viewed as weak. The elderly is not a burden to families. On the contrary, the elderly can achieve their own value through reading and lifelong learning and contribute to society while meeting their spiritual and cultural needs (7, 8).

Current research on the influencing factors of the physical and mental health of the elderly has been comprehensive and in depth. It covers living habits, Internet use, sleep quality, diet quality, physical activity, family intergenerational support, personal ability, social welfare, social economy, social participation, and social support (9–16). The existing research has made a comprehensive observation on the influencing factors of physical and mental health. Although it provides an effective direction for policy practice, it also has shortcomings. First, previous studies focus on the personal characteristics, health awareness, and social roles of the elderly. They seldom focus on the spiritual and cultural needs of the elderly. They lack attention to the endogenous motivation of reading among the elderly from the practical level and ignore the benefits of reading habits to the realization of self-worth and their effect on the physical and mental health of the elderly. Second, in-depth discussion on the internal influencing mechanism of reading habits on physical and mental health is scarce. Many studies focus on the surface phenomenon of whether the influencing factors are significant, but they fail to focus on the causal relationship and conduction path among variables. At present, the aging and overall education level of the elderly are constantly improving; thus, understanding the relationship between them and their internal mechanism is important. Finally, little attention has been given to the urban–rural heterogeneity of the elderly. Consistent with the development characteristics of urbanization, urban residents will have greater advantages in family income, education, and medical resources than rural residents. Such disparity will affect the physical and mental health of the elderly. In developing countries such as China, the heterogeneity of urban and rural elderly groups is significant. Therefore, the urban and rural perspective must be considered when examining the influencing factors of physical and mental health of the elderly.

This study uses the national dataset of the 2018 China Comprehensive Social Survey (CGSS2018) led by Renmin University of China for empirical analysis. The Probit model and ordinary least squares (OLS) method are used to estimate the influence of reading habits on physical and mental health of the elderly. Stepwise regression and the bootstrap method are used to explore the internal influencing mechanism of reading habits, and the instrumental variable (IV) method is used to solve endogeneity problems. From the perspective of urban and rural areas, this study tries to explain the heterogeneity of reading effect in the elderly groups with different family incomes, nature of job, and household registration by using interactive item regression.

The marginal contributions of this study are as follows. First, taking the reading habits of the elderly as explanatory variables enriches the multi-dimensional perspective research on the influencing factors of the physical and mental health of the elderly. Such an approach reveals the causal relationship among the variables, which has important practical significance in active aging. Second, on the basis of theory and experience, this study obtains structural analysis of the influencing mechanism of reading habits among the elderly on physical and mental health and quantifies the size and direction of its specific transmission effect. These findings can provide reference suggestions for the precise formulation of subsequent practical policies. Third, the results of this study can help policy makers formulate targeted support policies for resource-based vulnerable groups such as rural areas or low-income household to achieve stable development.

The structure of this paper is as follows: The second part presents the theoretical basis and research hypothesis, including the theoretical analysis and hypothesis of influence effect, influence mechanism, and heterogeneity. The third part discusses the data and methods, including the variables and econometric models of this study. The fourth part provides the empirical results and discussion. The explanatory results

include influence effect, influence mechanism, robustness test, and heterogeneity analysis. The fifth part is the conclusion.

Theoretical analysis and research hypotheses

Influencing mechanism hypothesis

Traditional reading behavior, as an important way to relieve loneliness and realize self-worth, is important to old people. Based on the socialization theory, socialization is subdivided into four parts in accordance with the different life cycle characteristics of individuals, in which the old age stage corresponds to re-socialization (17). The theory of re-socialization of the elderly holds that individuals in old age can still adapt to the society and maintain their physical and mental health by enriching their own behavior such as reading (18). In ancient Greece, reading was used as a psychotherapy tool, which was applied in practice. In the nineteenth century, the concept of reading therapy emerged, which was used to maintain the mental health of people (8). Afterward, Jacobs et al. found that reading activities can significantly reduce the mortality rate of male elderly people and positively affect the health of the elderly through a longitudinal study of community residents in Jerusalem (19). In addition, Zhang adopted the matching method of controlling mixed variables and found that illiteracy in the elderly population has adverse effects on their physical and mental health. The level of physical and mental health has decreased by 19.9%, which confirms the gain effect of reading. However, Zhang does not further discuss the influence of reading habits on the elderly (20). "Reading is beneficial to physical and mental health" is a deeply rooted traditional concept. However, whether good reading habits have a significantly positive effect on the physical and mental health of the elderly must be verified on the basis of the actual situation.

Therefore, hypothesis 1 is proposed: the reading habits of the elderly will have a positive effect on their physical and mental health.

In exploring the influencing mechanism of reading habits of the elderly on physical and mental health, multi-dimensional investigation and analysis must be conducted. First, studies have shown that reading activities can enrich spirituality, kill time, and promote self-development. However, spiritual abundance and the loneliness of reality often produce a strong sense of gap and increase the inner social interaction needs of an individual, thereby stimulating individual's motivation for social interaction (21). Wang found a significantly positive correlation between individual reading activities and social activities (22). Fuller found that reading behavior provides opportunities for people to participate in social activities and interpersonal interactions, which can promote identity or emotional connections among participants (23). Moreover, studies have shown that participating in social activities has a positive effect on the physical and mental health of the elderly (24, 25). Havighurst proposed in the activity theory that the elderly should not give up social activities simply because of their age, but they should keep certain social activities to maintain their active state, thereby achieving self-satisfaction and enhancing their physical and mental health (26). The theory of social interaction also advocates that the interaction between social interaction and individuals has a significant effect on their own social actions, and this social interaction is beneficial to their physical and mental health (27). Therefore, the reading habits of the elderly will stimulate their social communication needs, thereby improving their physical and mental health.

Second, the theory of social cognition emphasizes that people can adjust to environmental changes, and people's thoughts and emotions are greatly influenced by external environmental factors and their social cognition, which form the basis for new cognition and emotion (28, 29). Moreover, the higher their perception of social justice, the more positive social cognition and emotion will be produced, which will have a significantly positive effect on the health status of the elderly (30). However, with the continuous development of the digital age, information and news dissemination is gradually characterized by huge data volume and decentralization. The role of strict news censorship and screening in traditional media is slowly diminishing; vicious social events are being reported one after another, and media is becoming sensationalized. The negative bias theory in social psychology indicates that people tend to focus on negative information (31). Therefore, in such an environment, people gradually edify the sense of injustice to the whole society, resulting in weak individual social trust. Compared with other age groups, the elderly group has lower psychological security and weaker social suitability (32), which directly leads to a more significant sense of social injustice after reading relevant news. Therefore, the reading habits of the elderly may reduce their own perception and evaluation of social justice, which may have a negative effect on their physical and mental health.

Finally, studies have shown that keeping good reading habits in the elderly will significantly improve their willingness to learn (33). However, the separation theory proposed by Prasad advocates that the elderly are no longer suitable for high-pressure and high-intensity jobs because of their weak physical function; hence, they should carry out leisure and entertainment activities safely and spend their old age in peace (34). In addition, Yongduk concluded that the learning stress of the elderly has a direct and significant effect on health and quality of life, and the excessive willingness of the elderly to learn will cause excessive mental consumption and inhibit their physical exercise opportunities, thereby adversely affecting their health status (35). Therefore, the reading habits of the elderly can enhance their willingness to learn, but they will have a negative effect on their physical and mental health.

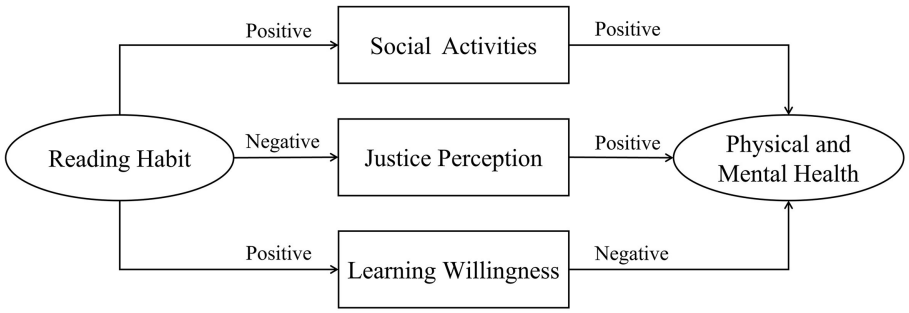

FIGURE 1
Mechanism model of the influence of reading habits on physical and mental health of the elderly.

On the basis of the abovementioned inferences, this study proposes Hypothesis 2: Social activities are the positive influencing mechanism of reading habits on the physical and mental health of the elderly, whereas social justice perception and learning willingness are the negative influencing mechanism. Figure 1 shows the specific transmission mechanism.

Although the research hypothesizes that social activities, social justice perception, and learning willingness may play a conductive role in the influencing mechanism of reading habits of the elderly on their physical and mental health, other influencing paths may play an intermediary role to explain these effects. Therefore, this study is exploratory in nature.

Heterogeneity hypothesis

A series of studies shows differences in family income and job nature between urban and rural residents apart from household registration (36–38). Focusing on the analysis of the influencing mechanism, the differences between urban and rural characteristics may lead to the heterogeneity of the influence of reading habits on the physical and mental health of the elderly.

First, most previous studies on reading habits hypothesized that families with different economic income will show differences in reading (39, 40). Although reading has shown the characteristics of digital transformation, it does not mean that you do not need to pay a certain amount for your own reading interest. However, low-income families may not have extra money to support their interest in reading, particularly for most elderly people who have lost their economic income. Second, compared with non-agricultural workers, rural workers cannot devote more leisure time and energy to reading activities because of their physical strength and energy demand. Over time, developing good reading habits becomes difficult. Moreover, relevant studies show that agricultural workers have longer working years. Even after passing the statutory retirement age, they will continue to work in agriculture until their physical condition cannot sustain manual labor (41). Finally, the elderly registered in rural areas have a deep-rooted traditional family concept, and they will take the initiative to take care of children from generation to generation and give their children more support to complete their own work tasks (42). Therefore, their leisure time will be occupied, and reading activities will be difficult to carry out. However, these internal and external constraints in reading activities of the abovementioned elderly groups promote the strong effect of reading activities on themselves and produce higher marginal utility, thereby making the gain effect of reading on physical and mental health more significant.

Therefore, hypothesis 3 is proposed: the positive effect of reading habits on physical and mental health is evident in low-income families, agricultural workers, and rural elderly groups.

Data and methods

Data sources

This study used the survey data of Chinese General Social Survey (CGSS) in 2018 to ensure the representativeness and universality of the research results. CGSS is a national survey led by China Survey and Data Center of Renmin University of China. The CGSS system comprehensively collected data from society, community, family, and individual. The survey adopted multi-layer random sampling and conducted a multi-dimensional survey of social conditions in the whole country at the micro level. The survey samples covered more than 10,000 families in all provinces, municipalities, and autonomous regions of Chinese mainland. It aimed to explore issues of great scientific and practical significance. Therefore, the data had national and comprehensive characteristics, good reliability, validity, and academic recognition. Compared with other databases, the data were more national, comprehensive, and random, and they had good reliability and validity and academic recognition. In the cross-sectional survey data of CGSS in

2018, a total of 12,787 valid samples were recovered. Based on the research needs, the samples of non-elderly people and the samples with missing information in the research scope were eliminated. Finally, 3,079 valid samples were obtained, which belonged to the large sample category and had no significant difference from the proportion composition of demographic variables in the original data.

Selection of main variables

Explained variable

The explained variable of this study is the physical and mental health level of the elderly. In this study, according to the definition standard of the elderly by the WHO, the sample data over 60 years old were selected for analysis. The physical and mental health level was quantified by the comprehensive evaluation of Chinese residents' physical and mental health level, and the actual physical and mental conditions of individuals were measured from a subjective perspective. In particular, participants were asked the following questions: "What do you think is your current health status?" "In the past 4 weeks, how often your health problems affected your work or other daily activities?" "How often do you feel depressed in the past 4 weeks?" The values of the three items were in accordance with the standards of Richter's five-point scale. During data processing, the rules of option assignment were as follows: the larger the value, the higher the health level of the interviewee. Finally, the three abovementioned evaluation scores were summed up to form a comprehensive index of the physical and mental health level, ranging from 3 to 15. The higher the value, the higher the physical and mental health level of the respondents.

Explanatory variables

The core explanatory variable of this study was the reading habits of the elderly, which is assessed through the question "Have you often engaged in reading/newspaper/magazine activities in your spare time in the past year?" (including but not limited to traditional paper reading methods). The options were "Never," "Several times a year or less," "Several times a month," "Several times a week," and "Everyday," which are assigned to 1–5, respectively. The higher the value, the higher the individual reading frequency. Therefore, this study explores whether the frequent reading activities of the elderly people lead to their better physical and mental health.

Mediating variables

Social activity (S_Activity). The social activity variable was measured by the item "Have you socialized/visited frequently in your free time in the past year?" The options include "Never," "Rarely," "Sometimes," "Often," and "Very Frequent," which are assigned to 1, 2, 3, 4, and 5, respectively. The higher the value, the more frequent the interviewee engages in social activities.

Social justice perception (J_Perception). The perceived variables of social justice were measured by the question "In general, do you think today's society is fair?" Quantitative measurement is carried out. Respondents can select from the following five options: "Totally unfair," "Relatively unfair," "not fair but not unfair," "relatively fair," and "Completely fair," which were assigned to 1, 2, 3, 4, and 5, respectively. The larger the value, the fairer the respondents think the society is today.

Willingness to learn (L_Willingness). The willingness to learn variable was measured by the item "Have you often recharged your learning in your free time in the past year?" The options include "Never," "Rarely," "Sometimes," "Often," and "Very Frequent," which are assigned to 1, 2, 3, 4, and 5, respectively. The higher the value, the stronger respondents' willingness to learn.

Control variables

This study controlled a series of variables, including individual characteristics and family characteristics, to reduce the estimation errors caused by missing variables (43–45). Individual characteristic variables include gender (Female), education level (Education, illiterate = 0, primary school = 1, junior high school = 2, high school or the same nature = 3, junior college = 4, undergraduate and above = 5), religious belief (Religion), age (Age), urban household registration (Urban), natural logarithm of annual income (in yuan), whether the respondent is a party member (CPC), whether the respondent participates in elections (Vote), and social class (S_Class, 1–10). Family characteristic variables include whether the father works in an office or an institution (F_Unit), whether the parents are party members (P_CPC), and the educational level of the parents (P_Education, taking the highest educational level). In addition, this study used provincial dummy variables to eliminate the influence of regional differences on the estimation results (46).

Descriptive statistics

Table 1 presents the descriptive statistics of related variables, which shows the distribution information of each variable. After deleting missing values and outliers, 3,079 samples can be used for regression analysis. The statistical results show that the average physical and mental health level of the explained variables was 10.498, indicating that most of the elderly were physically and psychologically healthy, and they were in the upper-middle level as a whole. The mean value of the explanatory of variable reading habits was 1.984, whereas the median value was only 1. This result indicated that the

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TABLE 1 Descriptive statistics.

Variable	*N*	Mean	P50	Sd	Min	Max
Health	3,079	10.498	11	2.649	3	15
Reading	3,079	1.984	1	1.431	1	5
Female	3,079	0.520	1	0.500	0	1
Education	3,079	1.514	1	1.290	0	5
Religion	3,079	0.122	0	0.328	0	1
Age	3,079	69.259	68	7.273	60	118
Urban	3,079	0.486	0	0.500	0	1
Income	3,079	8.087	9.306	3.554	0	13.487
CPC	3,079	0.147	0	0.354	0	1
Vote	3,079	0.605	1	0.489	0	1
S_Class	3,079	4.163	4	1.734	1	10
F_Unit	3,079	0.121	0	0.326	0	1
P_CPC	3,079	0.099	0	0.299	0	1
P_Education	3,079	0.647	0	1.016	0	5
S_Activity	3,079	2.729	3	1.144	1	5
J_Perception	3,079	3.328	4	1.016	1	5
L_Willingness	3,079	1.681	1	1.030	1	5

overall reading willingness of the elderly was low, and more of them remained at the level of occasional reading. Therefore, this study must explore the gain effect of reading habits on physical and mental health. In addition, the statistical results showed that most of the elderly were confined to the background of the times at that time. Their education level was generally low, with an average value of 1.514 and a median value of only 1, which was below the junior high school level. The gender ratio of the old people in the sample was relatively balanced, with an average age of 69.259. Moreover, of the included old people, 12.2% had religious beliefs, and 48.6% had urban household registration, indicating that the majority of the old people had rural household registration. Furthermore, the average logarithm of the existing economic income of the elderly was 8.087 (about RMB 3,252). Approximately 14.7% of the elderly were members of the Communist Party of China, and 60.5% have participated in voting in villages or neighborhood committees. The average education level of their parents was also low, which was lower than the primary school level. In general, the descriptive statistical results of all variables were consistent with the real situation in China, and multicollinearity was not a serious issue after testing.

Setting of the measurement model

This study constructed the following quantitative models based on the abovementioned literature review and theoretical framework to explore the influence of reading habits on the physical and mental health of the elderly:

$$Health = \beta_0 + \beta_1 \cdot Reading + \gamma X + \varepsilon$$

where Health is the explained variable "physical and mental health," Reading is the explained variable "reading habit," and X represents other control variables and model residuals; denotes model residuals; β_0, β_1, γ are the parameter and coefficient to be estimated. The following econometric models are constructed to explore the potential mediating effect of the willingness to read on the physical and mental health of the elderly:

$$\begin{aligned} Health = {} & \beta_0 + \beta_1 \cdot Reading + \beta_2 \cdot S_Activity + \beta_3 \cdot \\ & J_Perception + \beta_4 \cdot L_Willingness + \gamma X + \varepsilon \end{aligned}$$

where S_Activity, J_Perception, and L_Willingness denote the social activities, social justice perception, and willingness to learn of the elderly, respectively, to test the transmission mechanism of the influence of reading habits on the physical and mental health of the elderly. Given that the explained variables were ordered variables with values ranging from 3 to 15, the ordered response model was adopted to reflect the influence degree of each key explanatory variable in the model on the key explanatory variables. Considering the large range of values of the interpreted variables, which are similar to continuous variables, estimating and explaining the marginal effects were difficult. Therefore, this study was in accordance with Acemoglu and other practices, and it regarded the interpreted variables as continuous variables for model estimation (47). In addition, the double tests of ordered Probit and OLS were used to ensure the robustness of the estimation results.

Empirical results and discussion

Baseline regression

The results of ordered Probit and OLS regression are shown in Table 2. In reducing the estimation error caused by missing variables and directly comparing the control effects of control variables, Table 2 lists the regression results of uncontrolled variables, controlled individual characteristic variables, and all control variables one by one. The results show that ordered Probit and OLS regression methods have passed the significance test of 5%, which verifies that reading habits have a significantly positive effect on the physical and mental health of the elderly. A comparison of the model results shows that when the control variables are included in the model, the influence of reading habits on the physical and mental health of the elderly shows a downward trend. Thus, incorporating the control variables into the regression model is necessary. However, in contrast to

TABLE 2 Effect of reading habits on physical and mental health of the elderly.

	(1)	(2)	(3)	(4)	(5)	(6)
	Probit			OLS		
Reading	0.098***	0.036**	0.037**	0.253***	0.093**	0.096**
	(0.014)	(0.016)	(0.016)	(0.034)	(0.037)	(0.037)
Female		−0.113***	−0.112***		−0.268***	−0.264***
		(0.039)	(0.039)		(0.093)	(0.093)
Education		0.077***	0.081***		0.185***	0.193***
		(0.020)	(0.020)		(0.047)	(0.048)
Religion		−0.084	−0.083		−0.221	−0.218
		(0.062)	(0.062)		(0.149)	(0.149)
Age		−0.014***	−0.015***		−0.035***	−0.036***
		(0.003)	(0.003)		(0.006)	(0.007)
Urban		0.068	0.066		0.230*	0.226*
		(0.055)	(0.055)		(0.132)	(0.132)
Income		0.019***	0.019***		0.046***	0.046***
		(0.007)	(0.007)		(0.016)	(0.016)
CPC		−0.030	−0.024		−0.102	−0.088
		(0.057)	(0.057)		(0.132)	(0.132)
Vote		0.039	0.039		0.101	0.101
		(0.040)	(0.040)		(0.096)	(0.096)
S_Class		0.112***	0.112***		0.261***	0.262***
		(0.012)	(0.012)		(0.029)	(0.029)
F_Unit			0.052			0.115
			(0.063)			(0.146)
P_CPC			−0.095			−0.216
			(0.064)			(0.152)
P_Education			−0.015			−0.035
			(0.022)			(0.053)
_cons				10.795***	11.516***	11.609***
				(0.191)	(0.538)	(0.549)
Provincial effect	Yes	Yes	Yes	Yes	Yes	Yes
R^2	0.022	0.038	0.038	0.101	0.167	0.168
N	3,079	3,079	3,079	3,079	3,079	3,079

*Standard errors in parentheses, * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$.

column (2) to column (3) or column (5) to column (6), the regression coefficients of reading habits only change slightly. This result indicates that the problem of missing variables in this model is not serious, and the regression results obtained are robust. Finally, the regression coefficient in column (6) suggests that when other conditions remain unchanged, the physical and mental health level of the elderly will increase by 0.096 units for every unit of improvement in reading habits. Therefore, Hypothesis 1 holds true.

The regression results of control variables are consistent with previous studies, which verify the rationality of the regression model. For example, men have a higher level of physical and mental health than women, which is consistent with Fabrizio's gender difference research conclusion (48). In the regression results, the elderly with a high education level, high income, and high social class have better physical and mental health, which is consistent with the conclusion of previous studies (39, 40). Age has a significantly negative effect on the physical and mental health level of the elderly. Compared with the older elderly, the physical quality of the younger elderly is poor. Their mental health suffers from excessive discomfort and loneliness, thereby affecting the self-perceived health score, which is consistent with the conclusions of Lorem et al. (43). However, the estimation coefficients of family characteristic variables do not show a significant intergenerational influence as preset probably because the policy of encouraging more children was implemented in the early days of the New China. Hence, the families from this generation of elderly people were mostly "multi-child families," which led to relatively less energy and painstaking efforts of parents in family of origin, and the influence of natural family environment on their physical and mental health was not significant.

Endogenous analysis

The endogeneity of explanatory variables must be tested to avoid the estimation error of regression coefficient in the model caused by the endogeneity of explanatory variables, and if it exists, then it must be effectively controlled (49). Considering the endogenous test method of explanatory variables, the traditional Hausman test method follows the assumption of homogeneity of variance, which will fail in the case of heteroscedasticity. Therefore, the robust Durbin–Wu–Hausman (DWH) test in the case of heteroscedasticity is adopted in this process, and the results of DWH F are both significant at the 1% level. Therefore, the explanatory variable Reading is considered as an endogenous explanatory variable (50). Its endogeneity problems are primarily derived from the following aspects: First, although the variables that have an effect on the physical and mental health of the elderly have been controlled in the model estimation, some gaps may still exist. Considering that the data used in this study are cross-sectional, some unobservable variables with continuity and time characteristics may have been omitted and included in the disturbance term of the model, resulting in the correlation between explanatory variables and disturbance term, as well as estimation errors. Second, a bidirectional causal relationship may exist between explanatory variables and explained variables. Although this study focuses on exploring the influence of reading habits on the physical and mental health of the elderly, the physical and mental health level of the elderly will also affect their own reading habits. For example, the elderly with poor physical and mental state will be uninterested in all activities or may be ill in bed and unable to

carry out reading activities, resulting in the forced reduction of reading frequency.

Therefore, this study adopted the method of IVs to avoid the endogeneity problems of reading habits. Based on the findings of Evans et al. (51), the number of institutions and collection of public libraries in this province are used as tool variables of reading habits. The data are obtained from the 2019 Statistical Yearbook of Chinese Culture and Related Industries jointly edited by the National Bureau of Statistics and the Central Propaganda Department. The yearbooks contain statistical data related to cultural industries in the whole country, provinces, autonomous regions, and municipalities directly under the Central Government in 2018. On the one hand, Chen and other scholars have proven that different provinces in China will have different cultural backgrounds because of the implementation of policies, which creates conditions for multiculturalism, whereas the elderly groups in the same province have cultural background correlation to a certain extent (52). Given the characteristics of China's times and the independent development of various provinces, old people who often live in the same province have similar cultural backgrounds and reading habits. Great differences were also observed among different provinces. Often, major cultural capitals focus on the strategy of "reading for all," thereby building public reading space and enriching library collection and making residents in the whole province develop better reading habits. Therefore, the correlation condition of IVs selection is satisfied. On the other hand, as external environmental variables, the number of institutions and book collections of public libraries will not directly affect the physical and mental health level of the elderly; thus, they meet the exogenous IVs, which can be included in the model for the next stage of analysis (49).

After determining the IVs, they were included in the original regression model and re-verified by conducting IV-OProbit and 2SLS. The regression results are shown in Table 3. First, in the IV-Oprobit test, the error correlation in the equations of the two stages is significantly not 0 at the 1% level, which indicates that the reading habits of explanatory variables are endogenous in the model. Second, given that the Cragg–Donald Wald F statistics of the coefficients of the two IVs in the first stage of regression are 27.484, which exceeds the threshold of 10, a strong correlation between IVs and endogenous variables is proven. Moreover, the model does not have a weak IV problem (53). Furthermore, the significance value ($P = 0.101$) obtained by over-recognition test failed to pass the 5% significance standard, which proves that the exogenous IVs in the econometric model are valid. The regression coefficient of IVs in the first stage shows that the number of book collections will positively affect the reading frequency of the elderly. However, increasing the number of public library institutions on the basis of controlling the book collections will reduce the reading interest of the elderly. Finally, the Reading coefficient in the second stage

TABLE 3 Endogenous test of the influence of reading habits on physical and mental health.

	(1) First stage	(2) Second stage (IV-Oprobit)	(3) Second stage (2SLS)
Reading		0.570***	1.707***
		(0.071)	(0.354)
Mechanism	−0.002***		
	(0.000)		
Collection	0.000***		
	(0.000)		
Control variables	Yes	Yes	Yes
Durbin χ^2	30.223***		
Wu-Hausman F	30.374***		
Cragg-Donald Wald F	27.484***		
Corr(e1,e2)		−0.616***	
Wald chi-square		781.94***	379.54***
N	3,079	3,079	3,079

*Standard errors in parentheses, * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$, **Control variables include individual characteristics and family characteristics, which are the same in the following table.

model remains significantly positive, which can confirm the significantly positive effect of reading habits on the physical and mental health level of the elderly. A comparison of the regression coefficients of column (2) and column (3) shows that the positive effect of reading habits on physical and mental health of the elderly is underestimated, and the influence coefficient is significantly improved compared with the model estimation results before incorporating IVs. Overall, Hypothesis 1 remains significantly valid after eliminating the endogeneity of explanatory variables by conducting the IV method.

Mechanism analysis

This study included three intermediary variables from Persico's argumentation ideas, namely, S_Activity, J_Perception, and L_Willingness, in the benchmark regression model to explore the influencing mechanism of reading habits of the elderly on their physical and mental health. This study determined whether the transmission direction and influencing path existed by observing the change direction and degree of explanatory variable coefficients (54). The criteria for determining the forward conduction path are shown in Figure 2. If the independent variable X positively affects the mediator variable M, then the mediator variable M has the same positive effect on the dependent variable Y, and if this variable achieves positive transmission, then it is a positive conduction path. The negative transmission between the paths also forms a positive conduction path. After the incorporation of positive conduction

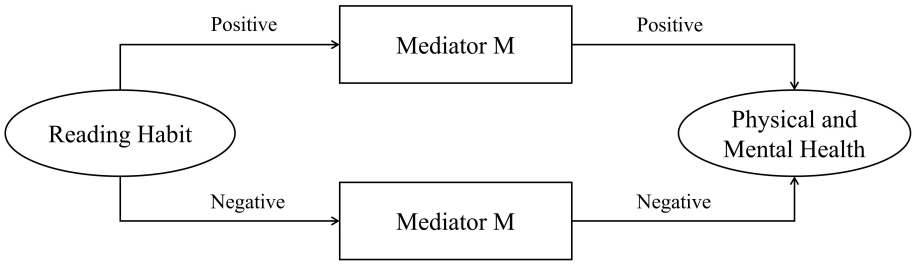

FIGURE 2
Positive conduction path schema of mediator variable M.

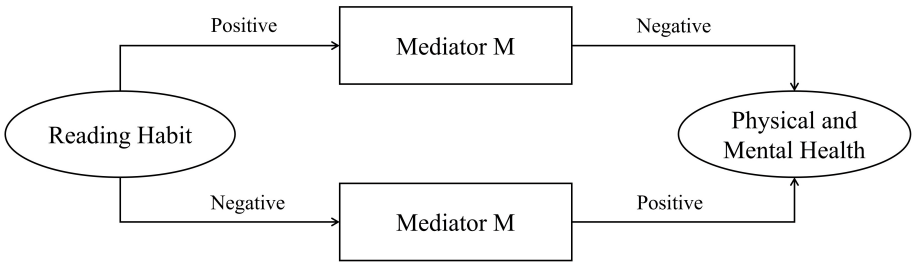

FIGURE 3
Negative conduction path schema of mediator variable M.

path into the mechanism, the direct effect of explanatory variable X on explained variable Y will be weakened, and the regression model coefficient will be reduced. However, if the role of intermediary variables is inconsistent before and after, then it is a negative conduction path (Figure 3). After being included in the model, the regression coefficient of the explanatory variable X will increase. Based on this finding, this research process carries out 2SLS estimation of the influencing mechanism, which not only eliminates the influence of endogenous explanatory variables on the estimation results, but also avoids the problem of accurately estimating the regression coefficient in IV-OProbit estimation. Apart from stepwise regression, this study explores whether the transmission path is valid (55). The specific test results are shown in Table 4. Columns (1) to (4) are the regression results, and column (5) is the final regression result after the two reverse conduction paths are included in the model. After completing the verification process of stepwise regression through 2SLS estimation, referring to Davidson's research, the bootstrap method is used to verify the mediating effect. The random sampling times are set to 2,000 times, and a 95% confidence interval is constructed. The confidence interval adopts bias-corrected and percentile test standards simultaneously to ensure the robustness of the final result (56).

The regression results present the following points: First, as shown in columns (2), (3), and (4), in the econometric model after controlling variables, the regression coefficients of

TABLE 4 Impact mechanism test (2SLS).

	(1) Health	(2) Health	(3) Health	(4) Health	(5) Health
Reading	1.707***	1.682***	1.864***	2.226***	2.429***
	(0.357)	(0.356)	(0.376)	(0.515)	(0.547)
S_Activity		0.134**			
		(0.053)			
J_Perception			0.275***		0.283***
			(0.061)		(0.067)
L_Willingness				−1.093***	−1.207***
				(0.311)	(0.330)
Control variables	Yes	Yes	Yes	Yes	Yes
N	3,079	3,079	3,079	3,079	3,079

*Standard errors in parentheses, * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$.

S_Activity and J_Perception are significantly positive, whereas the regression coefficients of L_Willingness are significantly negative. This result confirms the previous hypothesis of the influencing path. More frequent social activities and the perception of today's society can significantly improve the physical and mental health level of elderly individuals to a certain extent. However, the stronger the learning willingness of elderly individuals, the lower their physical and mental

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TABLE 5 Regression results of mediated variables.

Mediating variable	(1) S_Activity	(2) J_Perception	(3) L_Willingness
Reading	0.052***	−0.033**	0.380***
	(0.016)	(0.017)	(0.018)
R^2	0.014	0.032	0.228
N	3079	3079	3079

*Standard errors in parentheses, * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$.

health level. Second, looking at the coefficient of Reading, the core explanatory variable in column (2) decreases, whereas column (3) and column (4) increase. This result indicates that social activities have a positive transmission mechanism in the influence of reading habits on the physical and mental health of the elderly, whereas social justice perception and willingness to learn show negative transmission mechanisms. Compared with the benchmark regression coefficient value of column (1), the estimation coefficient of column (2) decreases by 0.025 or 1.5%, indicating that the positive conduction mechanism explained 1.5% of the influence of reading habits on the physical and mental health level of the elderly. In column (3) and column (4), the estimated coefficient increases by 9.2 and 30.4%, respectively, and the combined increase of the two negative conduction paths is 42.3% from column (5). Therefore, the negative mediating effects of social justice perception and willingness to learn are 9.2 and 30.4%, respectively. On the contrary, the comprehensive mediating effects of the two negative transmission mechanisms are 42.3%. Third, combined with the path judgment of the transmission mechanism and regression results, reading habits have a positive effect on social activities and willingness to learn and a negative effect on social justice perception. This inference is verified when three intermediary variables make orderly Probit regression on Reading (Table 5).

A comparison of the results verified by the Bootstrap method (Table 6) shows that the confidence intervals of indirect and direct effects of the three mediation paths do not contain 0, which indicates the mediation effect. All of them are partial mediation effects, which proves that the mediation path is significant. Therefore, the conclusion that the mediating effects are significant is robust, and Hypothesis 2 holds true.

Robustness test

Double verification methods are used to ensure the validity of the research results in the aforementioned research process and the robustness of the research conclusions. In addition, this study conducted a series of robustness tests. The specific regression results are shown in Table 7. Columns (4) and (8) are the final estimation results of the model after adding tool variables, which is convenient for reference and comparison of regression coefficients.

First, the explained variables are divided. The explained variable (Health) is composed of three items reflecting physical and mental health. Although such items can reflect the degree of individual physical and mental health, there is a gap between the emphasized health characteristics and specific performance. In the model regression, the explanatory variables only have a significant effect on one aspect. However, they show a significant final result on the overall physical and mental health level because of the comprehensive summary of indicators. Hence, the physical health level and mental health level of the elderly population serve as explanatory variables of the model for regression analysis to exclude the possibility of a significant local effect resulting in significant overall effect. The physical health level is assessed by the aforementioned question "What do you think is your current physical health status?" "In the past 4 weeks, how often your health problems affected your work or other daily activities?" The two items are summarized, and the assignment form is the same as the standard of the explained variable (Health) in the previous article. Finally, an ordered variable (PHealth) with a value ranging from 2 to 10 is constructed. Similarly, the level of mental health was determined by the item "How often have you felt depressed in the past 4 weeks?" An ordered variable (MHealth) with a value range of 1–5 is constructed, which is included in the econometric model and regression analysis carried out by IV-OProbit and 2SLS methods. Finally, the regression results in Table 7 can be obtained. The significance values of the coefficients pass the standard of 1%, which indicates that reading habits will have a significantly positive effect on the physical health and mental health of the elderly, and verify the robustness of the research results.

Second, the measurement standard of main variables has been changed. In the benchmark model, the research primarily uses the index of self-evaluation of physical and mental health to measure the physical and mental health level of the elderly, which is subjective. In this process, we refined "the number of visits with physiological or psychological diseases in the past year" into a new explained variable (OHealth) to ensure the robustness of the research results. The larger the value, the more visits, the worse the physical and mental health level, thereby achieving the objective measurement of individual's physical and mental health level. The final regression results show that reading habits have a significantly negative effect on the objective visits of the elderly at the 1% level. Under the objective indicators, the research conclusion that reading habits have positive effects on the physical and mental health of the elderly remains stable.

Finally, the data source was changed. In the aforementioned research process, the latest survey data published by China Comprehensive Social Survey in 2018 was used for analysis to test whether the research results are sensitive to research samples and survey time. Therefore, the data of China

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TABLE 6 Mediation effect test.

Mediating effect	Product of coef.			95% confidence interval			
	Estimate	SE	Z	bias-corrected		percentile	
				Lower	Upper	Lower	Upper
Indirect effect							
S_Activity	0.012	0.005	2.565**	0.004	0.022	0.003	0.021
J_Perception	−0.006	0.004	1.712*	−0.014	−0.000	−0.013	−0.000
L_Willingness	0.052	0.017	3.034***	0.019	0.086	0.018	0.085
Direct effect							
S_Activity	0.136	0.037	3.746***	0.062	0.201	0.063	0.202
J_Perception	0.150	0.036	4.196***	0.084	0.225	0.080	0.217
L_Willingness	0.092	0.041	2.261**	0.013	0.171	0.014	0.172

*Standard errors in parentheses, * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$.

TABLE 7 Robustness test: Replacement of variables.

Explained variable	(1) PHealth	(2) MHealth	(3) OHealth	(4) Health	(5) PHealth	(6) MHealth	(7) OHealth	(8) Health
	IV-Oprobit				2SLS			
Reading	0.556***	0.466***	−0.565***	0.570***	1.260***	0.447***	−0.564***	1.707***
	(0.076)	(0.090)	(0.082)	(0.071)	(0.270)	(0.123)	(0.162)	(0.357)
Control variables	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Corr(e1,e2)	−0.598***	−0.515***	−0.636***	−0.616***				
N	3,079	3,079	3,075	3,079	3,079	3,079	3,075	3,079

*Standard errors in parentheses, * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$.

Comprehensive Social Survey in 2017 are selected to re-estimate the econometric model. During verification, the number of institutions (Mechanism) and collection of public libraries in that year are still used as tool variables of reading habits, and the model regression is carried out by IV-OProbit and 2SLS methods. The final results show that the positive effects of reading habits on the physical and mental health of elderly individuals and the influencing paths remain significant in Table 8. Therefore, the previous research conclusions are robust.

Further discussion: Heterogeneity of reading effect

Given the differences of different family incomes, different work natures, and different registered permanent residence caused by different material living standards or concepts, reading habits of the elderly may have different effect on their physical and mental health (32–36). Hence, we carry out interactive regression and explore the heterogeneity of the influencing effects among samples by analyzing the interaction items between grouping variables and core explanatory variables. This approach allows us to analyze the influencing effects of willingness to read on the physical and mental health of the elderly from multiple angles (57).

First, the sample is divided into low-income families and high-income families with the average household income as the threshold, and the dummy variable Poor_family (0= high-income families, 1= low-income families) is generated. Second, the samples are divided into agricultural workers and non-agricultural workers based on the nature of work. When assigning variables, specific assignments are made in accordance with the nature of the current work. However, people who have no current work and only worked for agriculture are defined as agricultural workers because a large proportion of the elderly have retired and left their posts. In addition, by analyzing the sample characteristics of "never worked," we find that most of them are housewives in rural areas, who undertake all the housework in the family and follow the social division of labor of "men plow and women weave" in Chinese traditional culture. According to Wang and Liu, they can be regarded as "Silent Reserves" in society, which can be

TABLE 8 Robustness test: Replacement of data source.

	(1) Health	(2) Health	(3) Health	(4) Health	(5) Health
Reading	1.141***	1.100***	1.232***	1.324***	1.432***
	(0.325)	(0.321)	(0.332)	(0.419)	(0.427)
S_Activity		0.224***			
		(0.048)			
J_Perception			0.204***		0.197***
			(0.051)		(0.052)
L_Willingness				−0.593**	−0.650**
				(0.249)	(0.254)
Control variables	Yes	Yes	Yes	Yes	Yes
N	2943	2943	2943	2943	2943

*Standard errors in parentheses, * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$.

TABLE 9 Heterogeneity analysis.

Interaction effect	(1)	(2)	(3)	(4)	(5)	(6)
	Probit			OLS		
1.Poorfamily#c.Reading	0.065**			0.175***		
	(0.027)			(0.063)		
1.Farming#c.Reading		0.084**			0.186**	
		(0.038)			(0.087)	
1.Rural#c.Reading			0.066*			0.162**
			(0.035)			(0.080)
Control variables	Yes	Yes	Yes	Yes	Yes	Yes
Provincial effect	Yes	Yes	Yes	Yes	Yes	Yes
R^2	0.045	0.039	0.038	0.195	0.171	0.169
N	3,060	3,079	3,079	3,060	3,079	3,079

*Standard errors in parentheses, * $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$.

regarded as an agricultural production activity (58). Therefore, people who have never worked are classified as agricultural workers. This produces the dummy variable Farming (0 = non-agricultural workers, 1 = agricultural workers). Based on the household registration definition, the sample is divided into rural and urban people, and the virtual variable Rural is generated (0 = urban household registration, 1 = rural household registration).

Finally, the explained variables are interacted with the dummy variables generated above to explore their possible adjustment to the main effect. Table 9 shows the coefficients and significance of specific interaction items. Thus, the positive effect of reading habits on the physical and mental health of the elderly is more significant in low-income families, agricultural workers, and rural household registration groups. Hypothesis 3 is proven true.

Conclusions, policy implications, and limitations

Conclusions

Using the data of China Comprehensive Social Survey in 2018, Probit model, OLS model, IV method, and bootstrap method, this study analyzes the influence of reading habits of the elderly on their physical and mental health and its mechanism in detail. The following main conclusions are drawn.

First, the reading habits of the elderly have a significantly positive effect on their physical and mental health, that is, the better the reading habits of the elderly, the better their physical and mental health will be. Second, from the perspective of the influencing mechanism, the social activities, social justice perception, and willingness to learn of the elderly play an important intermediary role in the influencing path of reading habits on physical and mental health. Social activities are the positive transmission path, whereas social justice perception and willingness to learn are the negative transmission path. Third, the influence of the reading habits of the elderly on their physical and mental health is heterogeneous in many dimensions, such as family circumstances, work attributes, and household registration, that is, reading habits will show a stronger beneficial effect on the physical and mental health of the elderly from low-income families, working in agriculture, and having household registration in rural areas. Fourth, after dealing with the endogenous problem of explanatory variables through IVs or after subdividing the explanatory variables, replacing the main variables, and replacing the database, the regression results in the econometric model remain positive and significant, and the conclusions are robust.

Policy implications

Based on the current background of "world aging," the abovementioned research conclusions provide relevant policy enlightenment. The potential policy suggestions are as follows.

First, reading for all must be promoted, and the continuous reading habits of the elderly must be developed. Governments at all levels should carry out relevant reading promotion activities and corresponding publicity work, improve the availability of public reading, and stimulate the reading interest of the elderly. However, the principle that reading should also be controlled must be established to prevent excessive willingness to learn from damaging the physical and mental health of the elderly.

Second, a variety of social activities can be organized to encourage the elderly to participate in the community and integrate into society. As the main undertaker of public services, the government should be keenly aware of the psychological demands of the elderly for social activities and respond positively. Therefore, we should actively carry out relevant social

and league building activities to satisfy the social desires of the elderly in reading and improve their physical and mental health.

Third, special active pension policies must be formulated for the elderly to increase their sense of social justice. Governments at all levels should formulate targeted active pension policies and focus on these policies. Moreover, we should focus on the procedural justice and scientific rationality of working methods in the implementation of policies to weaken the sense of social injustice produced by the elderly and gradually eliminate its negative effect on the physical and mental health of the elderly when building a prosperous society.

Fourth, more public resources must be allocated to vulnerable elderly groups, and the heterogeneous influence of physical and mental health of urban and rural elderly groups must be bridged. In addition, the government should focus on "cultural poverty alleviation" by constructing more public libraries in rural areas and giving subsidies and corresponding assistance to households in some areas. We should also consider the humanistic care for the elderly and organize basic cultural publicity activities and reading assistance for them to achieve "cultural poverty alleviation," thereby generating effective benefits for their physical and mental health.

Limitation

This study has limitations. In the course of our research, the self-rated health level of the elderly is considered as the core explanatory variable. Although a large number of studies have shown that the self-rated health status has a good prediction and evaluation effect on personal health, the subjective possibility when applying causal path inference is strong, which will affect the final estimation result. In addition, given the limitation of cross-sectional survey data, we failed to make a dynamic survey on the influence of reading habits, which may omit variables with continuous characteristics. We can comprehensively explore the relationship between reading habits and physical and mental health of the elderly by using panel data or randomized controlled experiments.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: http://cgss.ruc.edu.cn.

Author contributions

WZ presented the ideas for this paper, developed the methodology, wrote the theoretical analysis, results, discussions, and conclusions. YZ provided theoretical guidance throughout the process, grasped the overall writing direction, and revised and edited the entire manuscript. JW provided methodological guidance and reviewed and edited the content. All authors have read and agree to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Improving health and social care services for slum-dwelling older adults: Perspectives of health professionals

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Background: Besides confronting the challenges of a growing older population, developing countries are dealing with limited resources and infrastructure, to ensure good health and social care services. One of these developing countries facing these challenges is Ghana. The healthcare system in Ghana currently does not have specialized geriatric services and is funded through the National Health Insurance Scheme (NHIS), private insurance companies and an out-of-pocket expenditure system. Social care services are important in improving Quality of Life (QoL) as it helps in building and strengthening relationships while also keeping slum-dwelling older adults active. There are various challenges with the health and social care of older adults in slums and practical ways to improve these have not been explored among the providers of this care.

Aims: This study, therefore, aimed to explore (1) the views of health professionals on older slum-dwelling adults' health and social care needs, access, and use, and (2) recommendations for improving access to health and social care services among slum-dwelling older adults.

Method: A qualitative exploratory descriptive approach was used among health professionals by conducting a focus group discussion (FGD) and interviews. A semi-structured interview guide was used to collect data from each participant.

Results: A total of 27 participants took part in the study. In the analysis of transcripts, 3 themes and 14 subthemes were conceptualized. Financial difficulties, queueing issues, distance to health facilities, health illiteracy and negative attitude of health professionals were identified as some barriers to the utilization of formal healthcare services. Social care services were described as non-existent, not structured, and having limited resources to cater for attendants. The health professionals also provided recommendations for improvement.

Conclusion: Health professionals in this study discussed barriers to access and use of health and social care services. Addressing these barriers is essential to improve the use of formal health and social care services and diminish health inequity among older adults.

KEYWORDS

health care service, social care services, slum dwellers, older adults, health professionals

What is known

- Barriers such as financial challenges, health illiteracy, long distances to services, long waiting times in healthcare facilities, and poor attitude of health professionals.

What study adds

- Formal social care services appeared to be next to non-existent.
- Available social care services are not structured.
- Recommendations for government agencies and NGOs to partner to provide formal social care services.
- Considerations for telehealth in slums to provide services for older adults.

Introduction

Adequate and sufficient healthcare and social services contribute to the quality of life (QoL) of older individuals and need to be present to promote healthy living (1, 2). Globally, societies are aging, and this is also the case for developing countries. Besides facing the challenges of a growing older population, developing countries are dealing with limited resources and infrastructure, to ensure good health and social care services. One of these developing countries facing these challenges is Ghana.

Ghana is a lower-middle-income country (according to the World Bank country classifications) with a total population of about 29.6 million inhabitants. Approximately 976,000 (3.2%) of the population are older adults (60 years and over). It was projected in 2013, that Ghana's older adult population will reach 2.5 million (7.2%) by 2025 and 6.3 million (11.2%) by 2050. As aging is often associated with frailty, multimorbidity and handicaps (3, 4), many older adults need help and support.

The healthcare system in Ghana currently does not have specialized geriatric services and is funded through the National Health Insurance Scheme (NHIS), private insurance companies and an out-of-pocket expenditure system (5–7). The NHIS is open to all Ghanaians, and one must be registered to enjoy its benefits. For formal workers, registration in the NHIS is free. Non-formal and private workers must pay a fee for NHIS registration and must renew their membership every year (5–7). As has been outlined by various authors, this is one of the deficits of the NHIS (8–10). Many people living in slums are part of this group of non-formal workers. Due to their lack of financial resources, they are often unable to pay the NHIS fee, and therefore, they often lack health care insurance. What also makes healthcare insurance less attractive is that most of the health conditions experienced by older adults are not being covered. For example, most cancer treatments, hearing and optic aids, as well as prostheses and physiotherapy, are not paid for by the NHIS (11, 12). As a consequence, many older adults living in Ghanaian slums do not have healthcare insurance. As they are often unable to pay for healthcare themselves, they usually do not receive the required care and support they need and are highly dependent on relatives.

A population in Ghana particularly vulnerable to this lack of access to care and support are older adults living in slums. Slums are characterized by uneven walkways, poor ventilation, improper housing structures, lack of water supply and poor sanitary conditions. As postulated by previous studies, slum environments as mentioned above may negatively impact the health and QoL of older adults (13–16). Therefore, older slum-dwellers in Ghana represent a particularly vulnerable population, who need adequate formal healthcare services.

However, access and utilization of formal healthcare services for Ghanaian older slum dwellers are problematic. Next to the already mentioned problems related to the insurance scheme, the first reason for this are the financial constraints of older adults in slums. Older adults living in slums used to be either farmers, fishermen or petty traders in their working lives and these professionals do not benefit from any formal pension schemes (9). Therefore, at 60 years and over, they possibly experience financial difficulties if there is no continual financial support from their jobs or relatives.

Largely, the services are not free for older adults below the age of 70 years. Considering that the general life expectancy is 64 years old, there is only a small group (those who live above

Abbreviations: FGD, Focus Group Discussion, NHIS, National Health Insurance Scheme.

70 years), benefiting from these free healthcare services (11). As stated earlier, the NHIS does not reimburse health facilities for services provided for most health conditions of older adults as it is not part of the insurance package. Therefore, a large group (older adults between 60 and 69 years old) still must pay for services that are not affordable for them (9).

The second reason for lack of access and utilization is that slums are usually situated rather far away from formal health care services (17, 18) and this is also the case in Ghana. As described in a study by Attafuah et al. (under review) on the health and social needs of older adults living in slums, participants stated that health facilities are not in the vicinity and make it difficult for patronage. Proximity to formal health care has been reported to be one of the hindrances to healthcare utilization (17, 18), not only in Ghana (19, 20) but also in other countries like Iran (21), Dhaka (22), and Indonesia (23).

The third reason is that older slum dwellers are often health-illiterate (24, 25). By health literacy, we mean the extent to which these older adults have the skills and available resources to access, recognize, consider, and use health information and services to make informed decisions regarding their health (26). As Nutbeam (27) explained, health literacy influences an individual's health behavior and is crucial to empowerment and a good QoL (28–30). The health literacy of older adults in slums is mostly very poor, which makes older adults' resort to spiritual healing. As described by Attafuah et al. (under review) most older adults living in Ghanaian slums trust traditional medicine more than evidence-based practices provided by formal care services.

The last reason for the lack of healthcare use is older adults argue that it seems as if health professionals in Ghana, often have a bad attitude toward older adults (30, Attafuah et al., under review). Not giving priority to older adults, not addressing them politely, and talking harshly to them were some bad attitudes and behavior mentioned by slum-dwelling older adults. All these factors taken together influence the access and use of health services by older slum dwellers negatively (20, 21, 31, 32). Therefore, it is important to see how the healthcare needs of the older slum dwellers can be met more appropriately, and how access to care can be improved.

Besides looking at the use of and access to healthcare services, it is also important for slum-dwelling older adults to be able to use social services. Social services such as counseling, health education, interaction with peers, and engaging in mind development games are important and meaningful for older adults and could be provided at a center in the community. Social care services are important in improving QoL as it helps in building and strengthening relationships while also keeping slum-dwelling older adults active. However, social services are few to non-existent in slums in Ghana (33, 34). A few day-care centers have been opened in some parts of Accra, the capital city. However, the fees that must be paid to make use of these services are not affordable to older adults in the slums.

A previous study by Attafuah et al. (under review), showed older slum-dwelling adults' perceptions of their health and social needs. Following up on that study, this study is seeking the views of professional caregivers regarding the current and future access to health and social care services of these older adults.

This study, therefore, aimed to explore (1) the views of health professionals on older slum-dwelling adults' health and social care access and use, and (2) recommendations for improving access to health and social care services among slum-dwelling older adults.

Methods

Study design

This study used a qualitative exploratory descriptive approach by conducting a focus group discussion (FGD) and interviews.

Study setting

Two private care homes and two hospitals located close to slums in Accra were purposively selected for this study. The care homes were chosen because of the social services they provide to possibly meet the social care needs of slum-dwelling older adults. The hospitals are the main providers of formal healthcare in the region.

Care homes in Ghana provide daycare services for older adults, for instance when relatives are going to work. Professionals working in these care homes are managers, registered general nurses, social care workers and health care assistants. They mostly provide services at home, i.e., community-based where they keep the older adult company and assist in laundry, and cooking among others. They rarely offer in-house residency services. With in-house daycare services, older adults gather for social activities, such as Christmas parties, indoor games on holidays and health talks.

The hospitals are both district hospitals with a 50–60 bed capacity. There are no specialized geriatric units in either hospital, but they provide medical and surgical services to older adult patients. Professionals working here include general nurses, community health nurses, public health nurses, midwives, and medical doctors. General nurses are usually in the outpatient department and the admission wards while the community and public health nurses carry out home visits to older adults in slums within the communities. Sometimes these home visits are conducted based on referrals from the general nurses.

Participants

To be included in this study, the following inclusion criteria were used: (1) being a registered general nurse, a community health nurse, a social worker, or a nurse manager, (2) being employed in one of the four health care facilities selected for this study, (3) having at least one year of working experience in their respective health professions, and (4) having cared for at least one slum-dwelling older adult. Additionally, participants should be able to communicate in English or Twi (a local Ghanaian language). Registered midwives were excluded.

Recruitment

To recruit participants, the first author PA contacted hospital managers by telephone to ask if they had staff members who were eligible according to the inclusion criteria. If this was the case, PA received telephone numbers to contact these staff members. The contact details of care home providers were taken from the internet. The managers recruited other health professionals from their facilities for the study. The invited professionals were contacted in person, *via* telephone, and met at a date and time convenient for the professionals for the interview. After informed consent was given, an appointment was made for an interview. Interviews were held either at the facility or in the community.

Study instrument

A semi-structured discussion/interview guide was used to collect data from each participant. The interview questions were classified into two sections: the first section focused on personal and professional information such as the participant's age, sex, work position, and work experience, and the second section was designed by the authors, based on literature to explore health professionals' views on slum-dwelling older adults' access to health and social care, facilitators, and barriers of care and recommendations on ways of improving healthcare and social services of these older adults. Questions in the discussion/interview guide included: (1) How do you perceive the current health and social services of slum-dwelling older people? (2) How would you describe older adults living in slums accessibility and use of hospital services/community care services/ access to aged care services? (3) What social care services are available in and around Teshie and Madina? (4) How can we improve accessibility and usage of health and social care services among slum-dwelling older adults? During the discussion/interview, additional open-ended questions were asked to enable deeper exploration of the issues. Participants were made to further describe their responses and obtain additional data using probing questions (35, 36). The guide was developed following the objectives of the study and the results of a previous study by the authors (Attafuah et al., under review). Expert consultations were done with IE, JS, and CL to ensure that the interview guide reflected the objectives of this study. The interview guide was pretested on two health professionals (a community health nurse and a general nurse) in a district hospital in the Greater Accra region to identify ambiguous questions and clarify them. This ensured the content validity of the interview guide. There was no need to change any questions after the pre-test. Participants involved in pretesting were not included in the final analysis of the data.

Data collection procedure

Data were collected between March and April 2022 using face-to-face audio-recorded interviews and one focus group discussion (FGD), all led by PA and supported by a research assistant, who tape-recorded the discussions/interview for between 50 min and 1 h. Only one FGD was done because, during the initial FGD, it was observed by the researchers that some participants felt intimidated by their senior colleagues for fear of victimization despite reassurances from the interviewer. Also, it was very difficult to get most categories of health professionals at the same time for a discussion. Individual interviews were the preferred option in most facilities.

At the start of the interview, the purpose of the study was explained orally and participants who agreed to participate were given an informed consent form to sign. The interviews were carried out in private offices at the health center or aged care center. For interviews with community health nurses, interviews were carried out in the hospital or their Community Health Planning and Services (CHPS) zones. Two interviews were conducted in Twi mixed with English as the participants jokingly said they don't understand some of the questions if stated in English. The rigor of the data collection process was ensured throughout the conduct of interviews and FGD. The credibility of participants was established through the method and analyst triangulation.

Ethical considerations

Ethical clearance (No. 37MH-IRB IPN 29/2022) was obtained from the Institutional Review Board of the 37 Military Hospital. Also, permission from the municipal assemblies of the study sites was obtained. Informed consent from individuals was sought. Additionally, information on voluntary participation and the right to withdraw from the study at any point were shared with all participants. Confidentiality and privacy were guaranteed as pseudonyms were used. Anonymity was maintained by assigning participants with special codes and confidentiality was also maintained by making sure all audio

tapes, transcribed data, field notes, and documented information given by the participants were stored and data encrypted. Access to the data is restricted to the research team alone.

Data management, analysis, and reporting

Interviews and discussions were transcribed verbatim by a research assistant and proofread by the first author to ensure the accuracy of the accounts of the health professionals thereby enhancing the reliability of the findings. Data analysis took place after the first author checked the audio recording and transcriptions. The data were processed using Atlas ti software version 9. A reflexive thematic analysis procedure from the critical realist and constructionist point of view was followed for the analyses of the data. Critical realists believe there is a reason why slum-dwelling older adults (from Attafuah et al., under review) expressed varying perceptions about health professionals based on their observations. Only health professionals can explain the "real" reason. Hence an interaction with health professionals themselves will better explain their actions as observed by the slum-dwelling older adults and provide recommendations to curtail them. Taking the critical constructionist view was to critically identify various ways of improving health and social care services through a discourse with the health professionals.

The first author familiarized herself with the data by listening to the audio and reading the transcribed data. Following the transcription, two experts who were fluent in both the local language (Twi) and English languages translated those transcribed Twi interviews to English adhering to the "back-to-back" translation rule. This ensured the preservation of the content and meaning of the data. Next, the transcripts were methodically coded by the first author, after which, the codes were organized under deducted themes. The consolidated criteria for reporting qualitative research (COREQ) were followed for this report (37).

Results

Background characteristics

A total of 27 participants took part in the study. Table 1 shows the distribution of age, gender, professional role, work experience, job title and qualification of participants in the study. The age of participants ranged between 23 and 63 years, of whom half were between 25 and 34 years of age. Most participants were female ($n = 25$), which reflects the current predominance of female health professionals in Ghana. The professional experience of participants ranged from 2 to 35 years and most participants had worked for more than 8 years ($n = 20$).

TABLE 1 Background characteristics of participants.

Characteristic	Frequency
Age group (years)	
30–35	6
36–40	4
41–45	8
46–50	3
51 and above	6
Total	27
Gender	
Male	2
Female	25
Total	27
Work experience (years)	
<5	3
5–10	10
>10	14
Total	27
Professional category	
General nurse	8
Community health nurse	11
Public health nurse	5
Social worker	2
Nurse manager	1
Total	27

All interviews lasted between 50 min and 1 h. Data saturation was reached after one FGD with 10 participants and 17 individual interviews (as described in the Methods Section, the FGD appeared to not be the best method to get an in-depth understanding of the theme and therefore individual interviews were performed). In the analysis, three themes and fourteen subthemes were conceptualized. This process is detailed in Figure 1 below.

Utilization of healthcare services

Participants discussed their perspectives on the reasons for the under-utilization of healthcare services among older adults living in slums. From these discussions, five themes emerged. The theme most often mentioned (by all 27 participants) was "financial difficulties". This was followed by "queues" ($n = 25$), "health illiteracy" ($n = 24$), and "unwelcoming health professionals" ($n = 20$, mostly nurses). Lastly, "proximity of health facilities" to the slums was mentioned by some participants as a factor influencing the utilization of healthcare

FIGURE 1
Chart showing themes and subthemes.

services. Below, the themes are described in more detail, including supporting quotes.

Financial difficulties

Health professionals mentioned that most slum-dwelling older adults face financial challenges and are not able to access the health facility for this reason. They explained that although some older adults have registered with the National Health Insurance Scheme (NHIS), most do not have an active card or are not registered at all. Besides, even with an NHIS registration, additional payments must be made. The narratives of 2 participants exemplify the theme "financial difficulties".

> *"… They pay for some of the services they receive at the hospital even with the introduction of the NHIS Card and this should not be. They are suffering especially financially…"* (PHN2).
>
> *"Most of them do not have health insurance. … so they find it difficult going to the hospital because they have to make payment for everything"* (CHN11).

Queues

Participants mentioned long waiting times at the health facility as an important reason to not access healthcare services. Professionals argued that the processes patients go through before seeing the doctor can be stressful for older adults. Because there are no special units for older adults, they are seen by the same doctors attending to the younger adults. Participants who work in the hospital said they sometimes select the patients and create a different queue for older adults although not every health professional does this.

> *"…when they come to the facility, they have to go to records first and search for their folders (*Patients records*) and it takes a long time before they come to have a physical assessment done and then be seen by a doctor… the process is tedious for them…"* (RGN 4).
>
> *"Although there are no special units for old people, we sometimes separate them from the young ones to minimize the waiting time…"* (RGN 1).

Health illiteracy

Participants discussed that not every old slum-dwelling adult was illiterate. However, health illiteracy remains a problem which influences the use of formal health services. Participants observed that most older adults in the slums attribute every ill-health to spiritual factors and will not usually use formal care services. They argued to see that some older adults receive medication from the hospital but do not adhere to the treatment regimen because of preferences for herbal preparation.

> *"I cannot vividly say yes, and I cannot say no, … in the setting in which we live, superstition supersedes a lot of things… most of them will rather use herbal medicine…"* (CHN 9).

Unwelcoming health professionals

Health professionals mentioned their attitude toward older slum-dwellers. They stated that older adults from slums were not treated with a lot of respect. Nurses were the health professionals mostly accused. Participants attributed the unwelcoming nature of most nurses to work challenges as well as personal problems.

> *"Well, I can say that during our training we did not receive much education on caring for older adults. So, the skills in attending to older adults may be missing… Also, especially at the OPD* (Outpatient Department)*, the patients can be many whilst staff on duty are few so they may be overwhelmed…"* (RGN 6).
>
> *"Our attitude … it's zero I won't even say one because if an old lady comes to the hospital and you being the health worker, for example, cannot give the older person priority care, … some of our people (*nurses*) are very rude. We all have our frustrations, but you should not displace them on the poor old patient… So, for our attitude, it is nothing to write home about"* (RGN 2).

The proximity of health facilities

Health professionals reported that poor quality of roads and uneven walkways, as well as the distance from the slum to the health facility influence utilization of health facilities.

> *"The poor road network and many untarred roads in the slums predispose the old people to falls so they would not be comfortable walking. Also, the place is far but there is no money for transportation. So, they stay at home and combine herbal mixtures till the complications begin to surface"* (CHN 9).

Access to social services: Non-existent, unstructured, and limited resources

Under the main theme 'access to social services', three subthemes emerged: social services being non-existent, social services being unstructured, and limited resources in available services to cater for all older adults in nearby slum communities.

Most health professionals (n=24) mentioned that social care services were non-existent in the slum communities nearby.

> *"A recreational place for old people? I have not heard of any around here…in the slums, everyone is thinking about the children* (playground) *and the government has not set up anything for the old people"* (PHN 5).

A few health professionals ($n = 3$) described a social care service but also described that this service did not have a guiding structure (schedule).

> *"There is a big tree in the community across the street. I know the old people go and sit there and have conversations. Sometimes we* (nurses) *gather them* (old people) *and give them a health talk. But they don't have any structured organization for their activities…"* (CHN 8).

Participants from the aged care centers stated that even though they provided some social care services such as local indoor games, health screening and health education to older adults from slum communities, resources were not available to make it freely and widely accessible.

> *"In our place, we accept the old people within the vicinity three times a week. We give them health talks, engage them in local games like Ludu and Oware* (local games with dice and pebbles) *and sometimes we allow them to tell stories. We feed them breakfast and lunch provided by benevolent people… However, because of the limited resources, we cannot transport people to the center so only the few who are nearby will attend…it's sad"* (SW2).

Recommendations for improvement

Under the main theme recommendations for improvement, six subthemes were identified: (1) review of NHIS policy, (2) review of pre-and post-training of nurses, (3) government support with available day-care centers, (4) liaising with non-governmental organizations (NGOs), (5) health promotion activities, and (6) placement of suggestion boxes around health facilities.

Review of NHIS policy

All participants suggested a review of the NHIS policy to make healthcare free for people 60 years and above. They also stated that including treatment for more disease conditions common among the aged population is essential.

> *"The NHIS policy should be reviewed if we want to improve the health and overall QoL of our older people especially those in the slums. They don't have the money so at least if they are registered free with no renewal costs, it will be a big relief!… they should also review the health conditions covered by the NHIS to include diseases of old people …"* (CHN 9).

Review of pre-and post-training of nurses

All nurses in this study spoke about the current training of nurses and lamented that a lot of nurses are being trained, but the quality of professionalism among nurses is questionable because of their approach to health care. They added that training should

result in intrinsic motivation and a professional attitude to care for older adults.

> *"The best way to curb and improve on this* [unwelcoming/unfriendly professionals] *is to encourage students in our various nursing training institutions to have the desire to care for people and also make gerontology an interesting course for nursing students to appreciate…"* (NM1).
>
> *"Training of students on not stigmatizing old people will possibly improve their attitude when they start practicing. Having regular workshops, post-training, on avoiding discriminatory actions toward old people in the slums may perhaps help"* (RGN 3).

Government supporting available daycare centers

Participants who were from the aged care centers advocated for governmental support so that services can spread to a wider catchment area.

> *"… Yes, we are trying our best with the little resources… if the government can factor us in their budget planning and help us financially, there will also be enough to care for older adults in the slums. A bus to transport people will be appreciated also…"* (SW 1).

Liaising with non-governmental organizations (NGOs)

Health professionals also suggested that NGOs and private individuals should collaborate and set up centers in communities to provide social services.

> *"…in the demarcated constituencies in every region, at least there should be one center where social services can be provided for old people. Just like playgrounds have been set up for the children, NGOs can also do something for the old people in the slum communities…."* (PHN 3).

Health promotion activities

All participants expressed that health promotion activities and free health screening to prevent and detect any health issues should be held frequently in the slums for older adults and their informal caregivers. They hoped that doing this will improve the health literacy of the slum-dwelling older adult while bringing health services to the doorsteps as the hospitals are far and the roads are not the best for the older adults. The narrative below by RGN 6 summarizes the perspective of all participants.

> *"…I will say that if we carry out health education and health promotion activities more often in the slums, we can improve the health literacy of the older adults…and also get closer to them..."* (RGN 6).

Suggestion boxes

Some health professionals working in the 2 hospitals suggested placing suggestion boxes in the compound of health facilities which should be regularly checked for patient complaints, especially regarding staff attitude.

> *"Suggestion boxes at vantage places will also be very helpful. Now it is compulsory to wear your name tag on duty so patients can easily identify us. Now patients can name health professionals who are rude and unprofessional … so that authorities can take appropriate action..."* (RGN 4).

Discussion

Previous studies have indicated general barriers to health care services however this study specifically focused on barriers for older slum-dwellers. This study explored the views of health professionals on the access to and use of health and social care services among older slum-dwelling adults and their recommendations for improvement. The participants in the study stated that slum-dwelling older adults' access to, and use of health and social care services was influenced by financial barriers, queues to access care services, the attitude of health professionals, long distance to health facilities, health illiteracy, and unavailability of formal social care services. All healthcare professionals interviewed commented that healthcare and social services for older adults need improvement. The general recommendations for improving health and social care services for older adults in slums that emerged from this study were: (1) review of NHIS policy to include free healthcare for adults aged 60 years and above, (2) review of pre-and post-training of nurses on geriatrics, (3) government support for day care centers for older adults, (4) liaising with non-governmental organizations (NGO's) to provide formal social care services and free registration of the health insurance, (5) health promotion activities by health professionals in slum communities, (6) provision of suggestion boxes around health facilities for compliments and complains.

The barriers to health care (financial challenges, health illiteracy, long distances to services, long waiting times in healthcare facilities and poor attitude of health professionals) described by participants in this study are not new, as they were also found in earlier studies performed in Ghana mentioned

by Braimah and Rosenberg (38) and Wuaku et al. (39), in India by Chauhan and Saxena (40) and in Thailand by Jirathananuwat (41).

Health professionals in this study stated that older adults in Ghanaian slums were aware they needed to pay for their health insurance cards as well as yearly renewals, but that they were financially unable to do so. This finding agrees with a study by Amiresmaili et al. (21) in Iran (which is comparable to Ghana as it is an emerging lower-middle-income country), where lack of financial support was a major barrier because of the low economic status of the slum-dwelling older adult in Ghana. As postulated by Amiresmaili et al. (21) reducing financial and non-financial barriers to accessing healthcare is likely to encourage the utilization of healthcare services. Recommendations of health professionals in this study regarding a review of the current NHIS policy (to ensure free healthcare for older adults 60 years and above instead of the current age range of 70years and over) resonate with previous studies in Africa which suggested that better insurance coverage improved access and use of healthcare services (18, 38, 39, 42).

From the focus group discussion, it emerged that the poor attitude of health professionals is also a barrier to the utilization of healthcare services by older adults in slums. Wang et al. (43) in their study of attitudes of Community health professionals also reported negative attitudes toward dementia patients which affected healthcare use in Changsha, China. This confirms a scoping study on low- and middle-income countries by Sarikhani et al. (44) which suggested that attitudinal barriers affect the utilization of healthcare services. Health professionals in this study recommended a review of the pre-and post-training of nurses to improve their attitude toward older adults in slums and make them more welcoming. This agrees with the recommendation by Wang et al. (43) that providing opportunities for education and training will be beneficial in improving the attitude of community health professionals and with more recent studies by Amsalu et al. (45) in Ethiopia, Tsiga-Ahmed et al. (46) in Nigeria and Tavares et al. (47) in Portugal.

Queueing at health facilities by older slum-dwellers was cited as a barrier to healthcare service access and use. This confirms previous studies by Oche et al. (48), Chauhan and Saxena (40), and Naz et al. (49) from Nigeria, India, and Pakistan, respectively. From these studies, older adults resorted to self-medication from pharmacies as this was an easier option compared to visiting the hospital. In more developed countries options for telehealth are being explored (50) but considering the literacy and economic level of older adults in Ghanaian slums, this will be a difficult initiative (but not impossible) to implement in this setting.

Lastly, the literature suggests that social care provided by family members is commonly seen in most African countries (51–53), moreover, from this study, formal social care services appeared to be next to non-existent (34, 54–56).

Strengths and limitations

A strength is that this study is the first of its kind which has explored the views of health professionals on improving health and social care services for slum-dwelling older adults in Ghana. The findings of this study can be used to guide the design and formulation of policies that aim at removing barriers to formal health and social care use among older adults in Ghanaian slums. A possible limitation of this study is the absence of physicians/medical doctors and other health professionals from the participants. These professionals were approached but they declined, stating they were unavailable or uninterested. Therefore, it is recommended for future studies to think of incentives that would make medical doctors and other health professionals interested to participate in such studies. Additionally, having a small number of participants from social services is a limitation, which makes external generalizability limited. Future studies should include more social workers as participants to provide more suggestions for better interventions to meet the social care needs of older adults in slums.

Implications for practice

This study stresses the need for health professionals in Ghana to change their attitude toward slum-dwelling older adults, which might be achieved through regular post-training workshops at the health facilities. Additionally, as health illiteracy is a contributing factor to low accessibility and use of healthcare services, this study encourages community and public health nurses to conduct activities aimed at improving health literacy among older adults in slums. A method could be health education at durbars in the communities or home visits to the older adults to interact with them. Lastly, health professionals in this study, are advocating for the government to support available day-care centers in Ghana to provide resources for the provision of social care services in these centers.

Implications for further research

Based on the results of this study, future research should focus on what social care services could improve the quality of life for slum-dwelling older adults. It is recommended to involve more social workers in these studies. Additionally, we recommend interventional studies to see if some of the practical strategies suggested in this study, can indeed remove some of the barriers intended to address. An example could be the post-training of nurses to address attitudinal barriers or health screening and health education to improve health literacy among older adults in slums. Lastly, similar studies can be replicated in other big regions of the country to ascertain any differences or similarities in the findings.

Conclusion

This study found barriers to health and social care access and use among slum-dwelling older adults, according to the perspective of health professionals. Addressing these barriers is essential to diminish the negative influence on their utilization of formal health and social care services and health inequity. Furthermore, the health professionals participating in this study suggested practical strategies to overcome these barriers, such as providing free healthcare for adults 60 years and over as well as ensuring a positive attitude of health professionals. It is hoped that these recommendations if adhered to, will improve the health and social care which is given to older adults.

Additionally, slum reforms and policymakers can implement these recommendations to help meet the health and social needs of older adults in slums. To be able to reach the goal of the Universal Health Coverage policy (12, 57) of "ensuring that all people have access to needed, quality health services without suffering financial hardship", Ghana needs to aim at improved healthcare for its population.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by Institutional Review Board 37 Military hospital. The patients/participants provided their written informed consent to participate in this study.

Author contributions

PA, IE, CL, AA, and JS conceptualized the study. PA conducted the interviews. PA and IE analyzed the data. All authors reviewed the sections Introduction and Discussion and read through the final manuscript before submission. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Potential productivity loss from uncorrected and under-corrected presbyopia in low- and middle-income countries: A life table modeling study

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Objective: To estimate the burden of potential productivity losses due to uncorrected and under-corrected presbyopia in LMICs among the working-age population in both the cross-sectional and longitudinal manner.

Methods: We extracted data for the prevalence of presbyopia from the Global Burden of Diseases (GBD), Injuries, and Risk Factors Study 2019. Data for the gross domestic product (GDP) per capita were extracted from the World Bank database and Central Intelligence Agency's World Factbook. We introduced life table models to construct age cohorts (in 5-year age groups) of the working-age population (aged from 40 to 64 years old) in LMICs, with simulated follow-up until 65 years old in people with and without uncorrected presbyopia. The differences in productivity-adjusted life years (PALYs) lived and productivity between these two cohorts were calculated. The potential productivity loss was estimated based on GDP per capita. The WHO standard 3% annual discount rate was applied to all years of life and PALYs lived.

Results: In 2019, there were 238.40 million (95% confidence interval [CI]: 150.92–346.78 million) uncorrected and under-corrected presbyopia cases in LMICs, resulting in 54.13 billion (current US dollars) (95% confidence interval [CI]: 34.34–79.02 billion) potential productivity losses. With simulated follow-up until retirement, those with uncorrected and under-corrected presbyopia were predicted to experience an additional loss of 155 million PALYs (an average loss of 0.7 PALYs per case), which was equivalent to a total loss of US$ 315 billion (an average loss of US$ 1453.72 per person).

Conclusions: Our findings highlight the considerable productivity losses due to uncorrected and under-corrected presbyopia in LMICs, especially in a longitudinal manner. There is a great need for the development of enabling eye care policies and programs to create access to eye care services, and

more healthcare investment in the correction of presbyopia in the working-age population in LMICs. This study could provide evidences for some potential health-related strategies for socio-economic development.

KEYWORDS

potential productivity loss, life table modeling, productivity-adjusted life years, presbyopia, low- and middle-income countries (LMICs)

Highlights

What is already known on this topic

- Tremendous number of people had uncorrected and under-corrected presbyopia in LMICs which would lead to negative impacts on their economic and human's quality of life.
- Global uncorrected and under-corrected presbyopia could result in significant productivity losses. However, productivity loss due to uncorrected and under-corrected presbyopia in LMICs in a longitudinal manner has not been studied.

What this study adds

- In 2019, a total of 54.13 billion (current US dollars) (95% confidence interval [CI]: 34.34-79.02 billion) potential productivity loss was estimated in LMICs.
- In a longitudinal manner, loss of PALYs per presbyopia case was estimated to be 0.7 and total potential productivity loss was predicted to be US$ 315 billion (an average loss of US$ 1453.72 per person).

How this study might affect research, practice or policy

- Considerable productivity losses due to uncorrected and under-corrected presbyopia in both the cross-sectional and longitudinal manner highlight a great need for great need for the development of enabling eye care policies and programs to create access to eye care services, and more healthcare investment in the correction of presbyopia in the working-age population in LMICs.

Introduction

Presbyopia, resulting from the progressive decline of the eye's accommodation ability, is an age-related impairment of near vision (1). Because of the global growth of life expectancy and the aging society, nowadays the number of people concerned by presbyopia was tremendous and growing rapidly (2). Various reasons such as large population, a high prevalence (ranges from 43.8 to 93.4%), lack of eye health resources and limited access to eye care service, poor awareness of presbyopia, low presbyopia spectacle-correction coverage rates (as low as 10%) and low compliance made low- and middle-income countries (LMICs) suffered more than 90% of the global burden of presbyopia vision impairment (3–6). And it has been estimated that willingness to pay for spectacles was significantly associated with salaries, near visual demand and an independent income source. Compared with people earning <$53.0, people earning more than $107.1 were 48 times more likely to purchase glasses (CI: 8.591–71.758), which explained the higher uncorrected presbyopia prevalence in LMICs in a way (7). Besides, global population aging was considered to be a significant risk factor contributing to presbyopia (8–10). Previous studies showed that 1.8 billion people were affected by presbyopia in 2015, making up 25% of the world population (95% confidence interval [CI], 1.7–2.0 billion). And 826 million people (95% CI, 686–960 million people) of these patients had vision impairment which could lead to difficulties with near vision tasks, because of no, or inadequate, vision correction (1). The number of people with disabilities owing to uncorrected presbyopia was 474.1 million in 2010, of which 448 million were in less- and least-developed countries, accounting for 94.5% of the total (3).

Typically, presbyopia occurs after age 40, and gradually aggravates until age 60. Presbyopia has been proved to lead to negative impacts on human's quality of life and ability to daily activities (11, 12): 53% of Indians (13), 58% of Brazilians (14), and 70% of rural Tanzanians (15) with functional presbyopia had difficulties with near vision tasks, which would further result in significant productivity losses, which includes absence from work and reduced efficiency at work (presenteeism) (16). This effect should be of concern especially given that the increases in retirement age and the employment of older workers have been observed in various countries (17). Therefore, it is important to estimate the productivity losses due to uncorrected presbyopia in LMICs to capture the economic burden of uncorrected presbyopia.

Previous studies have investigated the economic burden of presbyopia in different methods (18–20). Frick et al. estimated that the potential productivity losses due to uncorrected and under-corrected presbyopia could be US$ 25 billion or 0.037% of global GDP in the working-age presbyopia adults (≤65 years) in 2011 (18). Due to the high prevalence of uncorrected and under-corrected

presbyopia among people of working age in LMICs, the potential productivity losses could be large. However, the economic burden regarding productivity losses due to presbyopia in LMICs, has not been reported. Moreover, no study has thus far estimated the potential productivity loss due to uncorrected and under-corrected presbyopia in a longitudinal manner.

In the current study, we aimed to quantify the potential productivity loss due to uncorrected and under-corrected presbyopia in LMICs over an extended period of time, measured in terms of productivity-adjusted life years (PALYs) (21–23). PALY is a newly developed measurement akin to quality-adjusted life years, which can adjust years of life lived for productivity losses attributable to chronic health conditions at the population level (21).

Methods

The data sources

The prevalence of uncorrected and under-corrected presbyopia in each low- and middle-income country was sourced from the Global Burden of Disease Study (GBD) 2019, stratified by 5-year age groups. Gross domestic product (GDP) represented the sum of value added by all its producers. The data was sourced from the World Bank's World Development Indicator database of 2019 and the newest Central Intelligence Agency's (CIA) World Factbook. The employment-to-population ratio was defined as the proportion of a country's working-age population that was employed. Labor force participation rate was the ratio of the economically active population (including the employed and the unemployed) to the working-age population. We obtained the employment-to-population ratio and Labor force participation rate in 2019 from the International Labor Organization. In general, information for this indicator was derived from household surveys, mainly labor force surveys. More details about data in this article can be found in the Supplementary Tables S1, S2, S3.

The productivity index and PALY

The PALY, which has been described in previous studies, is a measure of disease burden that can be used to measure the impact of chronic health conditions on work productivity at the population level (21). Briefly, the PALYs are derived from multiplying years of life lived by productivity indices. This is similar to the calculation of quality-adjusted life years (QALYs). The productivity index represents the productivity of an individual in proportional terms, ranging from 1 (100% productive) to 0 (entirely non-productive). The productivity index can be derived from estimates of absenteeism (missed working days), and presenteeism (productivity reduction) in those with uncorrected presbyopia compared with those without uncorrected presbyopia. Absenteeism was defined as the number of lost work days per year due to uncorrected presbyopia, while presenteeism was defined as productivity reduction. The productivity reduction was estimated at 10.9% from previous studies (Supplementary Table S5), while absenteeism was assumed to be 0.

In order to calculate the potential productivity losses caused by uncorrected and under-corrected presbyopia among the working-age people in a longitudinal manner, we introduced the life table models to construct age cohorts (in 5-year age groups) of the working-age population (aged from 15 to 64 years old) in LMICs (24). Firstly, to estimate the burden of presbyopia, the uncorrected and under-corrected presbyopia subjects of the working-age, defined as the "presbyopia cohort", were followed up in a model simulation over their working lifetime (until the retirement age of 65 years). The same cohort was then re-stimulated but hypothetically assumed to be free of uncorrected and under-corrected presbyopia. This was defined as the "Non-presbyopia cohort". As uncorrected and under-corrected presbyopia is not a mortality condition, we assumed that no extra deaths in the "presbyopia cohort" compared with the "non-presbyopia cohort". Thus, in the current study, the differences in the results of the "presbyopia cohort" and "Non-presbyopia cohort" were quantified in terms of the PALYs. The WHO standard 3% annual discount rate was then applied to all years of life and PALYs (25).

Calculation of the potential productivity loss

To calculate the potential productivity loss due to presbyopia, we multiplied the number of total working-age cases (TC) by the productivity-adjusted life years (PALYs) lost due to presbyopia, employment-to-population ratio (ER), labor participation rate (LPR) and the gross domestic product (GDP) per capital together. The formula used to calculate the total productivity loss (TPL) was TPL = TC *ER*LPR*PALYs lost* GDP (PC).

Scenario and sensitivity analysis

Deterministic sensitivity analyses were performed to assess the impact of uncertainty around presbyopia-related productivity indices, and economic data inputs on the model. These included: upper and lower uncertainty bounds of presbyopia cases, upper and lower uncertainty bounds around productivity indices based on decreasing and increasing estimates of presenteeism by 25%. To assess the impact of the assumption of the WHO standard annual discount rate of 3.0%,

scenario analyses were performed in which the discount rate was 5.0 and 1.5%, respectively.

Results

In 2019, the number of global cases of uncorrected and under-corrected presbyopia in working age was 257.07 million, of which 92.7% (238.4 million) were in LMICs (entire data can be found in Supplementary Table S1). Table 1 shows the numbers of presbyopia cases and the productivity losses varying from regions in 5-year age groups (40–64 years old) in 2019. There were 238.40 million (95% confidence interval [CI]: 150.92–346.78 million) people suffering from uncorrected and under-corrected presbyopia in LMICs, which resulted in a productivity loss of 53.41 billion US$ (95% confidence interval [CI]: 34.34–79.02 billion) in 2019. And the percent of productivity losses to GDP in all LMICs is 0.17% (95% CI:0.11–0.25) in 2019. We estimated the productivity losses due to uncorrected and under-corrected presbyopia in every country of LMICs (Supplementary Table S6). The top 10 low- and middle-income countries with the highest productivity loss due to uncorrected and under-corrected presbyopia cases in 2019 are shown in Figure 1. Among all the LMICs, the top 3 countries with the greatest productivity losses were China (37.01 billion, 95% CI 23.63–53.86), India (3.61 billion, 95% CI 2.29–5.29), and Russian Federation (3.09 billion, 95% CI 1.95–4.52), respectively.

Table 2 demonstrates that the PALYs lived in those with presbyopia and the same cohort without presbyopia in 5 age groups (40–64 years old). Table 3 and Figure 2 show the productivity losses of presbyopia in LMICs from 2019 to retirement age. With simulated follow-up until retirement (Supplementary Table S4), we estimated that PALYs lived by the current cohort of people with uncorrected and under-corrected presbyopia in LMICs would be reduced by an estimate of 155 million PALYs (10.9%) over their working lifetime, compared with the same cohort assuming no presbyopia. This equated to 0.7 PALYs lost per person with presbyopia over the working lifetime. Based on the gross domestic product (GDP) per full-time worker in 2019, the loss in PALYs equated to a total of 315.20 billion US$ (95%CI 199.24–464.24) in lost GDP owing to reduced productivity, with an average of US$ 1453.72 lost per person with presbyopia. Longitudinally, the top 3 countries with the greatest productivity losses were China (219.36 billion, 95% CI 139.64–322.03), India (22.97 billion, 95% CI 14.54–33.87), and Russian Federation (14.19 billion, 95% CI 8.86–20.99), respectively. The detailed productivity losses of presbyopia in each country from 2019 to retirement age were shown in (Supplementary Table S7).

Table 4 shows the results of the Scenario and sensitivity analysis. The model was sensitive to a number of inputs such as cases of presbyopia, productivity indices, and the annual discount rate. Compared with the base case, at upper and lower uncertainty bounds of productivity indices estimates, PALYs lost to presbyopia were reduced and increased by 25%, respectively. Increasing the annual discount rate to 5% corresponded to a 9.71% reduction in PALYs lost, and a reduction in the annual discount rate to 1.5% leading to an 8.69% increase in PALYs lost.

Discussion

Collectively, our data demonstrate that uncorrected and under-corrected presbyopia created a considerable burden on the economy of LMICs in both the cross-sectional and longitudinal manner. A total of 238.40 million (95% confidence interval [CI] 150.92–346.78 million) presbyopia cases aged from 40 to 64 years old in 2019 were estimated to cause 54.13 billion US$ (current US dollars) (95% confidence interval [CI] 34.34–79.02 billion) reduction of productivity in LMICs. With simulated follow-up until retirement, those with uncorrected and under-corrected presbyopia were predicted to experience an additional loss of 155 million PALYs (an average loss of 0.7 PALYs per person), which was equivalent to a total loss of US$ 315.20 billion (an average loss of US$ 1453.72 per person).

Previous studies have reported the global potential productivity loss due to distant and near visual impairment (19, 26–28). By applying the near vision impairment disability weight (0.013), Frick et al. estimated that the potential productivity loss due to uncorrected and under-corrected presbyopia could be US$ 25 billion in the working-age presbyopia adults (≤65 years) in 2011 (18). In the current study, by using data from the GBD 2019, we estimated significant greater productivity loss compared with Frick's study, even in LMICs. One possible explanation is that we used the 10.9% of productivity reduction instead of the disability weight (1.3%). We believe that productivity loss calculation using disability weight has limitations. Firstly, disagreement exists regarding the disability weight in the literature (18, 29, 30). Secondly, disability weight may not represent a reduction of productivity. The relative increase of productivity was reported to range from 6 to 21.7%, which is greatly higher than the disability weight. For example, in a recent randomized controlled, investigator-masked trial, Reddy et al. showed that a 21.7% relative productivity increase could be made if presbyopia tea workers were corrected with spectacles in India (a typical country from the LMICs) (19).

The potential productivity loss due to uncorrected and under-corrected presbyopia in a longitudinal manner has not been studied previously. In the current study, we introduced the PALY metric and used the multistage life table models to quantify the future productivity losses among the working-age population. We estimated that uncorrected or under-corrected presbyopia leads to the loss of 0.7 PALYs per case in our simulation. And those with uncorrected and under-corrected presbyopia in LMICs were predicted to cause a total

TABLE 1 Productivity losses of presbyopia in LMICs in 2019.

Economies	Cases of uncorrected and under-corrected presbyopia by 40–64 y (millions $)	Productivity losses of uncorrected and under-corrected presbyopia (billions $)	GDP (trillions$)	Productivity loss/GDP (%)
Low-Income	12.98 (11.97–17.60)	0.52 (0.33–0.77)	0.49	0.11 (0.07–0.16)
Lower–Middle Income	119.95 (71.10–175.29)	7.57 (4.78–11.09)	7.72	0.10 (0.06–0.14)
Upper–Middle Income	105.47 (67.85–153.89)	46.04 (29.23–67.16)	24.02	0.19 (0.12–0.28)
Total	238.40 (150.92–346.78)	54.13 (34.34–79.02)	32.23	0.17 (0.11–0.25)

Captions: The Economies according to the GBD 2019 study of Low-and Middle-Income Countries: Low-Income Economies ($1,045 OR LESS); Lower–Middle Income Economies ($1,046 TO $4,095); Upper–Middle Income Economies ($4,096 TO $12,695). The number of presbyopia is derived from the GBD 2019 study. The number of cases and productivity losses by presbyopia are given in form of with 95% confidence interval.

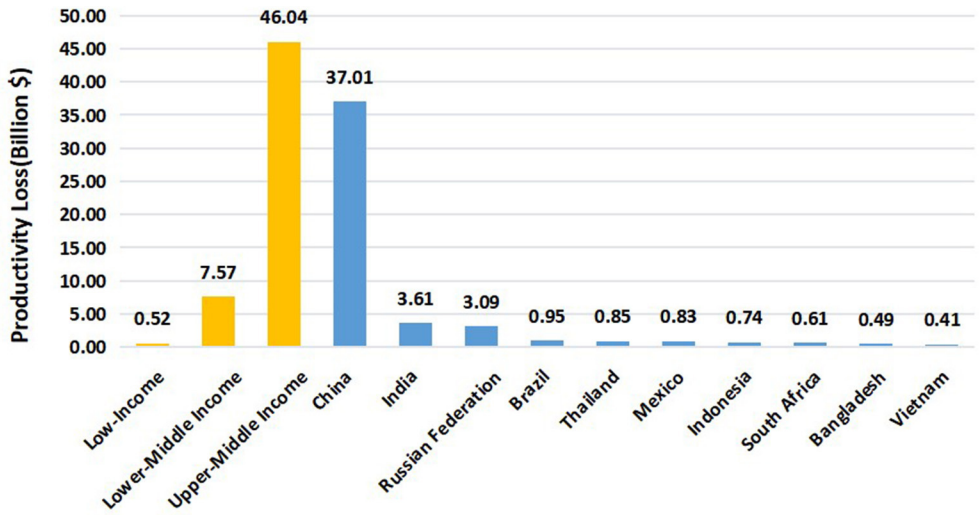

FIGURE 1
Productivity losses of presbyopia in LMICs and TOP10 countries of 40-64y (billion $) in 2019.

TABLE 2 Years of life lived in those with presbyopia, and in the same cohort assuming no presbyopia, over the working lifetime of the population simulated from life table modeling.

Five-year age group	Deaths in cohort with presbyopia (million)	Deaths in 'presbyopia cohort' assuming no presbyopia (million)	PALYs lived in cohort with presbyopia (million)	PALYs lived in 'presbyopia cohort' assuming no presbyopia (million)	PALYs lost per person with presbyopia
40–44	4.51 (2.90–6.68)	4.51 (2.90–6.68)	257 (165–380)	288 (185–427)	1.7
45–49	6.76 (4.16–10.28)	6.76 (4.16–10.28)	357 (220–544)	401 (247–611)	1.3
50–54	8.02 (5.18–11.54)	8.02 (5.18–11.54)	365 (236–524)	409 (265–589)	1.0
55–59	7.46 (4.59–10.84)	7.46 (4.59–10.84)	235 (145–342)	264 (162–384)	0.5
60–64	4.85 (3.14–6.98)	4.85 (3.14–6.98)	55 (36–80)	62 (40–90)	0.1
Total	31.60 (19.98–46.31)	31.60 (19.98–46.31)	1269 (802–1871)	1425 (900–2100)	0.7

TABLE 3 Productivity losses of presbyopia cases in LMICs from 2019 to retirement age.

Economies	Presbyopia cases in working age (millions $)	Productivity losses (billions $)
Low-Income	10.32 (6.50–15.15)	3.08 (1.92–4.57)
Lower–Middle Income	107.26 (67.94–156.58)	46.15 (29.03–68.22)
Upper–Middle Income	99.25 (62.98–144.73)	265.97 (168.29–391.45)
Total	216.82 (137.42–316.47)	315.20 (199.24–464.24)

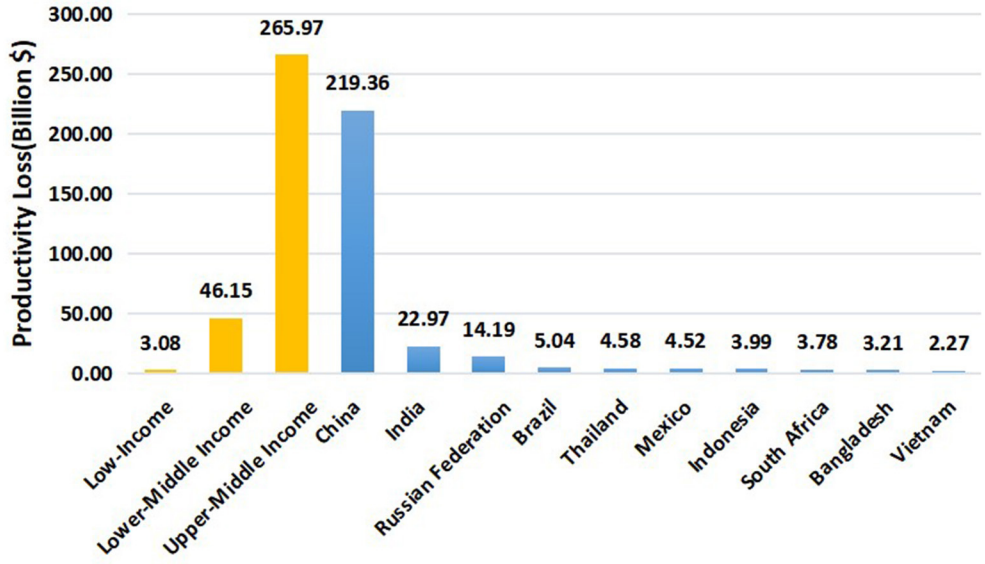

FIGURE 2
Productivity losses of presbyopia in LMICs and TOP10 countries (from 2019 to retirement age) in billion$.

TABLE 4 Sensitivity and scenario analyses to assess the impact of the uncertainties around productivity, and economic data inputs on PALYs lost in those with presbyopia in the population and the associated economic impact.

Analysis	PALYs lost	% Change in PALYs lost compared with base case	GDP lost (US$ billion)	GDP lost per person (US$)
Base	155295828.5		315	1453.72
1. Upper uncertainty bound of presbyopia cases	228879293.3	+ 47.38	464	1466.94
2. Lower uncertainty bound of presbyopia cases	98063705.35	– 36.85	199	1499.89
3. Productivity indices upper uncertainty bound	194119785.7	+ 25.0	394	1817.15
4. Productivity indices lower uncertainty bound	116471871.4	– 25.0	236	1090.29
5. Annual discount rate reduced to 5%	140222212.1	– 9.71	286	1318.97
6. Annual discount rate reduced to 1.5%	168787178.9	+ 8.69	341	1573.25

Sensitivity analysis 1 and 2 apply (1) the upper bound of the 95% CI and (2) the lower bound of the 95% CI around the presbyopia cases, holding all other model inputs constant.
Sensitivity analysis 3 and 4 apply (3) 25% increase and (4) 25% reduction in the productivity reduction rate estimates, holding all other model inputs constant.
Sensitivity analysis 5 and 6 apply an annual discount rate (5) increased to 5% (in line with the WHO standard annual rate) and (6) reduced to 1.5%.

loss of US$ 315 billion (an average loss of US$ 1453.72 per person) in our study. Although the burden of uncorrected presbyopia was also indispensable in high-income countries, people in these regions seem to have more opportunities to get the adequate optical correction (31). And Frick et al. found that the productivity loss of LMICs was much higher than high-income countries in 2011. The reasons for this difference might be complicated, including variations in wages, productivity, age structures, and employment rates (18). The poor are less able to afford spectacles for correction of presbyopia, so there is a great need for the development of enabling eye care policies and programs to create access to eye care services, and more healthcare investment in the correction of presbyopia in the working-age population in LMICs. It's worth to concern that a majority of the productivity loss by presbyopia in LMICs were estimated in the top 10 (89.77%), especially the top 3 (80.75%) countries (Figures 1, 2). Interventions to diagnose presbyopia (alongside other potential eye conditions) and increase spectacle coverage are highly recommended in these countries. Meanwhile, screening of presbyopia is beneficial to develop integrated eye care systems, because people with presbyopia are more likely to have sight-threatening diseases such as cataracts, glaucoma, and diabetic eye disease (6).

Clinically, there are several strategies to correct presbyopia (32). Correction with spectacles is known as the most common way that is simplest and cost-effective. Forms of spectacle lens include readers, single-vision glasses, bifocals, trifocals and progressive which are relatively mature now (33, 34). Single-vision or progressive contact lenses could also be used in presbyopia correction (35). Surgical approaches were considered to correct presbyopia too. But this way might be expensive and intractable which is an invasive procedure (35–40). Other options such as pharmacological therapies and ciliary muscle electrostimulation have not been widely applied in clinics yet (41, 42). Generally, obtaining spectacles is vital for the uncorrected presbyopia population, which was reported to be relative low cost (minimum price of a pair of spectacles: 8.6 to 12.9 US $) in previous studies (7, 43, 44). And a study in 2020 indicated that compared with the standard international cost of spectacles in 2006 (US $ 3.0) (45), the cost of which presbyopia people willing to pay for a pair of spectacles (US $ 19.0) was much higher. Moreover, the under-49 age group was 6.2 times more likely to get a pair of spectacles than the over-60 age group (7). Besides, a study in India suggested that most barriers to presbyopia correction were lack of 'felt need' (46%), 'lack of awareness' of presbyopia symptoms (16%), 'lack of access' (13%) and economic (13%) and personal reasons (12%)(46). So popularization of basic medical knowledge about presbyopia also plays an important role in the correction of presbyopia. We hope that the heavy productivity loss of the presbyopia population can attract the attention of the state, so as to expand the popularization of presbyopia and its correction. Additionally, we hope this study would inspire further related studies, such as near vision loss and socio-economic influence in LMICs, cost-effective strategies for presbyopia correction, and provision of eye care. And the ultimate goal is to improve the visual acuity and quality of life of presbyopia people through simple and effective means, of course, to a certain extent, to improve the economic level of the country.

This study has some limitations. Firstly, there were only 4 previous studies reporting the relative productivity reduction associated with presbyopia (Supplementary Table S5), and there were weaknesses in the GBD data source and methodology, including limited quality of data, and sparsity of population-based data, which could result in bias. Therefore, more robust data on presbyopia associated productivity reduction, especially from LMICs, is needed to improve our estimates. Secondly, the well-known limitation "life table assumption" in life table modeling should be noted, which means that age-specific mortality did not change over time in our modeling (46). Fortunately, presbyopia is non-fatal and the assumption was applied in both presbyopia and normal population, so the estimates would not change significantly. Thirdly, the productivity index applied in this study may not be generalizable to all LMICs, since not all economically productive activities were influenced by presbyopia in same degree. Many economically important activities, such as cooking, writing, reading, sewing, weeding, use of cell phones, and recognizing money, would be assigned with various weights in our further studies. Fourthly, this study only accounted the indirect costs of presbyopia in employment works, without considering the difficulties with near-vision tasks in unemployment work, like reading, writing, and using mobile phones, which were also important skills in production. Also, we did not take into account the onset of patients in the future (21), which could result in underestimate in productivity losses.

In conclusion, our findings highlight considerable productivity losses due to uncorrected and under-corrected presbyopia in both the cross-sectional and longitudinal manner in LMICs. There is a great need for the development of enabling eye care policies and programs to create access to eye care services, and more healthcare investment in the correction of presbyopia in the working-age population in LMICs. This study could provide evidences for some potential health-related strategies for socio-economic development.

Synopsis/precis

We found that uncorrected and under-corrected presbyopia in LMICs were predicted to cause a total loss of US$ 315 billion (an average loss of US$ 1453.72 per person) and a loss of 0.7 PALYs per case in low- and middle-income countries (LMICs).

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: https://www.healthdata.org/gbd/2019, https://databank.worldbank.org/source/world-development-indicators, https://www.cia.gov/the-world-factbook/. The other raw data supporting the conclusions of this article can be made available by the authors, without undue reservation.

Author contributions

Study design and manuscript writing and review: KQ and ZG. Data collection and analysis: QM, MC, and DL. Data analysis and interpretation: RZ, YD, SY, BC, HW, and JJ. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.983423/full#supplementary-material

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Depressive symptoms increase the risk of falls and injurious falls in Chinese adults aged ≥ 45 years: A 3-year cohort study

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Background: Falls and depressive symptoms are both public health concerns in China, but the effects of depressive symptoms on falls and injurious falls have not been thoroughly investigated.

Methods: This population-based prospective cohort study used data derived from adults aged ≥45 years acquired from the 2015 and 2018 China Health and Retirement Longitudinal Study. Data were analyzed from August 2021 to December 2021. Self-reported depressive symptoms were determined using a 10-item Center for Epidemiologic Studies Depression scale (CESD-10) with a total score range of 0–30. Item responses of 3–4 or 5–7 days were deemed indicative of specific depressive symptoms. The outcome variables were self-reported accidental falls and injurious falls.

Results: Of the 12,392 participants included in the study, 3,671 (29.6%) had high baseline depressive symptoms (CESD-10 scores ≥ 10), 1,892 (15.3%) experienced falls, and 805 (6.5%) experienced injurious falls during 2015–2018 follow-up. High depressive symptoms increased the risk of falls [odds ratio (OR) 1.34, 95% confidence interval (CI) 1.19–1.50] and injurious falls (OR 1.28, 95% CI 1.09–1.51) in a multivariable logistic regression model adjusted for major demographic, health-related, and anthropometric covariates. All of the 10 specific depressive symptoms except "felt hopeless" were associated with falls, and four specific symptoms significantly increased the risk of injurious falls; "had trouble concentrating" (OR 1.32, 95% CI 1.13–1.55); "felt depressed" (OR 1.32, 95% CI 1.12–1.55); "everything was an effort" (OR 1.23, 95% CI 1.04–1.45); and "restless sleep" (OR 1.18, 95% CI 1.02–1.40).

Conclusion: High depressive symptoms are significantly related to risk of falls and injurious falls. Four specific symptoms (had trouble concentrating, felt depressed, everything was an effort, and restless sleep) increase the risk of injurious falls in Chinese adults aged ≥ 45 years.

KEYWORDS

depressive symptoms, fall, injurious fall, cohort study (or longitudinal study), CHARLS

Introduction

As populations age, falls are becoming an increasing global health concern (1). Injuries resulting from severe falls such as fractures and traumatic brain injuries require medical treatment. These injuries can lead to chronic pain, disability, and even death (2, 3). Worldwide 37.3 million patients who suffer from falls require medical treatment each year, and falls cause the loss of >17 million disability-adjusted life-years (1). In 2019 the morbidity of falls in mainland China in adults aged >60 years was 3,799.4 per 100,000. The incidence rate of deaths associated with falls was 39.2 per 100,000, and that of disability-adjusted life-years associated with falls was 1,238.9 per 100,000 (4). Detecting, modifying, and preventing risk factors for falls in adults may reduce the number of falls, injurious falls, and associated complications.

Depressive symptoms are a mental problem characterized by sadness, loss of interest in activities, and reduced energy (5). They are typically measured by validated rating scales with established cutoffs such as the Epidemiologic Studies Depression scale (6). Depressive symptoms are consistently associated with falls (7–11). Two studies conducted in the United States and Canada demonstrated significant associations between baseline depressive symptoms and subsequent falls in community-dwelling older populations (7, 9). Systematic reviews (10, 11) also indicate a relationship between high depressive symptoms and an increased risk of falls in older adults. Notably, previous studies (7–11) have considered depressive symptoms as a dichotomous factor (e.g., present or not), or have used a total depression score. Such studies assumed that depressive symptoms are a single condition, and that all specific symptoms are fungible and equally valid indicators. Specific depressive symptoms such as sadness, sleep disorders, inattention, and suicidal ideation are distinct conditions, and they differ in significant respects such as potential biology, effect on injury, and risk factors (12). Moreover, most prior studies have concentrated on the role of depressive symptoms only on the occurrence of falls, while ignoring resulting injuries that required medical care (8–11), or they have only examined these relationships in older people (9–11).

The aim of the current study was to investigate associations between depressive symptoms—including elevated high depressive symptoms and specific depressive symptoms—and falls and injurious falls in Chinese populations aged 45 years and over.

Materials and methods

Study design

This study was a secondary analysis of data from the 2015 and 2018 China Health and Retirement Longitudinal Study (CHARLS). The CHARLS was a longitudinal survey-based study that aimed to be representative of residents aged 45 years and over in mainland China (13). It covered 28 provinces, 150 counties, and 450 villages/urban communities. A stratified (by per capita gross domestic product of urban districts and rural counties) multistage (county/district-village/community household) probability proportional to population size random sampling strategy was used. The first national survey was conducted in 2011, and the most recent was conducted in 2018. Through face-to-face interviews using a standardized questionnaire, detailed demographic and health-related data were acquired. The CHARLS was confirmed by the Biomedical Ethics Review Committee of Peking University, Beijing, China (IRB00001052–11015) (13).

Study participants

Participants who were included in both the 2015 cohort and the subsequent 2018 tracking survey were considered for inclusion in the present study. The exclusion criteria were (1) age <45 years; (2) a history of falls or a lack of fall information in 2015; (3) missing data on depressive symptoms in 2015; (4) refusing to answer questions on falls in the 2018 tracking survey; (5) died during the 2015–2018 follow-up period; and (6) lost to follow-up prior to the 2018 tracking survey. The final sample analyzed included 12,392 individuals (Figure 1).

Depressive symptoms

The Center for Epidemiologic Studies Depression scale comprised of ten items (CESD-10) in the CHARLS was used to measure depressive symptoms (13). Based on the number of days participants had experienced depressive symptoms in the past week, items were rated as < 1 day (0 points), 1–2 days (1 point), 3–4 days (2 points), or 5–7 days (3 points). The total CESD-10 score was the sum of all items, and possible scores ranged from 0 to 30. A CESD-10 score $\geq$ 10 was considered indicative of significant depressive symptoms (14). Participants with high depressive symptoms were divided into two subgroups; moderate (9–19) and higher (20–29). Using the method described by Jokela et al. (15), item responses of 3–4 or 5–7 days were deemed indicative of specific depressive symptoms.

Falls and injurious falls

In the survey falls were alluded to with the question "Have you fallen down?". Possible answers were "yes" or "no." If the answer was "yes," participants were asked a subsequent question, "How many times have you fallen down seriously enough to

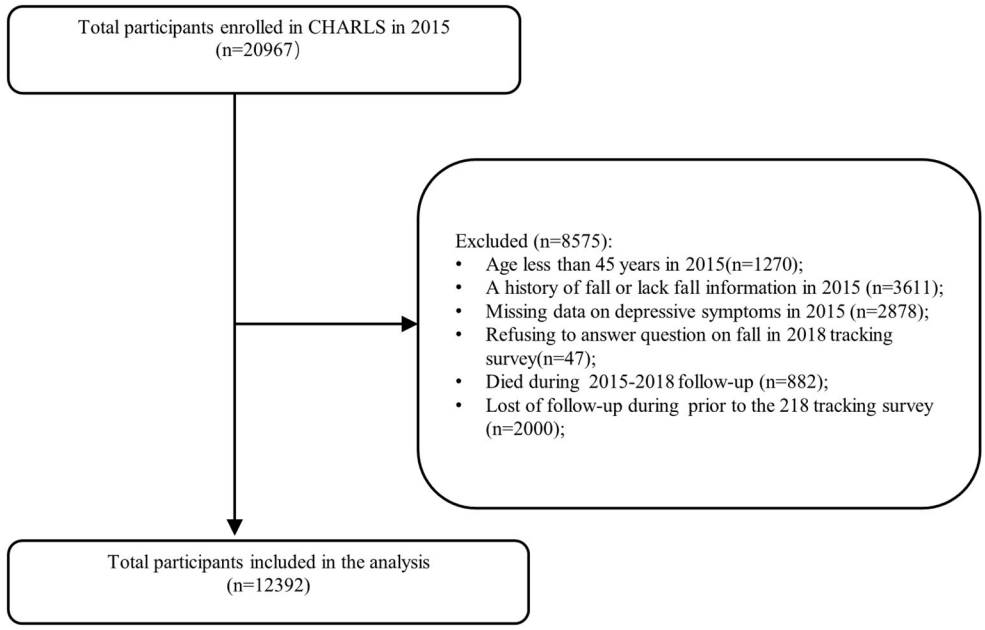

FIGURE 1
Flow chart of the participants.

need medical treatment?". Participants who reported needing medical treatment were defined as having had injurious falls. Outcome variables were treated as binary.

Assessment of covariates

Demographic information including age, gender, residence, marriage, and education were obtained *via* a structured questionnaire. Physician diagnoses of chronic comorbidities, including hypertension, diabetes, chronic lung diseases, heart diseases, kidney diseases, neuropsychiatric diseases, and arthritis or rheumatism were self-reported. Neuropsychiatric diseases were defined as the combination of stroke, emotional or mental problems, and memory-related diseases. Other health-related covariates included were drinking habits, smoking habits, body pains, and medication use.

Measurements of anthropometric indicators including systolic blood pressure, diastolic blood pressure, pulse, body mass index, waist circumference, handgrip strength, and peak expiratory flow were performed by trained research nurses. Handgrip strength was defined as the maximum strength of the dominant hand. Blood samples were provided by 68.5% (8,487/12,392) of the participants, and were used to assess white blood cells, platelets, hemoglobin, C-reactive protein, creatinine, glucose, and uric acid. Glomerular filtration rate was estimated using the Chronic Kidney Disease Epidemiology Collaboration's 2009 creatinine equation (16).

Statistical analysis

Data were analyzed from August 2021 to November 2021. Continuous variables are represented as means and standard deviations, or medians and interquartile ranges. Categorical variables are represented as frequencies and percentages. Differences between groups were assessed using the *t*-test, χ^2 test, analysis of variance, or Mann–Whitney *U*-test. There was 23.1% (2,866/12,392) of baseline data missing, and these data were imputed using the R-package missForest.

Multivariate logistic regression analyses were performed to identify odds ratios (ORs) and 95% confidence intervals (CIs). An extended model approach was used for covariate adjustment, where model 1 was adjusted for age and gender; model 2 was adjusted for age, gender, residence, marriage, education, smoking, and drinking; model 3 was adjusted for model 2 and included body pains, history of hypertension, diabetes, chronic lung diseases, heart diseases, kidney diseases, neuropsychiatric diseases, arthritis or rheumatism, hypertension medications, diabetes medications, heart medications, and neuropsychiatric medications; and model 4 was adjusted for model 3 and included systolic blood pressure, diastolic blood pressure, pulse, body mass index, waist circumference, handgrip strength, and peak expiratory flow. Potential nonlinear associations were also investigated *via* restricted cubic spine regression.

Post-hoc subgroup analyses were performed to investigate associations between some baseline characteristics and falls and injurious falls. *p*-values for interactions were determined *via*

likelihood ratio tests. Sensitivity analyses were performed to evaluate the robustness of results. First, further adjustment for laboratory indicators in model 4 was conducted in 8,538 participants who provided blood samples. Analyses were then repeated in 9,526 participants with non-imputed data.

Variance inflation factors with a cutoff value of 10 were generated to assess multicollinearity of the variables in the models. All analyses were performed in Stata version 16 and R version 4.1.1, and two-tailed p-values < 0.05 were considered statistically significant.

Results

Study participants and characteristics

The mean age of the 12, 392 study population was 58.0 years, 50.6% were men, and 29.6% had high depressive symptoms (CESD-10 score $\geq$ 10). Compared with those with low depressive symptoms (CESD-10 score $<$ 10), participants with high depressive symptoms were less likely to be male, younger, urban residents, and married. They were more likely to have no formal education, be nonsmokers and nondrinkers, and have body pains. Participants with high depressive symptoms also had a greater percentage of self-reported physician-diagnosed medical conditions and medication use, lower systolic and diastolic blood pressure, lower body mass index, smaller waist circumference, weaker handgrip strength, lower peak expiratory flow, and lower levels of white blood cells, hemoglobin, C-reactive protein, glucose, estimated glomerular filtration rate, and uric acid (Table 1). Baseline differences between included and excluded individuals are shown in Supplementary Table 1.

Associations between depressive symptoms and falls and injurious falls

During the follow-up period from August 2015 to August 2018, a total of 1,892 participants experienced falls, and 805 of those had injurious falls. The incidence rates of falls and injurious falls were higher in individuals with high depressive symptoms. High depressive symptoms independently predicted the occurrence of falls (OR 1.34, 95% CI 1.19–1.50) and injurious falls (OR 1.28, 95% CI 1.09–1.51) after adjustments for all covariates. These associations remained significant when depressive symptoms were divided into three categories (Table 2). All of the specific depressive symptoms except "feel hopeless" were significantly associated with falls, and four of the specific symptoms were significantly associated with injurious falls; "had trouble concentrating" (OR 1.32, 95% CI 1.13–1.55), "felt depressed" (OR 1.32, 95% CI 1.12–1.55), "everything was an effort" (OR 1.24, 95% CI 1.04–1.45), and "restless sleep" (R 1.20, 95% CI 1.02–1.40) (Table 3). In restricted cubic spine regression analysis. there were linear positive associations between total CESD-10 score and the risks of falls and injurious falls (nonlinearity; $p = 0.15$ for falls, $p = 0.54$ for injurious falls) (Figure 2).

Subgroup and sensitivity analyses

Subgroup analyses were conducted to stratify associations between depressive symptoms (high vs. low) and falls and injurious falls by risk factors (Figure 3). The effects of depressive symptoms on falls were more pronounced in participants aged 45–65 years ($p = 0.022$ for interaction), and the association between depressive symptoms and injurious falls was stronger in female participants ($p = 0.006$ for interaction) and non-diabetic participants ($p = 0.047$ for interaction). The effects of depressive symptoms on falls and injurious falls remained after further adjustment for laboratory indicators in 8.538 participants with blood sample data (Supplementary Table 2), and in repeat analyses in 9,526 participants with non-imputed data (Supplementary Table 3).

Discussion

In the current study depressive symptoms were positively associated with falls and injurious falls during a 3-year follow-up period in middle-aged and older adults. Specifically, high depressive symptoms at baseline increased the risks of falls and injurious falls. Most specific depressive symptoms were independently associated with falls, and four specific symptoms ("had trouble concentrating", "felt depressed", "everything was an effort", and "restless sleep") were significantly associated with injurious falls.

The population selected for the study was individuals without a history of falls within the previous 2 years, based on the possibility that falls themselves may lead to depressive symptoms (17, 18). The results of the present study corroborate prior studies with regard to positive associations between high depressive symptoms and falls and injurious falls. Patients with depressive symptoms had a nearly three times greater risk of falling than those without depressive symptoms (19). In another longitudinal survey high depressive symptoms estimated by the Center for Epidemiological Studies Depression Scale 8-item short-form were associated with an increased risk of falls 2 years later (20). Systematic reviews (10, 11) also indicate relationships between high depressive symptoms and increased risks of falls in elderly adults. In the current study high depressive symptoms were a significant predictor of injurious falls, which is consistent with a prior study (7). Compared with these previous studies, this study not only had much larger sample size over a wider age range (≥45 years old at baseline) and a longer follow-up time,

TABLE 1 Baseline characteristics of 12,392 participants by depressive symptoms.

Characteristics	Participants, no. (%)			
	Total sample	Depressive symptoms		
	($N = 12,392$)	Low, <10 ($N = 8,721$)	High, ≥10 ($N = 3,671$)	*P*-value[a]
Age, y	58.00 (51.00, 65.00)	58.00 (51.00, 65.00)	59.00 (52.00, 66.00)	<0.001
Man	6,266 (50.56)	4,815 (55.21)	1,451 (39.53)	<0.001
Rural residence	4,814 (38.85)	3,682 (42.22)	1,132 (30.84)	<0.001
Married	10,367 (83.66)	7,476 (85.72)	2,891 (78.75)	<0.001
Educational level				<0.001
No formal education	4,675 (37.73)	2,884 (33.07)	1,791 (48.79)	
Primary school	3,577 (28.87)	2,597 (29.78)	980 (26.70)	
Middle or high school	3,646 (29.42)	2,820 (32.34)	826 (22.50)	
College or above	494 (3.99)	420 (4.82)	74 (2.02)	
Smoke[b]	5,571 (44.96)	4,142 (47.50)	1,429 (38.93)	<0.001
Drink[b]	5,826 (47.05)	4,294 (49.27)	1,532 (41.77)	<0.001
Body pains[b]	3,178 (25.65)	1,325 (15.20)	1,853 (50.48)	<0.001
History of comorbidities				
Hypertension[b]	3,754 (30.45)	2,506 (28.87)	1,248 (34.19)	<0.001
Diabetes[b]	973 (7.91)	624 (7.20)	349 (9.61)	<0.001
Chronic lung diseases[b]	1,524 (12.36)	869 (10.01)	655 (17.97)	<0.001
Heart diseases[b]	1,661 (13.48)	1,016 (11.71)	645 (17.71)	<0.001
Kidney diseases[b]	714 (5.80)	390 (4.49)	324 (8.90)	<0.001
Neuropsychiatric diseases[b]	558 (4.52)	261 (3.00)	297 (8.13)	<0.001
Arthritis or rheumatism[b]	3,897 (31.58)	2,246 (25.86)	1,651 (45.17)	<0.001
History of medication use				
Hypertension medications[b]	2,806 (22.92)	1,848 (21.41)	958 (26.54)	<0.001
Diabetes medications[b]	675 (5.49)	433 (5.00)	242 (6.66)	<0.001
Heart medications[b]	1,069 (8.69)	618 (7.13)	451 (12.41)	<0.001
Neuropsychiatric medications[b]	250 (2.06)	117 (1.36)	133 (3.78)	<0.001
Systolic blood pressure, mmHg[b]	127.00 (19.21)	127.36 (19.02)	126.17 (19.60)	0.005
Diastolic blood pressure, mmHg[b]	75.15 (11.14)	75.46 (11.08)	74.44 (11.25)	<0.001
Pulse, /min[b]	73.83 (10.46)	73.85 (10.49)	73.79 (10.40)	0.813
Body mass index, kg/m^2[b]	24.01 (3.64)	24.15 (3.62)	23.70 (3.69)	<0.001
Waist circumference, cm[b]	85.79 (12.69)	86.36 (12.49)	84.48 (13.05)	<0.001
Handgrip strength, kg[b]	30.98 (10.50)	32.24 (10.40)	28.06 (10.14)	<0.001
Peak expiratory flow, l/min[b]	327.79 (122.77)	339.59 (124.13)	300.51 (115.05)	<0.001
Laboratory indictors[c]				
White blood cell, 10^9/L	5.95 (1.66)	5.98 (1.64)	5.89 (1.69)	0.023
Hemoglobin, g/dL	13.77 (1.79)	13.88 (1.79)	13.53 (1.78)	<0.001
Platelet, 10^9/L	203.42 (66.06)	203.01 (65.20)	204.37 (68.02)	0.393
C-reactive protein, mg/L	1.40 (0.70, 2.60)	1.40 (0.70, 2.50)	1.40 (0.80, 2.70)	0.023
Estimated glomerular filtration rate, mL/min/1.73 m^2	99.32 (17.14)	100.17 (17.27)	97.34 (16.68)	<0.001
Glucose, mg/dL	95.50 (88.29, 106.31)	95.50 (88.29, 106.31)	95.50 (86.49, 106.31)	0.037
Uric acid, mg/dL	4.95 (1.36)	5.03 (1.37)	4.77 (1.31)	<0.001

Data are shown as means ± standard deviation, median (interquartile range), or numbers (percentages).

[a] *P*-value was based on χ^2 or analysis of variance or Mann-Whitney *U*-test where appropriate.

[b] Missing data: 1 (0.01%) for smoke, 9 (0.07%) for drink, 3 (0.02%) for body pains, 63 (0.50%) for hypertension, 94 (0.76%) for diabetes, 64 (0.52%) for chronic lung diseases, 72 (0.58%) for heart diseases, 74 (0.60%) for kidney diseases, 54 (0.44%) for neuropsychiatric diseases, 51 (0.41%) for arthritis or rheumatism, 152 (1.23%) for hypertension medications, 105 (0.85%) for diabetes medications, 87 (0.70%) for heart medications, 273 (2.20%) for neuropsychiatric medications, 2,165 (17.47%) for systolic blood pressure, 2,167 (17.49%) for diastolic blood pressure, 2,170 (17.51%) for pulse, 2,115 (17.07%) for body mass index, 2,109 (17.02%) for waist circumference,2,170 (17.51%) for handgrip strength and 2,197 (17.73%) for peak expiratory flow.

[c] Measured in subpopulation of 8,487 (68.50%) participants.

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TABLE 2 The association between depressive symptoms and falls and injurious falls in 3-year follow-up (2015–2018).

Depressive symptoms	Event	Incidence rate, per 1,000 person-years	OR (95%CI)			
			Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]
Falls	1,892	50.89				
Categories						
Low, <10	1,140	43.57	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
High, ≥10	752	68.28	1.62 (1.46–1.80)	1.58 (1.42–1.76)	1.37 (1.22–1.53)	1.34 (1.19–1.50)
Categories						
Low, <10	1,140	43.57	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Moderate, 10 to <21	576	63.43	1.49 (1.34–1.67)	1.46 (1.31–1.64)	1.30 (1.15–1.46)	1.27 (1.13–1.43)
Higher, ≥21	176	91.10	2.29 (1.90–2.76)	2.22 (1.84–2.68)	1.79 (1.46–2.18)	1.73 (1.41–2.11)
p for trend			<0.001	<0.001	<0.001	<0.001
Injurious Falls	805	21.65				
Categories						
Low, <10	475	18.16	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
High, ≥10	330	29.96	1.59 (1.37–1.85)	1.51 (1.30–1.76)	1.32 (1.12–1.55)	1.28 (1.09–1.51)
Categories						
Low, <10	475	18.16	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Moderate, 10 to <21	252	27.75	1.48 (1.26–1.74)	1.42 (1.20–1.67)	1.26 (1.06–1.50)	1.23 (1.03–1.46)
Higher, ≥21	78	40.37	2.12 (1.63–2.73)	1.97 (1.51–2.55)	1.64 (1.23–2.15)	1.55 (1.16–2.03)
p for trend			<0.001	<0.001	<0.001	<0.001

OR, odds ratio; CI, confidence interval.
[a]Model 1 was adjusted for age and gender.
[b]Model 2 was adjusted for age, gender, residence, marital status, educational level, smoking status, drinking status.
[c]Model 3 was adjusted as model 2 plus body pains, history of hypertension, diabetes, chronic lung diseases, heart diseases, kidney diseases, neuropsychiatric diseases and arthritis or rheumatism; and use hypertension medications, diabetes medications, heart medications, neuropsychiatric medications.
[d]Model 4 was adjusted as model 3 plus systolic blood pressure, diastolic blood pressure, pulse, body mass index, waist circumference, handgrip strength and peak expiratory flow.

TABLE 3 Association between specific depressive symptoms and falls and injurious falls.

	Event (%)	OR (95% CI)[a]	
		Falls	Injurious falls
Depressive symptoms number[b]		1.08 (1.05–1.10)	1.06 (1.03–1.10)
Items[c]			
Bothered by little things	3,237 (26.12)	1.22 (1.09–1.37)	1.11 (0.94–1.30)
Had trouble concentrating	3,149 (25.41)	1.31 (1.17–1.46)	1.32 (1.13–1.55)
Felt depressed	3,113 (25.12)	1.34 (1.20–1.50)	1.32 (1.12–1.55)
Everything was an effort	3,023 (24.39)	1.26 (1.12–1.41)	1.23 (1.04–1.45)
Felt hopeless	5,339 (43.08)	1.06 (0.96–1.17)	1.02 (0.88–1.18)
Felt fearful	1,025 (8.27)	1.31 (1.11–1.54)	1.12 (0.88–1.41)
Restless sleep	3,854 (31.10)	1.15 (1.03–1.28)	1.20 (1.02–1.40)
Felt unhappy	3,810 (30.75)	1.18 (1.06–1.31)	1.11 (0.95–1.29)
Felt lonely	1817 (14.66)	1.21 (1.05–1.38)	1.17 (0.96–1.41)
Could not get going	1166 (9.41)	1.22 (1.04–1.43)	1.21 (0.97–1.50)

OR, odds ratio; CI, confidence interval.
[a]Model was adjusted for age, gender, residence, marital status, educational level, smoking status, drinking status, body pains, history of hypertension, diabetes, chronic lung diseases, heart diseases, kidney diseases, neuropsychiatric diseases and arthritis or rheumatism; and use hypertension medications, diabetes medications, heart medications, neuropsychiatric medications; and systolic blood pressure, diastolic blood pressure, pulse, body mass index, waist circumference, handgrip strength and peak expiratory flow.
[b]Sum of Specific Depressive Symptoms.
[c]Measured by the 10-item Center for Epidemiologic Studies Depression Scale (Having specific depressive symptoms were identified by defining item responses as 3–4 days or 5–7 days).

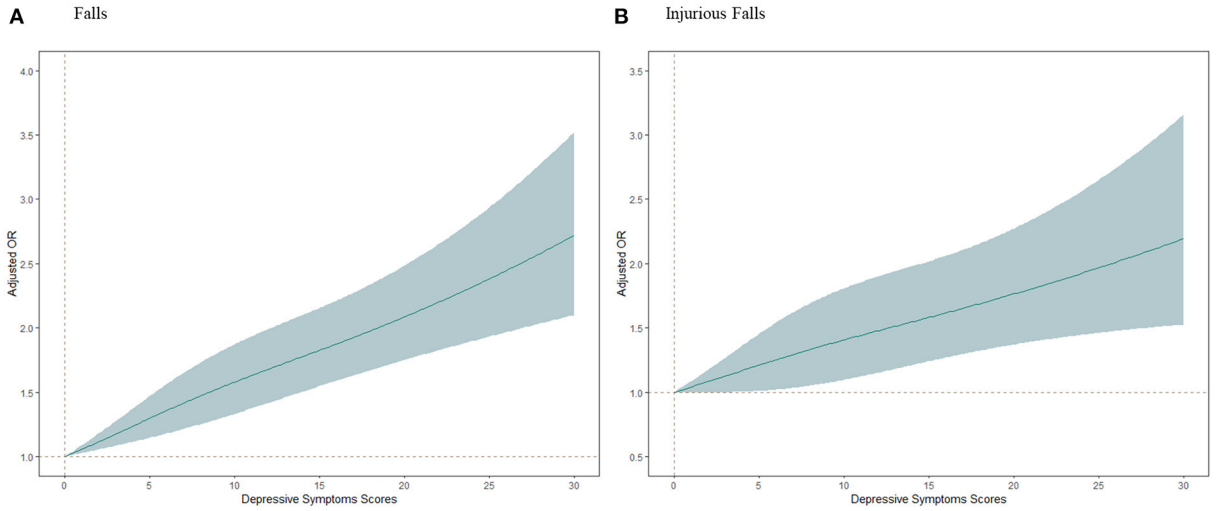

FIGURE 2
Adjusted odds ratios (ORs) of falls and injurious falls according to depressive symptoms scores. Graphs show ORs for falls **(A)** and injurious falls **(B)** adjusted for age, gender, residence, marital status, educational level, smoking status, drinking status, body pains, history of hypertension, diabetes, chronic lung diseases, heart diseases, kidney diseases, neuropsychiatric diseases and arthritis or rheumatism; and use hypertension medications, diabetes medications, heart medications, neuropsychiatric medications; and systolic blood pressure, diastolic blood pressure, pulse, body mass index, waist circumference, handgrip strength and peak expiratory flow. Data were fitted by a restricted cubic spline generalized linear regression model. The depressive symptoms score ranges from 0 to 30, with the highest score representing the highest risk of depressive symptoms. Solid lines indicate ORs, and shaded part indicate 95% confidence intervals (CI).

but also paid attention to the influence of specific depressive symptoms on falls and injurious falls.

The effects of specific depressive symptoms on falls and injurious falls have not been fully investigated. In a cross-sectional investigation attention interference and loss of executive control were associated with falls in elderly adults (21). Poor attention during gait increased the risk of falls in elderly people (22). Australian assisted-living-care residents with <6 h sleep had a higher likelihood of experiencing multiple falls after 1 year (23). Poor sleep quality, insomnia, and increased sleep disturbances were associated with increased likelihood of recurrent falls (24). A fear of falling that reduces activity and further decreases gait quantity and quality increases the likelihood of falling (25). In a longitudinal study perceived social isolation was reportedly related to a 33% increase in fall risk (26). The present study is the first to investigate the influences of specific depressive symptoms as determined *via* a depression rating scale on falls and injurious falls.

There are several possibilities with respect to mechanisms underlying associations between depressive symptoms and falls and injurious falls. Numerous risk factors for falls such as psychomotor retardation and gait alteration are common in older people with depressive symptoms in epidemiological investigations (27, 28). Individuals with depressive symptoms also tend to exhibit cognitive deficits that affect attention, executive functions, and processing speed, which can all increase the risk of falls and injurious falls (29). By influencing levels of inflammatory cytokines, vitamin D levels, and some hormone concentrations, depressive symptoms may lead to factures (29, 30). Lastly, multiple somatic comorbidities related to falls are often associated with depression (31). Women are more likely to experience depressive symptoms than men (32), which may be the reason why depressive symptoms is more strongly associated with injurious falls in women. Prior studies supported that people with diabetes were at a significantly higher risk of falls and injurious falls than people without diabetes across (33, 34). This study found stronger associations of depressive symptoms with injurious falls among non-diabetes participants and possible reason was selection bias.

The strengths of the current study include the evaluation of specific depressive symptoms, its prospective design, inclusion of the outcomes of injurious falls, the long follow-up period, and adjustments for various confounding factors. The study also had some limitations. First, data pertaining to falls and chronic comorbidities were self- reported, which may have resulted in bias. Second, the CESD-10 was used to evaluate depressive symptoms rather than clinical diagnosis. However, our findings do highlight the importance of assessing depressive symptoms to avoid falls and injurious falls in adults aged ≥45 years. Additional specific depressive symptoms associated with falls and injurious falls may be discovered *via* the use of other validated rating scales. Third, the findings may not fully apply to other countries because the study was conducted in Chinese adults aged 45 years and over. Fourth, the study

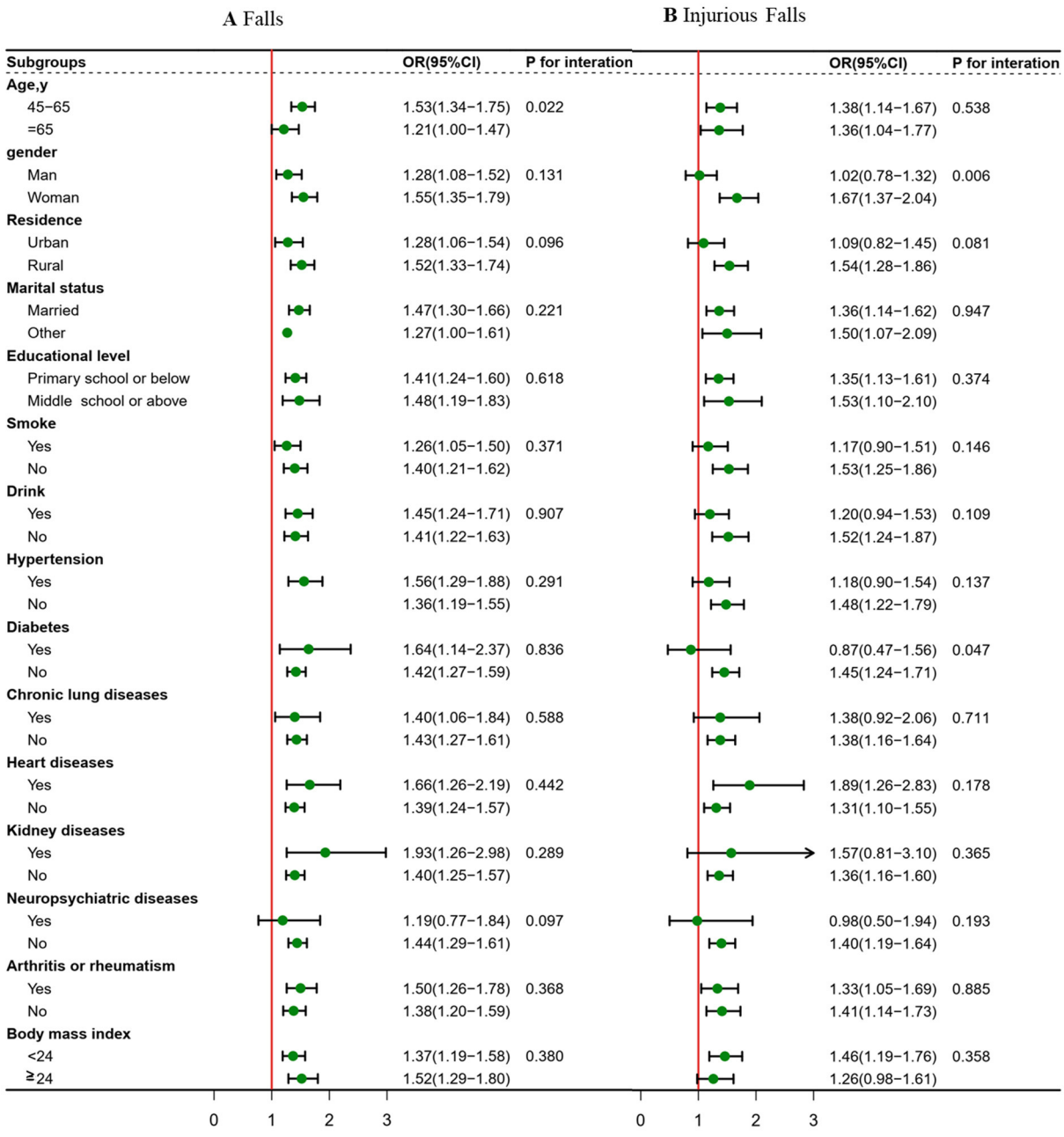

FIGURE 3
Association between depressive symptoms (high vs. low) and falls and injurious falls risk stratified by different factors. Graphs show odds ratios (OR) and 95% confidence intervals (CI) for falls **(A)** and injurious falls **(B)** adjusted for age, gender, residence, marital status, educational level, smoking status, drinking status; and history of hypertension, diabetes, chronic lung diseases, heart diseases, kidney diseases, neuropsychiatric diseases and arthritis or rheumatism; and systolic blood pressure, diastolic blood pressure, pulse, body mass index, waist circumference, handgrip strength and peak expiratory flow.

bears the characteristic limitations of *post-hoc* subgroup analysis. Despite adjustments for many confounding factors, residual confounding factors may still exist. Fifth, the falls or injuries cases within the first follow-up year should be excluded in the sensitivity analysis to exclude an inverse causal relationship. It was difficult to conduct limited by the availability of data.

Conclusion

In the current study middle and older aged adults with high depressive symptoms were at increased risk of falls and injurious falls, and the presence of specific depressive symptoms increased the risk of injurious falls. These results

are significant from a public point of view in the light of population aging. We should not only pay attention to whether or not have depressive symptoms, but also need to pay attention to the specific symptoms of depression such as "had trouble concentrating", "felt depressed", "everything was an effort", and "restless sleep". Tailored fall- prevention programs should be established for adults with specific depressive symptoms related to injurious falls.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

QZ and HB: designed and conducted the study. HB, SL, and DJ: statistical analysis. HB, LW, and ZT: drafting of the manuscript. HB, LW, ZT, and YD: administrative, technical, or material support. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.964408/full#supplementary-material

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Individualized prediction of chronic kidney disease for the elderly in longevity areas in China: Machine learning approaches

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Background: Chronic kidney disease (CKD) has become a major public health problem worldwide and has caused a huge social and economic burden, especially in developing countries. No previous study has used machine learning (ML) methods combined with longitudinal data to predict the risk of CKD development in 2 years amongst the elderly in China.

Methods: This study was based on the panel data of 925 elderly individuals in the 2012 baseline survey and 2014 follow-up survey of the Healthy Aging and Biomarkers Cohort Study (HABCS) database. Six ML models, logistic regression (LR), lasso regression, random forests (RF), gradient-boosted decision tree (GBDT), support vector machine (SVM), and deep neural network (DNN), were developed to predict the probability of CKD amongst the elderly in 2 years (the year of 2014). The decision curve analysis (DCA) provided a range of threshold probability of the outcome and the net benefit of each ML model.

Results: Amongst the 925 elderly in the HABCS 2014 survey, 289 (18.8%) had CKD. Compared with the other models, LR, lasso regression, RF, GBDT, and DNN had no statistical significance of the area under the receiver operating curve (AUC) value (>0.7), and SVM exhibited the lowest predictive performance (AUC = 0.633, p-value = 0.057). DNN had the highest positive predictive value (PPV) (0.328), whereas LR had the lowest (0.287). DCA results indicated that within the threshold ranges of ~0–0.03 and 0.37–0.40, the net benefit of GBDT was the largest. Within the threshold ranges of ~0.03–0.10 and 0.26–0.30, the net benefit of RF was the largest. Age was the most important predictor variable in the RF and GBDT models. Blood urea nitrogen, serum albumin, uric acid, body mass index (BMI), marital status, activities of daily living (ADL)/instrumental activities of daily living (IADL) and gender were crucial in predicting CKD in the elderly.

Conclusion: The ML model could successfully capture the linear and nonlinear relationships of risk factors for CKD in the elderly. The decision support system based on the predictive model in this research can help medical staff detect and intervene in the health of the elderly early.

KEYWORDS

prediction, chronic kidney disease, elderly, machine learning, longevity areas, China

Introduction

Chronic kidney disease (CKD) has become a major public health problem worldwide and has caused a huge social and economic burden, especially in developing countries (1). In 2017, the number of CKD patients worldwide reached 697.5 million, amongst which nearly one-sixth (132 million) were in China (2). CKD plays an important role in the development of end-stage renal disease (ESRD) (3), all-cause mortality (4), non-vascular health outcomes (5) and hospitalisations (6). The prevalence of CKD increases with age, and this problem is exacerbated by the aging of the Chinese population. The 2015 Annual Data Report of the China Kidney Disease Network showed that nearly half of CKD patients in China are over 60 years old (7). A study reported that the prevalence of CKD (Stages III–IV) in men and women between 55 and 64 years old is 6.1 and 13.1%, respectively; in the corresponding population of 75–84 years old, the prevalence of CKD is increased to 33.2 and 41.7% (8). In addition, the average age of patients with ESRD in China is 59 years; the patients with ESRD in China are younger than those in the USA (62.8 years) and Japan (64.7 years) (9). Therefore, the early identification, intervention and establishment of effective treatment strategies for potential Chinese CKD patients are crucial in controlling the number of Chinese CKD cases. The elderly population is a high-risk group in terms of CKD. Close attention must therefore be devoted to the elderly population.

Several studies have analyzed the association between CKD and its risk factors, which mainly include the following types of indicators: (1) demographic characteristics, such as sex (10), age (11), and marital status (12); (2) unhealthy lifestyle, including smoking (13), and alcohol consumption (14); (3) mental and physical health, including instrumental activities of daily living (IADL) and activities of daily living (ADL) (15), cognition (16), depression (17), body mass index (BMI) (18), and waist circumference (19); (4) chronic diseases, such as hypertension (20), diabetes (21), heart disease (22), stroke and cerebrovascular diseases (23) and cancer (24); and (5) biology medical indicators, including serum albumin (25), blood urea nitrogen (21), total cholesterol (26), triglyceride (27), urea acid (28), and hemoglobin (29). However, most algorithms for predicting CKD are based on a small number of patients and clinical predictors, and their predictive accuracy is usually uncertain (21, 30–32). The main research method used at present is multiple linear regression. The multiple linear regression model is based on the least squares method and assumes that the variables are independent of one another. However, the relationship between dependent and independent variables is complex and nonlinear, with high-dimensional correlation (33–36). Therefore, the performance of this model in terms of sensitivity and specificity is insufficient for use in predicting CKD.

Machine learning (ML) techniques have many advantages, including robustness to parametric assumptions, high power and accuracy, capability to model nonlinear effects, availability of numerous well-developed algorithms and capability to model high-dimensional data (37). ML techniques can be used to design data-driven models and algorithms with predictive capabilities in an unpredictable manner to achieve good results. ML models have been widely used in medical and health fields to assess disease risks and provide information for the establishment of clinical decision support systems, including predicting disease outcome (38), recommending treatment methods (39), and personalized medicine (40). Therefore, ML technology is an effective means for the early diagnosis of CKD.

To the authors' knowledge, no previous study has used ML methods combined with longitudinal data to predict the risk of CKD amongst the elderly in China in 2 years. Therefore, this study utilizes survey data from the Healthy Aging and Biomarkers Cohort Study (HABCS) in China as a sample to predict CKD amongst the elderly in longevity areas in China by using six ML models.

Materials and methods

Study design and setting

The HABCS datasets were collected by the Center for Healthy Aging and Development Studies (CHADS) of National School of Development at Peking University and the Chinese Center for Disease Control and Prevention (CDC) from in-depth studies in the eight longevity areas in the Chinese Longitudinal Healthy Longevity Survey (CLHLS) 5th, 6th, and

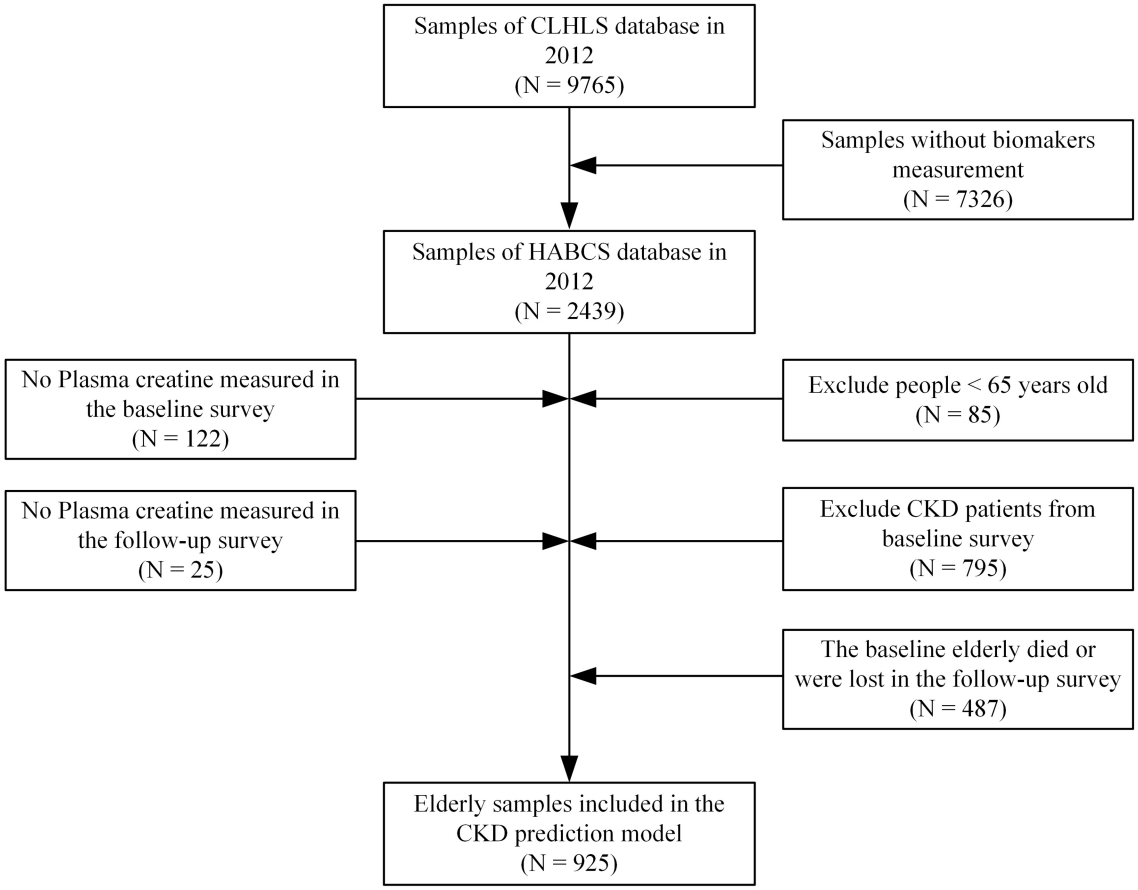

FIGURE 1
Study samples selection process.

7th waves in 2009, 2012, and 2014. We selected the surveyed individuals in 2012 as the baseline survey sample and the surveyed individuals in 2014 as the follow-up survey sample. The selected elderly did not have CKD in the baseline survey. The specific sample selection process is shown in Figure 1. The research conducted in this study was performed in accordance with the Declaration of Helsinki.

Data collection

Questionnaire data

The CLHLS questionnaire data contained information on the research subjects' family structure, living arrangements and proximity to children, ADL, capacity for physical performance, self-rated health, self-evaluation of life satisfaction, cognitive functioning, chronic disease prevalence, care needs and costs, social activities, diet, smoking and drinking behaviors, psychological characteristics, economic resources and care giving and family support amongst elderly respondents and their relatives.

Laboratory examination

In this study, blood and urine samples of subjects corresponding to CLHLS samples in HABCS were collected for laboratory examination. Hemoglobin concentration (HC), which was amongst the indicators we collected for the laboratory examination, was measured on-site. The clinical test center of Capital Medical University used the Hitachi 7,180 automatic biochemical analyser produced in Japan and commercial diagnostic reagents produced by Roche Diagnostics company to examine other indicators, including plasma albumin, serum creatinine, blood urea nitrogen, blood urea acid, total cholesterol and triglyceride (41).

Study variables

Outcome variable

This study defined whether the sample in the follow-up survey met the diagnostic criterion of CKD as the outcome variable. When the sample met the diagnostic criterion of CKD, it was assigned a value of 1; otherwise, it was given a value of 0.

The diagnostic criteria and definition for CKD were based on the Guidelines for the Screening, Diagnosis and Prevention of CKD published in China in 2017 and the Kidney Disease Outcomes Quality Initiative of the American Kidney Foundation (42). These two documents are very authoritative in China and the United States. The diagnostic criterion of CKD in these two documents was defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2. eGFR was calculated with the CKD-EPI equation, which is expressed as follows (43):

$$\begin{aligned} \text{eGFR} = 141 \times \min(\text{Scr}/\kappa, 1)\alpha \times \max(\text{Scr}/\kappa, 1) - 1.209 \\ \times 0.993\ \text{Age} \times 1.018(\text{if female}) \end{aligned}$$

where Scr is serum creatinine expressed in mg/dL, κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of Scr/κ or 1 and max indicates the maximum of Scr/κ or 1.

Predictors

We selected 22 variables of the respondents in the 2012 baseline survey as predictors of CKD, and these included the following: (1) demographic characteristics, such as gender (male vs. female), age (a continuous variable) and marital status (has a spouse vs. no spouse); (2) unhealthy lifestyle, including smoking (yes vs. no) and alcohol consumption (yes vs. no); (3) mental and physical health, including IADL/ADL (a continuous variable), cognitive function (a continuous variable), depression (yes vs. no), BMI (a continuous variable) and waist circumference (a continuous variable); (4) chronic diseases, such as hypertension (yes vs. no), diabetes (yes vs. no), heart disease (yes vs. no), stroke and cerebrovascular diseases (yes vs. no), cancer (yes vs. no), and blood disease (yes vs. no); and (5) biology medical indicators, including serum albumin (a continuous variable), blood urea nitrogen (a continuous variable), total cholesterol (a continuous variable), triglyceride (a continuous variable), urea acid (a continuous variable), and hemoglobin (a continuous variable).

In this study, we determined whether a respondent had hypertension based on whether the respondent was diagnosed with hypertension by a doctor. The diagnosis of Chinese doctors is based on the "China Guidelines for the Prevention and Treatment of Hypertension", in which hypertension is defined as systolic blood pressure over 140 mmHg, diastolic blood pressure over 90 mmHg.

A modified version of Lawton's scale was used to measure impairments in IADL amongst the elderly samples (44). The scale includes the following self-reported activities: visiting neighbors, shopping, cooking a meal, washing clothes, walking continuously for 1 km at a time, lifting a weight of 5 kg, continuously crouching and standing up three times and taking public transportation. These items had three response categories, namely, "yes, independently", "yes, but need some help" and "no, can't"; the three options were coded 3, 2 and 1, respectively. Impairment in ADL was measured using the Katz scale (45), which covers the following activities: bathing, dressing, going to the toilet, transferring indoors, continence and eating. The response categories of ADL were consistent with IADL's and coded similarly. We calculated the total score of 14 items as a respondent's final score, with a maximum of 42 points.

The measurement for depression used two levels of indicators, and an answer of "yes" to any question is considered a representation of depression (coded as 1, otherwise 0). The two questions were as follows: (1) Have you had a time in the last 12 months when you felt sad, blue or depressed for 2 weeks or more? (2) Have you had a time in the last 12 months lasting 2 weeks or more when you lost interest in most things, such as hobbies, work or activities, that you usually find pleasurable?

Statistical analysis

In the training set (70% random sample), we developed different ML models to predict the probability of CKD for the elderly. The data structure of this study contains both predictor variables and outcome variables, so the ML prediction models were based on supervised learning algorithm. Meanwhile, the outcome variable is a binary variable, so this study focused on the classification problem, so as to solve the identification of CKD in the elderly. Therefore, we have constructed six ML classification algorithms based on supervised learning, logistic regression (LR), LR with lasso regularization (lasso regression), random forest (RF), gradient-boosted decision tree (GBDT), support vector machine (SVM) and deep neural network (DNN). A systematic comparison of the strengths and weaknesses of six machine learning algorithms was shown in Table 1 (46).

LR

Logistic Regression is a ML algorithm which is used for the classification problems, it is a predictive analysis algorithm and based on the concept of probability (47). We implemented LR algorithm in an R and the used the glm function to fit the model.

Lasso regression

Lasso regularization automatically deletes unnecessary covariates, and only the most significant variables are retained in the final model. We used 10-fold cross validation to obtain the optimal value of the regularization parameter (lambda) with minimum mean squared error (MSE) (48). The optimal lambda values were used for variable selection. The methods presented above are implemented in an R package called glmnet. minMSE is automatically calculated using arguments s = "lambda.min" in the cv.glmnet function.

TABLE 1 A systematic comparison of the strengths and weaknesses of six machine learning algorithms.

Supervised ML[a] algorithms	Strengths	Weaknesses
LR[b]	(1) Easier to implement, interpret.	(1) It tends to underperform when there are multiple or non-linear decision boundaries.
	(2) It makes no assumptions about distributions of classes in feature space.	(2) It is not flexible enough to naturally capture more complex relationships. DNN can easily outperform this algorithm.
	(3) It has a nice probabilistic interpretation of model parameters	(3) It requires average or no multicollinearity between independent variables.
	(4) It can interpret model coefficients as indicators of feature importance.	(4) Unless multinomial, generic LR can only classify variables that have two states (i.e., dichotomous).
Lasso regression	(1) It can be regularized to avoid overfitting.	(1) It leads to dimensionality reduction, which means the model is built using a lower dimensional dataset. This generally leads to a high bias errror.
	(2) Lower dimensional dataset is computationally efficient.	(2) It could be computationally expensive.
	(3) Outputs have a nice probabilistic interpretation.	(3) A poor value for hyperparameter might make the model performance worse.
RF[c]	(1) It outputs importance of variable.	(1) No interpretability.
	(2) Individual decision trees can be trained in parallel.	(2) A large number of trees can make the algorithm too slow and ineffective for real-time predictions.
	(3) It reduces overfitting, since RF takes the average value from the outcomes of its constituent decision trees.	(3) Overfitting can occur easily.
	(4) There is no need for feature normalization.	(4) It favors those variables or attributes that can take high number of different values in estimating variable importance.
	(5) Scales well for large datasets.	
	(6) RF is harder to overfit than GBDT.	
GBDT[d]	(1) Often provides predictive accuracy that cannot be beat.	(1) GBDT are more sensitive to overfitting if the data is noisy.
	(2) Lots of flexibility - can optimize on different loss functions and provides several hyperparameter tuning options that make the function fit very flexible.	(2) Training generally takes longer because of the fact that trees are built sequentially.
	(3) No data pre-processing required.	(3) GBDT are harder to tune than RF. There are typically three parameters: number of trees, depth of trees and learning rate, and each tree built is generally shallow.
	(4) Handles missing data, imputation not required.	
	(5) GBDT are better learners than RF.	
SVM[e]	(1) More robust compared to LR	(1) Memory intensive
	(2) Can model non-linear decision boundaries, and there are many kernels to choose from.	(2) A time-consuming approach if applied to a huge database.
	(3) Fairly robust against overfitting, especially in high-dimensional space.	(3) It is trickier to tune due to the importance of picking the right kernel, and don't scale well to larger datasets.
		(4) RF are usually preferred over SVM
DNN[f]	(1) They are usually outperformed by tree ensembles for classical ML problems.	(1) A black box approach for a statistical modeler we have very little control on what the model does.

(Continued)

TABLE 1 (Continued)

Supervised ML[a] algorithms	Strengths	Weaknesses
	(2) Can detect complex nonlinear relationships between dependent and independent variables.	(2) Non-repetitive results and instability.
	(3) Strong gradual corruption ability.	(3) It require much more expertise to tune (i.e., set the architecture and hyperparameters).
	(4) Corruption of one or more cells of ANN[g] does not prevent it from generating output.	(4) It needs parallel processing environment.

[a]ML, machine learning; [b]LR, logistic regression; [c]RF, random forests; [d]GBDT, gradient-boosted decision tree; [e]SVM, support vector machine; [f]DNN, deep neural network; [g]ANN, artificial neural network.

RF

RF is a meta-estimator that fits a number of decision tree classifiers in various sub-samples of the dataset and uses averaging to improve the predictive accuracy and control overfitting (49). In this study, we used out-of-bag estimation to measure the prediction errors. In addition, we used *R* ranger and caret packages to construct RF models.

GBDT

GBDT produces a prediction model in the form of an ensemble of weak prediction models, builds the model in a stage-wise manner and generalizes them by allowing the optimisation of an arbitrary differentiable loss function (50). In this study, we used 10-fold cross-validation to measure the prediction error and used the XGBoost package in R software to construct GBDT models.

SVM

SVM is a discriminative classifier that is formally defined by a separating hyperplane. In other words, given labeled training data (supervised learning), the algorithm outputs an optimal hyperplane that categorizes new examples (46). The radial basis function (RBF) kernel in the SVM function was used in this study.

DNN

DNN is an artificial neural network (ANN) with multiple layers between the input and output layers. DNN searches for the correct mathematical manipulation to turn the input into the output, whether it is a linear relationship or a non-linear one (51). In DNN, we constructed a three-layer feedforward model with an adaptive moment estimation optimiser by utilizing the Keras package. For DNN, we developed the final models by randomly and manually tuning the hyperparameters, such as the number of layers and hidden units, learning rate, learning rate decay, batch size and epochs, by using the Keras package. To minimize potential overfitting, we used batch normalization that normalizes the means and variances of layer inputs.

Model evaluation

In the test set (30% random sample), we used the AUC value and prospective prediction results [sensitivity (Eq. 1), specificity (Eq. 2), accuracy (Eq. 3), positive predictive value (PPV) (Eq. 4), and negative predictive value (NPV) (Eq. 5)] to evaluate the performance for each ML model. We selected the threshold value of expected prediction results based on receiver operating curve (ROC) (i.e., the value with the shortest distance to the perfect model). A widely used test to compare the difference between two AUCs relies on the method developed in a seminal paper by DeLong et al. (52) (henceforth "the DeLong test"). The DeLong test was applied to compare the differences in the ROC curves of different ML models. Decision curve analysis (DCA) was performed to calculate the clinical "net benefit" for the six ML prediction models in comparison with default strategies of treating all or no patients. Net benefit was calculated across a range of threshold probabilities, which is defined as the minimum probability of a disease at which further intervention would be warranted, as follows: net benefit = sensitivity × prevalence – (1 – specificity) × (1 – prevalence) × w, where w is the odds at the threshold probability (53). To obtain an in-depth understanding of the contribution of each predictor to the ML model, we also calculated the importance of variables in the GBDT and RF model for each result.

$$\text{Sensitivity} = \frac{TP}{TP + FN} \quad (1)$$

$$\text{Specificity} = \frac{TN}{TN + FP} \quad (2)$$

$$\text{Accuracy} = \frac{TN + TP}{TN + TP + FN + FP} \quad (3)$$

$$\text{Positive predictive value} = \frac{TP}{TP + FP} \quad (4)$$

$$\text{Negative predictive value} = \frac{TN}{TN + FN} \quad (5)$$

Here, true negatives (TN) and true positives (TP) indicate the elderly that were accurately identified as not suffering depression and suffering depression, respectively; false negatives (FN) and false positives (FP) indicate the elderly that were inaccurately identified as not suffering depression and suffering depression, respectively.

Results

Characteristics of elderly samples with CKD in HABCS 2012

As shown in Table 2, amongst the 925 elderly in HABCS 2014, 289 (18.8%) had CKD. The age of the elderly with CKD (87.34 ± 10.73) was higher than that of the elderly without CKD (78.67 ± 10.44). The female elderly with CKD (25.4%) had a larger proportion than the male elderly (12.4%). The marital status of married but not living with spouse (15.2%) for the elderly accounted for a larger proportion than the marital status of married and living with spouse and divorced (9.6 and 9.1%, respectively). The cognitive function score of the elderly with CKD (19.34 ± 5.80) was lower than that of the elderly without CKD (21.01 ± 3.99). The elderly who smoked (12.0%) had a larger proportion than the elderly who did not smoke (20.1%). The ADL/IADL score of the elderly with CKD (36.57 ± 6.79) was lower than that of the elderly without CKD (39.08 ± 5.42). The plasma albumin level of the elderly with CKD (39.04 ± 5.36) was lower than that of those without CKD (41.23 ± 4.51). The total cholesterol level of the elderly with CKD (4.18 ± 0.97) was lower than that of the elderly without CKD (4.36 ± 0.94). The hemoglobin level of the elderly with CKD (126.55 ± 20.61) was lower than that of the elderly without CKD (132.4 ± 22.32). The elderly with hypertension (26.1%) had a larger proportion than the elderly without hypertension (15.8%).

Afterward, we performed binary logistic regression to analyze the crude and adjusted odds ratios for the elderly with CKD (vs. non-CKD) for each predictor. The elderly with a high age had a higher risk of CKD compared with the elderly with a low age [adjusted odds ratio (OR) = 1.066; 95% confidence interval (CI): 1.041–1.092]. The female elderly had a higher risk of CKD than the male elderly (adjusted OR = 1.897; 95% CI: 1.152–3.122). The elderly with a marital status of married but not living with spouse had larger odds of CKD than the elderly with a marital status of married and living with spouse (adjusted OR = 1.837; 95% CI: 1.161–2.907). The elderly with low plasma albumin had a higher risk of CKD than the elderly with high plasma albumin (adjusted OR = 0.928; 95% CI: 0.885–0.973). The elderly with high urea acid had a higher risk of CKD than those with low urea acid (adjusted OR = 1.004; 95% CI: 1.001–1.006). The analysis showed that the elderly with hypertension (adjusted OR=1.957; 95%CI: 1.298–2.951) had a higher risk of CKD than those without hypertension.

Prediction appearance for elderly with CKD by using the six ML models

A comparison of the ROC curves of the six ML models for elderly with CKD is shown in Figure 2A and Table 3. We further compared the models by using the DeLong test. LR, lasso regression, RF, GBDT and DNN showed no statistical significance (AUC > 0.7), implying that these models had similar predictive power. In our study, SVM had the lowest predictive performance (AUC = 0.633, p-value = 0.06). The threshold values of LR, lasso regression, RF, GBDT, SVM, and DNN were 0.127, 0.138, 0.272, 0.050, 0.180, and 0.352, respectively. SVM had the highest accuracy (0.732, 95% CI: [0.677–0.782]), and LR had the lowest accuracy (0.634, 95% CI: [0.576–0.690]). SVM had the lowest sensitivity (0.460), and DNN had the highest sensitivity (0.760). The specificity of SVM was the highest (0.716), and the specificity of the LR was the lowest (0.612). DNN had the highest PPV (0.328), whereas LR had the lowest PPV (0.287). DNN had the highest NPV (0.930), whereas SVM had the lowest NPV (0.874). DCA (Figure 2B) showed that within the threshold ranges of ∼0–0.03 and 0.37–0.40, the net benefit of GBDT was the largest, and within the threshold ranges of ∼0.03–0.10 and 0.26–0.30, the net benefit of RF was the largest.

Importance of CKD predictors for the elderlys

The importance of the predictors in the RF and GBDT models is shown in Figure 3. Age was the most important predictor variable in both models. In addition, blood urea nitrogen, serum albumin, uric acid, BMI, marital status, ADL/IADL and gender were crucial in predicting CKD amongst the elderly.

Discussion

This study was based on the panel data of 925 elderly individuals in the 2012 baseline survey and 2014 follow-up survey of the HABCS database. The data included the socioeconomic status, unhealthy lifestyle, chronic diseases and other biological indicators of each elderly person. We used six ML models (LR, lasso regression, RF, GBDT, SVM, and DNN) to predict the risk of CKD in the elderly 2 years later. The results showed that the ML model has excellent performance in predicting the risk of CKD in the elderly. The DCA result indicated that all ML models can generate a huge net benefit within various thresholds, and each ML model has its own advantages derived from its net benefit within different threshold ranges.

TABLE 2 Characteristics and odds ratio of elderly with depression presenting to the CLHLS 2014.

Predictors		All elderly N[a] (%)	Elderly with CKD[b] N (%)	Elderly with non-CKD N (%)	p-value	Crude OR[c] (95%CI[d])	Adjusted OR[g] (95%CI)
Age		80.27 ± 11.01	87.34 ± 10.73	78.67 ± 10.44	<0.001	1.072 (1.056–1.089)	1.066 (1.041–1.092)
Gender	Male	499 (53.9)	62 (12.4)	437 (87.6)	<0.001	Reference	Reference
	Female	426 (46.1)	108 (25.4)	318 (74.6)		2.394 (1.697–3.377)	1.897 (1.152–3.122)
Marital status	Married and living with spouse	500 (54.1)	48 (9.6)	452 (90.4)	<0.001	Reference	Reference
	Married but not living with spouse	414 (44.8)	121 (29.2)	293 (70.8)		3.889 (2.699–5.603)	1.837 (1.161–2.907)
	Divorced	11 (1.2)	1 (9.1)	10 (90.9)		0.942 (0.118–7.515)	0.794 (0.082–7.723)
Cognitive function		20.70 ± 4.43	19.34 ± 5.80	21.01 ± 3.99	<0.001	0.929 (0.899–0.961)	1.010 (0.967–1.056)
Smoking	No	725 (78.4)	146 (20.1)	579 (79.9)	0.009	Reference	Reference
	Yes	200 (21.6)	24 (12.0)	176 (88.0)		0.541 (0.340–0.860)	0.891 (0.496–1.603)
Drinking	No	747 (80.8)	142 (19.0)	605 (81.0)	0.31	Reference	Reference
	Yes	178 (19.2)	28 (15.7)	150 (84.3)		0.795 (0.511–1.239)	1.222 (0.704–2.122)
ADL/IADL[e]		38.62 ± 5.78	36.57 ± 6.79	39.08 ± 5.42	<0.001	0.939 (0.916–0.963)	1.027 (0.989–1.068)
BMI[f]		22.59 ± 16.10	24.86 ± 35.20	22.08 ± 6.21	0.31	1.009 (0.995–1.022)	1.025 (0.999–1.052)
Waist circumference		82.55 ± 32.10	82.97 ± 11.18	82.45 ± 35.13	0.74	1.000 (0.996–1.005)	1.001 (0.997–1.006)
Plasma albumin		40.83 ± 4.75	39.04 ± 5.36	41.23 ± 4.51	<0.001	0.906 (0.874–0.940)	0.928 (0.885–0.973)
Blood urea nitrogen		6.29 ± 1.64	6.43 ± 1.75	6.25 ± 1.61	0.23	1.067 (0.965–1.179)	1.133 (1.012–1.267)
Total cholesterol		4.33 ± 0.95	4.18 ± 0.97	4.36 ± 0.94	0.03	0.813 (0.679–0.974)	0.925 (0.727–1.177)
Triglyceride		0.99 ± 0.61	0.97 ± 0.56	1 ± 0.63	0.59	0.931 (0.703–1.234)	1.142 (0.808–1.613)
Urea acid		270.37 ± 79.02	270.21 ± 74.89	270.4 ± 79.97	0.98	1.000 (0.998–1.002)	1.004 (1.001–1.006)
Hemoglobin		131.33 ± 22.12	126.55 ± 20.61	132.4 ± 22.32	0.001	0.987 (0.979–0.995)	0.998 (0.989–1.008)
Hypertension	No	691 (74.7)	109 (15.8)	582 (84.2)	<0.001	Reference	Reference
	Yes	234 (25.3)	61 (26.1)	173 (73.9)		1.883 (1.318–2.689)	1.957 (1.298–2.951)
Diabetes	No	903 (97.6)	165 (18.3)	738 (81.7)	0.59	Reference	Reference
	Yes	22 (2.4)	5 (22.7)	17 (77.3)		1.316 (0.479–3.617)	1.736 (0.556–5.416)
Heart disease	No	853 (92.2)	154 (18.1)	699 (81.9)	0.38	Reference	Reference
	Yes	72 (7.8)	16 (22.2)	56 (77.8)		1.297 (0.724–2.322)	1.068 (0.541–2.108)
Stroke and cerebrovascular diseases	No	871 (94.2)	160 (18.4)	711 (81.6)	0.98	Reference	Reference
	Yes	54 (5.8)	10 (18.5)	44 (81.5)		1.010 (0.498–2.050)	0.567 (0.252–1.273)
Cancer	No	922 (99.7)	169 (18.3)	753 (81.7)	0.50	Reference	Reference
	Yes	3 (0.3)	1 (33.3)	2 (66.7)		2.228 (0.201–24.711)	2.232 (0.162–30.816)
Blood disease	No	913 (98.7)	168 (18.4)	745 (81.6)	0.88	Reference	Reference
	Yes	12 (1.3)	2 (16.7)	10 (83.3)		0.887 (0.193–4.085)	1.511 (0.279–8.191)
Depression	No	869 (93.9)	160 (18.4)	709 (81.6)	0.92	Reference	Reference
	Yes	56 (6.1)	10 (17.9)	46 (82.1)		0.963 (0.476–1.950)	1.024 (0.468–2.242)

[a]N represents the samples; [b]CKD, chronic kidney disease; [c]OR, odds ratio; [d]CI, confidence interval; [e]ADL/IADL, activities of daily living/instrumental activities of daily living; [f]BMI, body mass index. [g]An adjusted OR is an odds ratio that controls for other predictor variables in the binary logistic regression.

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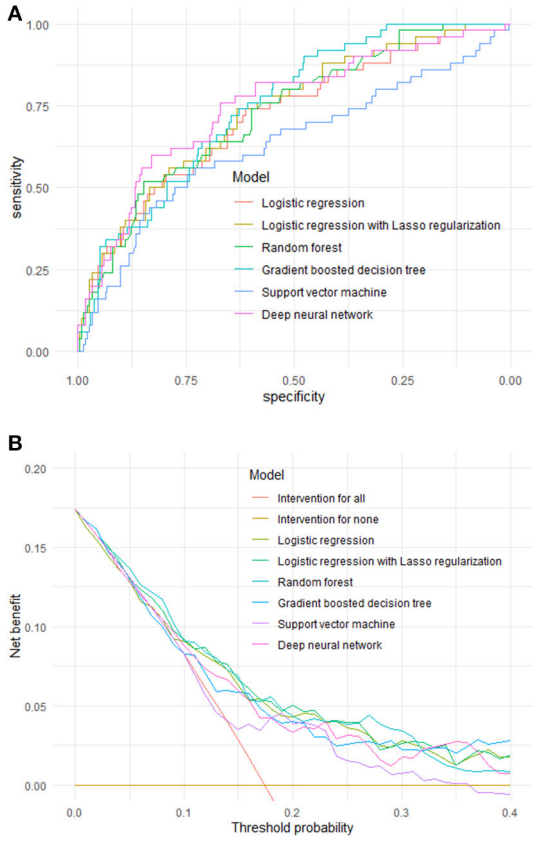

FIGURE 2
Predictive performance of six machine learning models for elderly with CKD **(A)** ROC curve. The x-axis represents specificity (probability of negative test given that the elderly did not have the CKD), and the y-axis represents sensitivity (probability of a positive test given that the elderly had the CKD). **(B)** Decision curve analysis. The y-axis is benefit and the x-axis is preference. The benefit of a test or model is that it correctly identifies which patients do and do not have disease (in our example, CKD).

This study found that the elderly with old age, female, married but not living with a spouse, low plasma albumin, high urea acid and hypertension have a high risk of CKD, which is consistent with the results of several studies (1, 54, 55). Previous studies on CKD risk prediction did not analyze the elderly individually (56–58). The age of respondents in several previous studies was 40 or over 50, but according to the prediction results of the ML model, the AUC value of these studies are all above 0.7. The AUC value of the ML model in this study was between 0.716 and 0.750, which is effective in predicting CKD in the elderly.

Several studies have shown that the ML prediction model is driven by automatic prediction based on the most objective indicators (59, 60). It can use the complex nonlinear relationship between predictors to improve prediction performance. When the sample size is sufficient, the predictive performance of the ML algorithm is good. However, in certain sample screening procedures, the sample size is insufficient. Therefore, we must ensure that the ML algorithm can obtain good prediction performance with a small sample size. In this study, although we selected a relatively small data set of 925 elderly people, the sample size meets the requirements of power analysis and can be used to perform high-precision prediction tasks. The AUC value of most models is close to 0.7, and the performance of linear models is better than that of other types of models. In this study, due to the small amount of data, the linear classifiers could separate samples ideally, and the highly complex ML models (e.g., SVM) demonstrated powerful learning capabilities but were prone to overfitting. The forecast accuracy was thus reduced. SVM performed the worst in this study because the Euclidean distance on which SVM relies is not the best way to deal with the classification of CKD in the elderly. Therefore, the linear model performed better in our study.

When predicting the risk of CKD in the elderly 2 years later, we should determine a threshold for identifying CKD and non-CKD in the elderly. If a model has high PPV and NPV, then it is theoretically ideal. However, in practice, we need to weigh high PPV and high NPV based on the actual situation. In this study, because the proportion of elderly people suffering from CKD is small, we needed to consider the PPV results of different models. This task allows researchers to measure the prediction of the model so that many potential high-risk CKD groups can be screened out. In addition, we used DCA to analyse the net benefits of six ML models at different thresholds. The results can help medical service providers provide flexible model selections based on their professional knowledge to guide clinical decision-making.

This is the first survey to comprehensively study the practicality of different modern ML models in predicting CKD in the elderly in China. The decision support system based on the predictive model in this research can help medical staff detect and intervene in the health of the elderly early, and it can provide scientific evidence for clinical treatment, disease prevention and community health management.

Our study has several limitations. Firstly, only 22 predictors were considered. We restricted our analyses to predictive modeling with known or possible risk factors, including demographic indicators, biomarkers of kidney function and kidney damage, such as ethnicity, serum cystatin C and renalase. Hence, our conclusion cannot be generalized to data sets with numerous predictors. In future studies, we can continue to add more specific predictors to help improve the prediction performance, such as the size and cortical thickness of the kidney. Secondly, the diagnostic criteria for chronic diseases were mainly based on self-reported medical history, and related variables were obtained through questionnaire surveys. No clear test diagnosis was performed. Thus, deviations may be present. Thirdly, the sample size used was relatively small; the tuning

TABLE 3 Prediction performance of elderly with CKD using 6 machine learning models.

Model	AUC[a]	*p*-value[d]	Threshold	Accuracy	Sensitivity	Specificity	PPV[b]	NPV[c]
Logistic regression	0.716	Reference	0.127	0.634 (0.576–0.690)	0.740	0.612	0.287	0.918
Logistic regression with Lasso regularization	0.734	0.28	0.138	0.652 (0.593–0.707)	0.740	0.633	0.298	0.920
Random forest	0.729	0.71	0.272	0.686 (0.629–0.740)	0.640	0.696	0.308	0.902
Gradient boosted decision tree	0.750	0.34	0.050	0.659 (0.601–0.713)	0.720	0.646	0.300	0.916
Support vector machine	0.633	0.06	0.180	0.732 (0.677–0.782)	0.460	0.789	0.315	0.874
Deep neural network	0.750	0.56	0.352	0.686 (0.629–0.740)	0.760	0.671	0.328	0.930

[a]AUC, area under the receiver operating curve; [b]PPV, positive predictive value; [c]NPV, negative predictive value.
[d]p-value is the result of Delong test of AUC curve based on the comparison of each machine learning model.

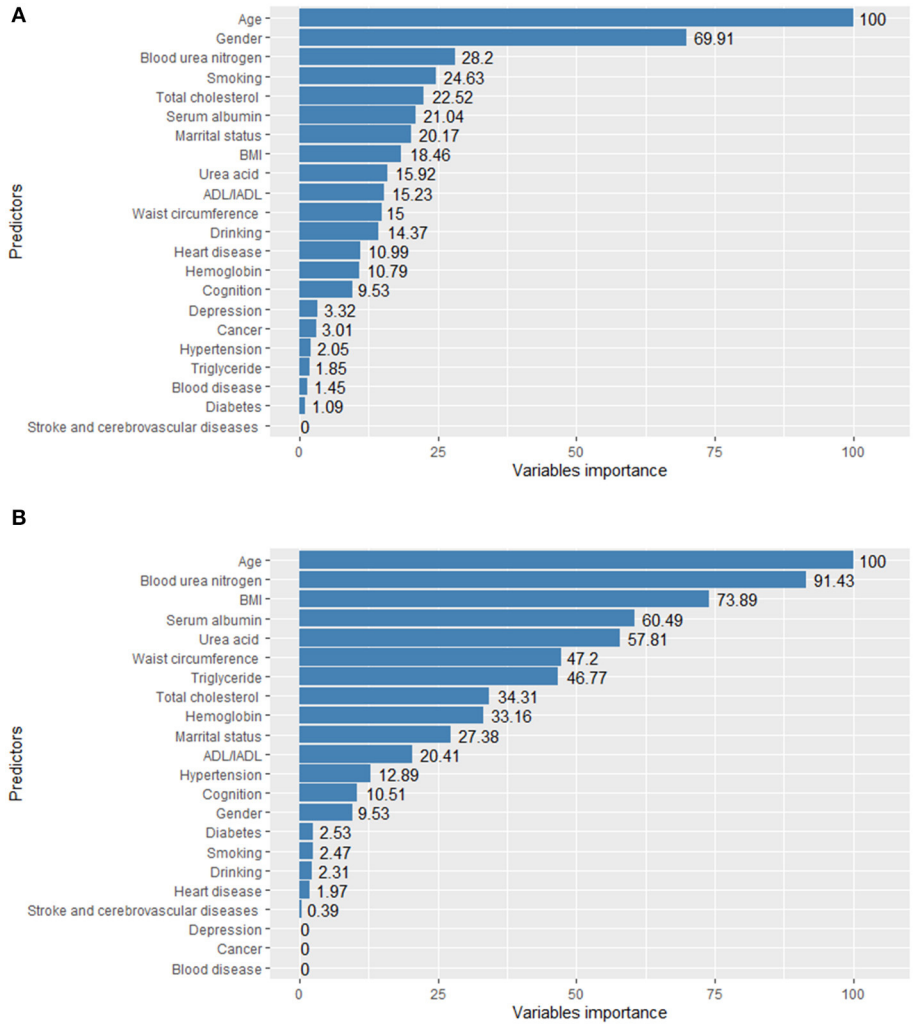

FIGURE 3
Variable importance of RF **(A)** and GBDT **(B)** model for elderly with CKD.

parameters could be optimized further to avoid overfitting. In follow-up research, we can consider recruiting more participants for model testing and evaluation. Lastly, the capability to diagnose depression amongst the elderly depends on local medical resources, and indications and clinical thresholds may vary between emergency departments and clinicians.

Conclusion

We established and compared six ML models that can predict the risk of CKD 2 years later based on the socioeconomic characteristics, unhealthy lifestyle, chronic diseases and biomedical indicators of the elderly. The LR, lasso, RF and ML models, including GBDT and DNN, demonstrated a high overall predictive capability, and the different models showed high net benefit at different threshold levels. We also found that age, blood urea nitrogen, serum albumin, uric acid, BMI, marital status and ADL/IADL exerted an important influence on model predictability, whereas the other predictors were not as important. Further research is required to test the effect of using the system in a clinical environment.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: https://opendata.pku.edu.cn/dataset.xhtml?persistentId=doi:10.18170/DVN/WBO7LK.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee of Peking University (IRB00001052-13074). The patients/participants provided their written informed consent to participate in this study.

Author contributions

DS and NW are the guarantors and contributed to the conception and design of the project. DS, KH, and XZ contributed to the analysis and interpretation of the data. DS, XZ, and YC contributed to the data acquisition and provided statistical analysis support. DS drafted the article. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Oral health-related multiple outcomes of holistic health in elderly individuals: An umbrella review of systematic reviews and meta-analyses

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Background and aims: Along with an aging population, exploring the impact of oral health on holistic health and determining exact outcomes in elderly individuals are important in both scientific research and clinical practice. Significant increase in the number of systematic reviews shows that oral health can directly or indirectly affect the overall health of elderly people physically, mentally and socially. To systematically collate, appraise, and synthesize the current evidence, we carried out an umbrella review of the impacts of oral health on holistic health in elderly individuals.

Methods: A systematic reviews and meta-analyses search was performed in the major databases PubMed, MEDLINE, Web of Science and the Cochrane Library from inception to February 1, 2022, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The JBI (Joanna Briggs Institute) Critical Appraisal Checklist for Systematic Reviews and Research Syntheses was referred to assess methodological quality, and the GRADE (Grading of Recommendations, assessment, Development, and Evaluation working group classification) was used to assess the quality of evidence for each outcome included in the umbrella review.

Results: Out of 1,067 records, a total of 35 systematic reviews were included. Respiratory diseases, malnutrition, age-related oral changes, frailty, cognitive impairment, depression and poor quality of life were identified as seven key outcomes that affect the physical, mental and social health of elderly individuals. Meanwhile, three intervention measures of oral health were summarized as (i) more rigorous and universal scales, (ii) dental cleaning and denture installation, and (iii) improving self-awareness regarding oral care.

Conclusions: Evidence showed that oral health can significantly affect holistic health, and the diverse oral diseases directly lead to multiple health outcomes in elderly individuals. Clear high-quality evidence revealed that oral health is strongly associated with seven health outcomes covering physical, mental, and

social levels, which directly corresponds to holistic health, and impacts the quality of life of elderly individuals. Such the results remind the importance of oral care in public health, and further studies need to be conducted to verity more specific association between oral health and other chronic diseases.

Systematic review registration: https://www.crd.york.ac.uk/PROSPERO/#recordDetails, identifier: CRD42022315315.

KEYWORDS

oral health, holistic health, elderly individuals, multiple outcomes, umbrella review

Introduction

With the rapid aging of the population worldwide, the holistic health of elderly individuals has become a crucial issue in both developing and developed countries (1, 2). In general, holistic health is defined as a state of complete physical, mental and social functioning, not only the absence of disease and frailty (3), which has been increasingly studied, especially among older people. With increased life expectancy (4), the risks of multiple chronic communicable/non-communicable physical diseases, mental impairments and social disorders are increasing continuously (5, 6). In addition, people have become increasingly aware that the occurrence of such diseases tends to be a cross result; namely, there is always a strong correlation between one poor health outcome and multiple complications, which, however, is severely neglected (7). Typically, as one of the most crucial issues among elderly individuals, people realize that poor oral health is significantly associated with holistic health and can result in multiple health outcomes (8–11). Furthermore, instead of primarily addressing oral diseases or oral hygiene itself, an increasing number of studies in recent years have focused on revealing the correlation between oral health and different common diseases in elderly individuals (12–14).

For instance, evidence has shown that 15% of cases of community-acquired pneumonia or other respiratory diseases, which are considered some of the most common chronic diseases among elderly individuals, are significantly associated with oral bacteria (15). Correspondingly, it has been reported that once regular oral nursing care is lacking, the pathogenic microorganisms colonizing the oral microbiome are strongly correlated with the aggravation of respiratory diseases, including aspiration pneumonia, chronic obstructive pulmonary disease (COPD), and even COVID-19, in elderly individuals in residential care (16–18). Simultaneously, older people with poor awareness of autonomous oral care not only take higher risks of periodontitis and/or dental caries related to oral diseases, but the higher load of microorganisms easily gives rise to frailty (11, 16), loss of function (19) and multiple chronic comorbidities (20, 21). Tooth loss and a decline in chewing ability are also considered to be accompanied by malnutrition and low quality of life (22, 23). In addition, poor oral health can directly and indirectly impact the mental health of elderly individuals and lead to cognitive impairment (24) and depression (25, 26). Moreover, it has also been reported that understanding the economic burden of oral diseases is essential to evaluate the societal relevance of preventing and addressing oral diseases (27).

Although there is an increasing amount of research and systematic reviews on the impacts of oral health on different health outcomes, and published articles on corresponding topics have covered a variety of general health outcomes among elderly individuals, such studies have mainly focused on the association between oral health and some specific diseases; a body of work describing the current landscape of intervention and nursing measures that links oral health and the diverse outcomes covering physical, mental, and social health is still missing (28, 29). Accordingly, it is still challenging for practitioners and decision-makers to find, interpret, and utilize related evidence in daily nursing and medical processes.

The aim of this umbrella review, therefore, is to provide an overall examination and synthesis of the available qualitative and quantitative evidence on the oral health of elderly individuals from a higher-level perspective and explain the impact of oral health on multiple outcomes of holistic health among elderly individuals. On this basis, the objectives of the review are to assess, identify, analyse, and synthesize the evidence on (1) an exact correlation between oral health and multiple outcomes of holistic health in older people and (2) solutions and suggestions, including effective interventions in clinical practice for nursing care.

Materials and methods

The protocol of this study was registered in PROSPERO registry (CRD42022315315), and the review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA).

TABLE 1 PICOS criteria for inclusion of studies.

Item	Criteria	Description
Participation	Does the study involve elderly individuals?	Yes
Intervention	NA	
Comparator	NA	
Outcomes	Does the study report effect on oral health-related multiple outcomes of holistic health?	a. Respiratory diseases b. Malnutrition c. Frailty d. Diabetes mellitus e. Cardiovascular conditions f. Age-related oral changes g. Cognitive impairment h. Depression i. Poor quality of life
Study design	Is the study a systematic review?	Systematic reviews with/without meta-analyses are considered.

NA, not available.

Eligibility criteria

Studies were selected based on the following eligibility criteria: (a) included a systematic review with/without meta-analyses on oral health among older people; (b) investigated the association of different multiple outcomes of holistic health among older people; and (c) included older people as the study population, which exactly corresponds to populations, interventions, comparators, outcomes and study designs (PICOS) as presented in Table 1.

Data sources and search strategy

The electronic databases PubMed, MEDLINE, Web of Science, and the Cochrane Library were systematically searched for review articles to identify systematic reviews with meta-analyses of observational or interventional studies that researched the multiple oral health-related outcomes of holistic health among older people. The following research strategy was used to conduct the literature search: (oral health or oral diseases) AND (systematic review∗ OR meta-analysis*), using truncated terminology for all areas (see Supplementary Table 1). We limited search to reviews written in English or Chinese published before February 2022. Searches were restricted by the level of evidence (systematic review and meta-analysis, or other evidence syntheses). Literature reviews or other types of non-systematic reviews were excluded. In addition, we checked reference lists and performed lateral searches using the "related articles" option in PubMed and the "cite by" option in Web of Science. The reference lists of eligible papers and relevant clinical guidelines were also searched (see research strategy in Supplementary Table 1). All searches were carried out on 1 February 2022.

Selection of reviews

Two of the authors (FL and SS) worked together to remove duplicates with EndNote reference management software, reviewed titles and abstracts for relevance, and finally selected the papers, which required the agreement of both reviewers. Disagreements were resolved through consensus or discussion with the third researcher (XH).

Quality appraisal

Review articles included in the final analysis were critically evaluated using the "JBI Critical Appraisal Checklist for Systematic Reviews and Research Syntheses" (JBI CAC for SRRS) by two reviewers (30), and no reviews were eliminated according to their results from this instrument. The JBI assessment tool consists of 11 questions (see the detailed checklist in the Supplementary material). Every question is assessed with four possible answers: Yes, No, Unclear or Not Applicable. Each "Yes" response gains one point, and all other answers receive zero points. Based on the sum of the points, the quality of papers was divided into three groups: low (0–4), moderate (5–8), and high (9–11) quality (31). The quality of the evidence (QoE) supporting each bottom-line statement was rated by using a method of the GRADE approach for primary evidence (1 = very low; 2 = low; 3 = moderate; 4 = high) (Box 1) (32, 33). This method takes into account the study design (meta-analysis; yes or no) and JBI CAC rating of the included systematic reviews.

Data extraction and synthesis

The following data were extracted from each manuscript: (1) the name of the first author and publication year; (2) the study design, number of primary studies included in the meta-analysis, the study characteristics and the total number of participants; (3) the respective outcome according to the eligibility criteria; and (4) risk estimates and corresponding confidence intervals and the respective significance level. If relevant data were not available in the respective papers, we sent email inquiries to the corresponding authors. If the author did not reply or could not provide the missing data, we marked the missing information as "No". Reviews and primary studies were classified as quantitative, qualitative or mixed methods studies. The primary studies in each review were tabulated to assess the overlap between reviews. Effectiveness was investigated by categorizing the different outcomes reported

and tabulating the data, including an indication of whether the effects of the intervention were positive, negative or not statistically significant.

Results

Selection of relevant reviews

A total of 1,066 records identified through database searching and 1 additional record identified through other sources were imported into the reference management programme EndNote X9.3.1. After examining the records in this programme, 400 duplicates were removed, and 667 records remained. Next, two authors independently screened the titles and abstracts of the remaining records, and 579 papers were excluded because they did not meet the inclusion criteria. Furthermore, based on the inclusion and exclusion criteria, 53 of the 88 articles were excluded after full-text review because these studies did not focus on elderly individuals, did not mention outcomes of holistic health, or did not include systematic reviews with/without meta-analyses. Finally, 35 review papers met the inclusion criteria and were included in the analysis and synthesis of this study. Figure 1 illustrates the detailed selection of the review papers. The detailed information of the papers is shown in Table 2, which summarizes the elements of the selected reviews, indicating the diversity of research designs, participant groups and outcomes addressed by the authors.

Participants and settings

Six of the included papers were from the Netherlands, five were from the United States, five were from Brazil, four were from China, three were from Canada, two were from Australia, Iran and Sweden, and one was from the United Kingdom, Italy, Japan, Spain, Denmark and Belgium, respectively. The average number of authors was 5.3 ± 1.9. The publishing year of the papers ranged from 2003 to 2021. The average number of databases referred was 4.5 ± 1.6.

The most common groups of participants investigated were elderly individuals living in hospitals or nursing homes. Meanwhile, community-dwelling or institutionalized/non-institutionalized older adults were also the main participant groups investigated in the primary studies. In addition, three studies considered all elderly individuals in general. Among the included reviews, total participants ranged from 618 to 121,547, while 13 of the included papers did not report the total number but presented the ranges of the ages of the elderly participants instead.

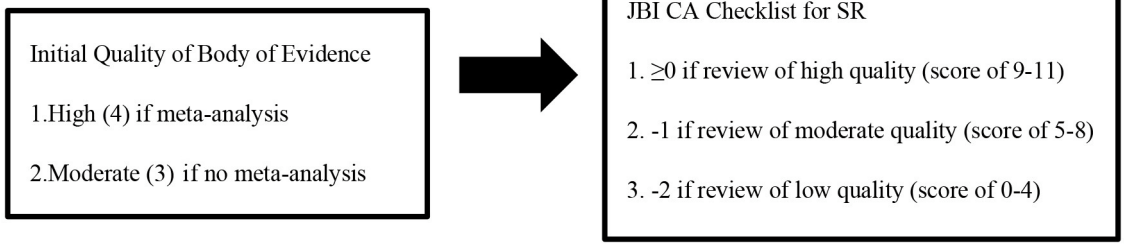
Designs and characteristics of the reviewed articles

Most of the included systematic reviews consisted of cross-sectional and longitudinal studies, and 12 reviews consisted of randomized controlled trials (RCTs). The summarized findings of the included reviews came from between 4 and 68 primary studies. Eleven reviews also conducted meta-analyses with/without RCT results that were relevant to the present umbrella review.

Critical assessment and risk of bias in the included review papers

The corresponding detailed critical assessment and risk of bias of the reviews are shown in Supplementary Table 2. Eight papers were evaluated as medium quality, and the others were graded as high quality.

BOX 1 Method used to rate the quality of the evidence supporting each bottom-line statement.



CA, critical appraisal; SR, systematic reviews.

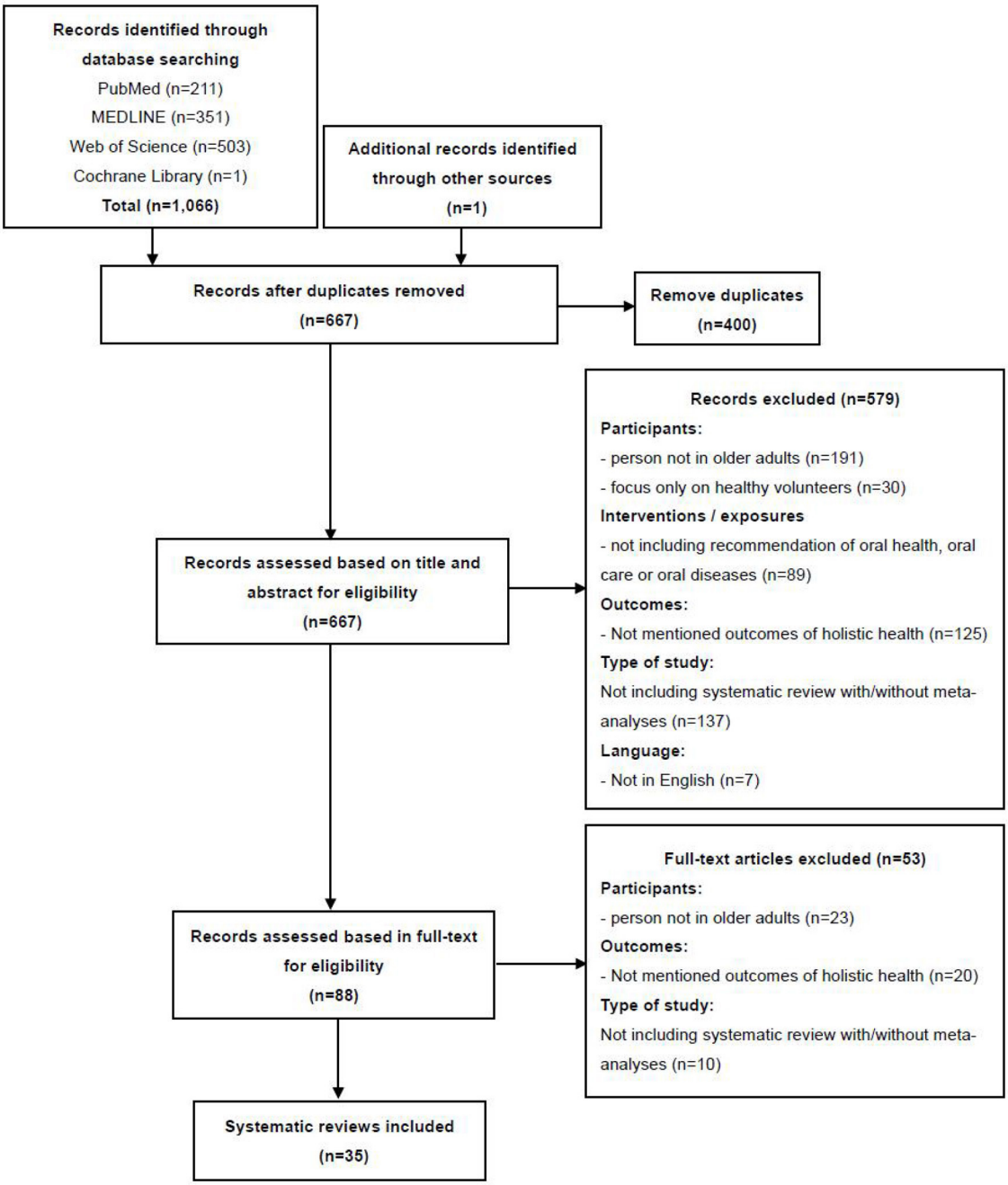


FIGURE 1
PRISMA flowchart.

Key data synthesis results

The included papers showed a varied range of the impacts of oral health on holistic health among older people. According to the definition of holistic health, three secondary level subthemes can be conceptualized to meaningfully generalize the comprehensive outcomes.

In terms of the research topics, the subthemes based on the main theme can be identified as (i) physical outcomes ($N = 23$); (ii) mental outcomes ($N = 6$); and (iii) social outcomes ($N = 6$), as shown in Supplementary Table 3.

Physical outcomes

Twenty-three systematic reviews provided data on physical outcomes, of which 7 included a meta-analysis. Nine systematic reviews (2 with a meta-analysis) (29, 30) focused on respiratory diseases (13, 15, 50–56), 5 (2 with a meta-analysis) (39, 40) on age-related oral changes (39–43), 6 (3 with a meta-analysis) (28, 36, 38) mainly on malnutrition and 3 (none with a meta-analysis) on frailty (29, 57, 58).

Respiratory diseases

All the corresponding reviews, in general, showed that oral health is crucially related to the incidence of aspiration pneumonia, and various poor oral hygiene factors are considered significant risk factors for different respiratory diseases. Five systematic reviews with low to high quality scores showed that the prevalence of cariogenic and periodontal pathogens in saliva and dental plaque as well as dental decay due to poor oral hygiene are potential risk factors for pneumonia and chronic obstructive pulmonary disease (13, 15, 50, 55, 56). One systematic review of moderate quality pointed out that higher plaque scores were strongly associated with a previous history of respiratory tract infection (50). In particular, one moderate-quality review mentioned that the detection and isolation rates of *Candida albicans, Staphylococcus aureus*, methicillin-resistant *S. aureus, Pseudomonas aeruginosa,* and even *Escherichia*, which are strongly related to mortality due to aspiration pneumonia, are much higher among older people with poor oral health (13).

On the other hand, 6 systematic reviews (2 with meta-analyses) of moderate to high quality showed that regular oral care intervention and cleaning are significant factors for preventing aspiration pneumonia in older people (13, 15, 51–54). Mechanical and/or topical chemical disinfection or antibiotics such as povidone iodine can greatly reduce the incidence of nosocomial pneumonia (15, 52). Both the meta-analyses of high quality examined the impacts of oral hygiene on the incidence rate of hospital aspiration pneumonia (HAP) and showed that while there was no evidence verifying whether professional oral care was better or worse than routine oral care, it demonstrated that professional oral care can truly reduce mortality from HAP (51, 53). One review of low quality pointed out that tooth brushing, denture cleaning and regular professional oral health care are the best interventions to reduce the incidence of aspiration pneumonia (56). Combined with the quality and results of the included reviews, respiratory diseases should be considered to be closely associated with poor oral health.

Age-related oral changes

Poor oral health adds to the burden of the change in the microenvironment for older people (43), which directly aggravates dental/root caries and periodontitis in both developing and developed countries among institutionalized elderly individuals (42). Two high-quality meta-analyses that assessed the salivary flow rate of elderly people showed that the prevalence of hyposalivation in older people is higher than that in other populations, but there was no clear evidence to verify the relevance between the level of salivary production and function in elderly people (39, 40). Simultaneously, as a counterpart of the outcome, 1 systematic review of moderate quality showed that one of the reasons for oral changes in older people over 65 is long hospital stays or being institutionalized in a residential home (41), which therefore demonstrated the importance of developing protocols for elderly individuals' oral health care and providing more professional training to caregivers. Combined with the quality and results of the included reviews, malnutrition should be considered to be closely associated with poor oral health.

Malnutrition

Five reviews of low to high quality showed that the condition of the dentition is strongly associated with the prevalence of malnutrition in elderly individuals (28, 35–38), of which 2 quantitative meta-analyses of high quality pointed out that the nutritional status of elderly individuals with good dentition or dentures is significantly better than those with fewer functional tooth units or anodontia (28, 36). Meanwhile, 3 reviews of low to high quality demonstrated that masticatory problems, which have been identified as independent predictors for low BMI and serum albumin level, weight loss and protein-energy malnutrition (37), are also key for malnutrition (28, 35, 37). Elderly people with chewing problems had nearly twice the risk of malnutrition, and importantly, a lack of tooth/denture cleaning lack of autonomy for oral care, no access to the dentist and being edentulous placed elderly individuals at higher risk of malnutrition (28). On the other hand, two systematic reviews of moderate quality also showed that soft tissue problems, including tongue with blisters, dry or cracked lips and other functional loss, may hinder the intake of nutrients, which can also lead to malnutrition among older people (34, 37). Combined with the quality and results of the included reviews, malnutrition should be considered to be closely associated with poor oral health.

Frailty

The evidence for frailty in elderly individuals is complex. Two systematic reviews of moderate quality analyzed the

TABLE 2 Main characteristics of the articles included in the systematic umbrella review.

References, review design	Aim or objective	Search strategy	Type of studies: total number + design	Setting of participants. Total number of participants (if available)	Study outcomes related to holistic health
Nutrition					
Algra et al. (34) Systematic review	To examine the association between malnutrition and oral health in older people.	Databases: 4, PubMed, CINAHL, DOSS, and Embase. Langue: limited to English and Dutch. Date: from January 2000 to May 2020.	10 studies: 9 cross-sectional studies + 1 longitudinal cohort study	Nursing homes, dental clinics, community community-welling older people, or hospital units (acute care units or rehabilitation). Total $N = 9,093$.	The association between malnutrition and oral health, the state of hard and soft tissues of the mouth, salivary flow, and xerostomia
Hussein et al. (28) Systematic review and meta-analysis	To evaluate whether poor oral health is associated with a higher risk of malnutrition based on MNA or MNA-SF in older adults.	Databases:4, PubMed, Web of Science, Cochrane Library and EMBASE. language: English. Date: up to June 2020.	33 studies: 28 cross-sectional studies + 5 cohort studies	Community-dwelling older adults, interviewed at home or in emergency rooms or hospital wards, institutionalized older adults, living in nursing homes or assisted living facilities. Total $N = 27,559$	MNA or MNA-SF
Tada and Miura (35) Systematic review	To assess the association of mastication with food and nutrient intake in the community dwelling elderly.	Databases:4, PubMed, Web of Science, Cochrane Library, and Scirus. Langue: English. Date: between 1991 and 2013.	35 studies: 28 cross-sectional studies + 7 intervention studies	Community dwelling elderly (Non-institutionalized healthy elderly, dental school hospitals.) Total *N* not reported.	Food intake or nutrient intake
Toniazzo et al. (36) Systematic review and meta-analysis	To compare the nutritional status and oral health in older individuals.	Databases:3, Medline-Pubmed, Scopus and EMBASE. Language: no restrictions. Data: up to October 28th 2016.	26 studies: 23 cross-sectionals + 1 case-control + 1 cohort + 1 clinical trial	Non-institutionalized older adults. Total $N = 13,257$.	The malnutrition or risk of malnutrition related with oral health
Van Lancker et al. (37) Systematic review	To determine whether an association exists between oral health and malnutrition in the elderly in a long-term care facility.	Databases:3, Medline, CINAHL and Cochrane Library. Language: in English, Dutch, French, or German. Date: between January 1985 and May 2011.	16 cross-sectional studies	Long-term care facility. Total *N* not reported, number of included patients varied between 40 and 3,088.	The association between oral health status and malnutrition

(Continued)

TABLE 2 (Continued)

References, review design	Aim or objective	Search strategy	Type of studies: total number + design	Setting of participants. Total number of participants (if available)	Study outcomes related to holistic health
Zelig et al. (38) Systematic review and meta-analysis	To determine the association between tooth loss and nutritional status by the validated nutrition screening or assessment tool.	Databases:5, PubMed, Scopus, CINAHL, Web of Science, and MEDLINE. Language: English. Date: between January 2009 and December 2019.	7 studies: 6 cross-sectionals and 1 cohort	Adults living in the community and institutions. Total *N* = 7,897.	Associations between tooth loss and nutritional status
Age-related oral changes					
Affoo et al. (39) Systematic review and meta-analysis	To determine whether salivary flow decreases as a function of aging.	Database:7, PubMed, EBSCOhost, Web of Science, Cochrane library, EMBASE, Dissertations and Theses, and Scopus databases. Language: English. Date: up to June 2013.	47 cohort studies	All general elderly. Total *N* not reported, number of included patients varied between 15 and 1,427.	The aging process is associated with reduced salivary flow in a salivary-gland.
Pina et al. (40) Systematic review and meta-analysis	To determine the prevalence of hyposalivation in older people.	Database:6, Embase, LILACS, Medline, PubMed, Web of Science and Google Scholar. Language: no restrictions. Date: up to February 2019.	13studies: 10 cross-sectional studies + 3 cohorts	All general elderly. Total *N* = 3,885	The prevalence of hyposalivation
Ruiz-roca et al. (41) Systematic review	To ascertain the oral health status of older people patients admitted to institutions or hospitalized for a long period of time.	Database: 2, PubMed and Cochrane Library. Language: English and/or Spanish and/or Portuguese. Date: 1 January 2014 to 1 January 2019.	5 studies: 2 cross-sectional + 2 cohorts + 1 case-control study	Older hospitalized for long term at least 7 days. Total *N* = 773	Poorer results in patients institutionalized in the periodontal index score
Chan et al. (42) Systematic review	To provide an update on caries prevalence in older adults around the globe.	Database: 5, PubMed, Scopus, Embase/Ovid and Web of Science, Google Scholar. Language: English. Date: January 2016 to March 2021.	39 (8 additional) cross-sectional surveys	Community, residential homes, and hospitals. Total *N* not reported.	Caries prevalence

(Continued)

TABLE 2 (Continued)

References, review design	Aim or objective	Search strategy	Type of studies: total number + design	Setting of participants. Total number of participants (if available)	Study outcomes related to holistic health
López et al. (43) Systematic review	To review the burden of caries and periodontitis in the elderly, changes with age that can explain this burden, and the vulnerability to disease of elderly populations.	Database: 2, PubMed, Medline. Language: NA.	18 studies	All general elderly. Total *N* not reported.	Caries and periodontitis burden
Quality of life					
van de Rijt et al. (44) Systematic review	To identify oral health factors associated with OHQoL in the elderly and to give a comprehensive overview of the body of literature for each oral health factor separately.	Databases:5, PubMed, Embase, EBSCO/CINAHL, EBSCO/PsycINFO, and Wiley/ Cochrane Library. Language: no restrictions. Date: up to April 3, 2019.	68 studies: 9 RCTs (randomized clinical trials) + 6 cohort studies + 53 cross-sectional studies	In community or in institutional care. Total $N = 47,770$.	OHQoL
Wong et al. (45) Systematic review	To describe recently reported oral health levels, the OHRQoL and the associated factors.	Databases:6, Cochrane Library, JBI, MEDLINE, EMBASE, CINAHL, Google Scholar. Language: English. Date: between July 2009 and June 2019.	25 studies: 22 cross-sectional studies + 3 case-control studies	Institutionalized homes, long-term care, nursing homes and residential homes. Total $N = 10,958$.	OHQoL
Azami-Aghdash et al. (46) Systematic review and meta-analysis	To assess oral health-related quality of life in older people.	Database: 7, PubMed, EMBASE, Scopus, SID, MagIran, Cochrane Library, google scholar. Language: English. Date: from 1st Jan 2000 to 30th Jan 2017.	40 studies: The type of included studies was not mentioned	All general elderly. Total $N = 22,416$.	OHQoL
Baniasadi et al. (47) Systematic review and meta-analysis	To determine the relationship between poor OHRQoL and oral health determinants.	Database: 4, PubMed, Scopus, Cochrane Library and Web of Science. Language: English. Date: before 1 December 2019.	19 studies: 18 cross-sectional studies + 1 cohort study	All general elderly. Total *N* not reported.	The association between poor OHRQoL and oral health.

(Continued)

TABLE 2 (Continued)

References, review design	Aim or objective	Search strategy	Type of studies: total number + design	Setting of participants. Total number of participants (if available)	Study outcomes related to holistic health
de Medeiros et al. (48) Systematic review	To evaluate whether treatment with new complete dentures improves quality of life in elderly patients.	Database: 6, MEDLINE/PubMed, Scopus, LILACS, SciELO, Web of Science, and Cochrane Library. Language: in English, Spanish, Portuguese. Data: up to March 2018.	7 studies: 6 RCTs + 1 cohort study	Residential or nursing homes, sheltered accommodations, private homes, or hospitals. Total $N = 618$.	Quality of life in elderly patients with new complete dentures
Ming et al. (49) Systematic review and meta-analysis	To increase understanding of OHRQoL among patients with AD and explore factors that may affect OHRQoL.	Database: 6, PubMed, Cochrane Library, Medline, EBSCO, ProQuest, and EMBASE. Language: English. Date: until August 30, 2018.	6 studies: 5 cross-sectional designs + 1 nRCT	All general elderly. Total $N = 632$.	The association between OHRQoL and AD
Respiratory diseases					
Azarpazhooh et al. (50) Systematic review	To investigate evidence for a possible etiological association between oral health and pneumonia or other respiratory diseases.	Database: 9, Ovid MEDLINE, Cumulative Index to Nursing & Allied Health Literature, Cochrane library, Database of Abstracts of Reviews of Effects, EMBASE, Health and Psychosocial Instruments, HealthSTAR, PubMed, and Google Scholar. Language: English. Date: from the earliest record until July 2005.	10 studies: 9 case-control + 1 cohort study	In nursing homes and especially in ICUs. Total *N* not reported.	Outcomes related to respiratory diseases
Khadka et al. (13) Systematic review	To determine potentially pathogenic microorganisms in oral specimens of older people with aspiration pneumonia and the effect of POHC in reducing aspiration pneumonia risk.	Database:7, PunMed/MEDLINE, CINAHL, EMBASE, Cochrane library, PROQUEST, Google Scholar, and Web of Science. Language: English. Date: published between January 2001 and December 2019.	12 studies: 4 cross-sectionals + 5 cohort + 3 interventions (9 observational studies included a followed-up period ranging from 6 months to 9 years or until participants were no longer living.	Older adults in residential care. Total *N* not reported.	Aspiration pneumonia as an outcome and describing oral microorganisms.

(Continued)

TABLE 2 (Continued)

References, review design	Aim or objective	Search strategy	Type of studies: total number + design	Setting of participants. Total number of participants (if available)	Study outcomes related to holistic health
Liu et al. (51) Systematic review and meta-analysis	To assess effects of oral care measures for preventing nursing home-acquired pneumonia in residents of nursing homes and other long-term care facilities.	Database: 6, Cochrane Library, MEDLINE Ovid, Embase Ovid, CINAHL, ClinicalTrails. Gov, WHO. Language: no restrictions. Date: up to 15 November 2017.	4 RCTs	Residents of nursing homes and other long-term care facilities. Total $N = 3,905$.	Outcomes related to home-acquired pneumonia.
Loeb et al. (52) Systematic review	To assess the effectiveness of prevention of AP in older adults: compensatory strategy/positioning changes, dietary interventions, pharmacologic therapies, oral hygiene, and tube feeding.	Database:5, MEDLINE, EMBASE, Cochrane Library, CINAHL, and HealthSTAR databases. Language: no restrictions. Date: from 1997 to 2001.	8 RCTs	Older adults in nursing homes. Total $N = 1,234$.	Primary outcome: AP; Secondary outcomes: related to the effects of aspiration that were assessed included dehydration, gross aspiration, nutritional intake, and death.
Scannapieco et al. (15) Systematic review	To determine if interventions that improve oral hygiene reduce the rate of pneumonia in high-risk population.	Database: 4, MEDLINE, pre-MEDLINE, MEDLINE Daily Update, and Cochrane library. Language: English. Date: from 1966 through March 2002.	30 studies: 21 case-control studies + cohort studies + 9 RCTs.	Elder patients or institutionalized patients in nursing homes. Total $N = 3,172$.	Primary outcome: reduced rate of pneumonia or lung disease, Secondary outcomes: improved lung function. Patients-centered outcomes: quality life issues, Adverse outcomes: intraoral adverse effects, increased rate of pneumonia.
Sjögren et al. (53) Systematic review and meta-analysis	To compare the effect of intensified oral care interventions given by dental or nursing personnel on mortality in elderly adults in hospitals or nursing homes with the effect of usual oral care.	Database: 3, PubMed, Cochrane library, and HTA. Language: English, Danish, Norwegian, or Swedish. Date: published since January 1, 1996.	5 RCTs	Elderly adults in hospitals or nursing homes. Total N not reported.	The outcome was mortality from HAP

(Continued)

TABLE 2 (Continued)

References, review design	Aim or objective	Search strategy	Type of studies: total number + design	Setting of participants. Total number of participants (if available)	Study outcomes related to holistic health
Sjögren et al. (54) Systematic review	To investigate the preventive effect of oral hygiene on pneumonia and respiratory tract infection, focusing on elderly people in hospitals and nursing homes.	Database: 2, Medline, Cochrane library. Language: Dutch, English, German, and any of the Nordic languages (Danish, Finnish, Icelandic, Norwegian, Swedish). Date: from 1996 to 2007.	15 studies: 5 RCTs + 10 nRCTs	Elderly people in hospitals and nursing homes. Total *N* not reported.	Pneumonia and respiratory tract infection, death from pneumonia
van der Maarel-Wierink et al. (55) Systematic review	To systematically review the risks for aspiration pneumonia in frail older people and the contribution of bad oral health among the risk factors.	Database: 5, PubMed (Medline), Web of Science, Cochrane Library, EMBASE, and CINAHL. Language: English. Date: January 2000 to April 2009.	21 studies: 1 case-cohort + 12 cohort + 7 case-control + 1 cross-sectional design	Frail elder people in hospitalized, institutionalized, or frail home-dwelling. Total *N* not reported.	The risks of aspiration pneumonia
van der Maarel-Wierink et al. (56) Systematic review	To systematically review the literature on oral health care interventions in frail older people and the effect on the incidence of aspiration pneumonia.	Database: 5, PubMed, Web of Science, Cochrane Library, EMBASE and CINAHL. Language: English. Date: from January 2000 to July 2010.	5 RCTs	Hospitalized or institutionalized people. Total *N* not reported.	The incidence of aspiration pneumonia
Frailty					
Slashcheva et al. (29) Systematic review	To updating the evidence for association between oral health characteristics and frailty status, identifying gaps in translational dental research and application of frailty assessment into clinical practice.	Database: 5, MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, Embase, Cochrane library and Scopus. Language: English. Date: Until to 2 January 2020.	26 studies: 17 Cross sectional studies + 9 longitudinal studies	All general elderly. Total $N = 37,925$.	Association between oral health characteristics and frailty status

(Continued)

TABLE 2 (Continued)

References, review design	Aim or objective	Search strategy	Type of studies: total number + design	Setting of participants. Total number of participants (if available)	Study outcomes related to holistic health
Tôrres et al. (57) Systematic review	To assess the relationship between frailty or one of its components and poor oral health.	Database: 5, PubMed, EMBASE, Cochrane library, LILACS, and SciELO. Language: English, Spanish, or Brazilian Portuguese. Date: from 1991 to July 2013.	12 studies: 7 cross-sectional + 5 cohort studies.	The frail elderly. Total *N* = 7,884.	Different oral health predictors and covariates that are associated with frailty or its components.
Hakeem et al. (58) Systematic review	To systematically review longitudinal studies on the association between oral health and frailty indicated by any validated scale or index.	Database: 3, MEDLINE, EMBASE and LILACS. Language: no restriction. Date: up to July 2018.	5 longitudinal studies	No considerations were given for the recruitment settings (nursing or care homes, hospitals, community dwelling), nor the general health status. Total *N* not reported.	Association between oral health and frailty
Cognitive impairment					
Nangle et al. (59) Systematic review	To focus on how oral health relates to specific cognitive abilities in older adults.	Database: 4, PubMed, Scopus, PsychINFO, and Web of Science. Language: English. Date Until August, 2018.	23 studies: 19 cross sectionals + 3 longitudinal + 1 interventional	NA Total *N* = 121,547.	Relationship between oral health and cognitive decline in late adulthood
Lauritano et al. (60) Systematic review	To present a literature review of oral health status and the need for oral care in people with dementia, as compared to people without dementia and also of the relationship between periodontal disease and cognitive impairment.	Database: 3, PubMed, CINAHL, and Cochrane Library. Language: no restrictions. Date: within 2019.	56 studies: 19 cohort + 9 case-control + 26 cross-sectional + 2 RCTs	Participants must have been diagnosed with dementia, and should be 60 years or older. Total *N* = 15,263.	Role of tooth loss due to periodontal disease in progression of dementia.
Delwel et al. (61) Systematic review	To provide a comprehensive literature overview following a systematic approach of the level of oral hygiene and oral health status in older people with dementia with focus on oral soft tissues.	Databases: 3, PubMed, CINAHL, and the Cochrane Library. Language: Dutch, English, and German. Date: performed on 12 January 2017.	36 studies: 14 cross-sectional studies + 10 case-control studies + 10 + cohort studies + 2 RCTs	Nursing homes, Community, Non-institutionalized, institutionalized, assisted living, acute bed geriatric hospital, psychiatric hospital, long-term care homes. Total *N* = 9,182.	Oral hygiene and oral health status

(Continued)

TABLE 2 (Continued)

References, review design	Aim or objective	Search strategy	Type of studies: total number + design	Setting of participants. Total number of participants (if available)	Study outcomes related to holistic health
Delwel et al. (62) Systematic review	To provide a systematic overview including a quality assessment of studies about oral health and orofacial pain in older people with dementia, compared to older people without dementia.	Database: 3, PubMed, CINAHL, and the Cochrane Library. Language: no restrictions. Date: up to now.	37 studies: 11 cohort + 6 case-control studies + 19 cross-sectional + 1 RCT	All general elderly. Total *N* = 7,806.	Oral health status
Wu et al. (63) Systematic review	To systematically review longitudinal studies examining the association between oral health and cognitive decline.	Database:3, PubMed, Medline, CINAHL. Language: English. Date: January 1993 and March 2013.	56 studies: 40 cross-sectional studies + 16 longitudinal studies	All general elderly. Total *N* not reported.	The risk of cognitive decline or incident dementia
Depression					
Cademartori et al. (64) Systematic review and meta-analysis	To systematically review the literature in order to investigate association between depression and oral diseases.	Database: 5, PsychInfo, PubMed, Scielo, Scopus, and Web of Science. Language: no restriction Date: until 20 April 2018	15 studies: 14 cross-sectional studies + 1 longitudinal study	All general elderly. Total *N* not reported.	Dental caries/periodontal disease/tooth loss

AD, Alzheimer's disease; AP, aspiration pneumonia; DOSS, Dentistry and Oral Sciences Source; MNA, mini nutritional assessment; MNA-SF, mini nutritional assessment short form; NA, not available; OHRQoL, oral health-related quality of life; POHC, professional oral hygiene care.

factors including the number of teeth, chewing ability, oral function and the accumulation of oral health problems and showed that the prevalence of frailty, which is expected to increase rapidly in the aging population, is significantly related to oral health (29, 58), while 1 review of low quality that also included dental service use and Geriatric Oral Health Assessment Index scores claimed that poor oral health has not been evaluated longitudinally to show an association (57). This is because the assessment of frailty remains easily ignored in translational dental research and clinical practice (29). Therefore, combined with the quality and results of the included reviews, although evidence showed a positive association between oral health and frailty, the diversity of the included samples resulted in the outcome variable, and frailty should not be considered a clear outcome of poor oral health.

Mental outcomes

Six systematic reviews provided data on mental outcomes (59–64), of which 1 included a meta-analysis (64). Five systematic reviews (none with a meta-analysis) focused on cognitive impairment (59–63), and 1 (with a meta-analysis) focused mainly on depression (64).

Cognitive impairment

One qualitative systematic review of low quality provided evidence of an association between learning and memory and complex attention and executive function and oral health in elderly individuals, of which most of the primary studies independently identified one or more significant unadjusted associations or adjusted covariates correlated with oral health

(59). Correspondingly, the remaining 4 review articles of low to moderate quality focused on verifying the relation between oral health and dementia based on various oral assessment criteria (60–63). While one review of low quality showed that a few studies claimed that there was ambiguous evidence to demonstrate the association between oral health and dementia (63), most of the included studies reported that the risk of prevalence of orofacial pain, gingival bleeding or inflammation and dental caries is much higher in people with senile dementia (60–62). Together, these data suggest a positive effect of improving dental care and designing corresponding oral scales for earlier identification and effective interventions for preventing cognitive impairment in older people (59). Combined with the quality and results of the included reviews, cognitive impairment should be considered a possible outcome of poor oral health.

Depression

One systematic review with a meta-analysis of high quality studied the correlation between oral health and depression, which is the main cognitive disability in elderly individuals worldwide (64). The review quantitatively analyzed the outcome of oral diseases, where depression was considered the main potential result. Generally, although more longitudinal research to test causal and temporal relationships between depression and oral health status needs to be conducted, the existing results showed a positive association between depression and oral diseases in older people. Combined with the quality and results of the included reviews, depression should be considered a possible outcome of poor oral health.

Social outcomes

Six systematic reviews provided data on social outcomes (44–49), of which 3 included a meta-analysis (46, 47, 49). The included reviews focused on analyzing the association between oral health and quality of life, which can be reflected by oral health-related quality of life (OHQoL) or the Geriatric Oral Health Assessment Index (GOHAI).

Quality of life

Four systematic reviews of moderate to high quality showed that a higher number of teeth, occluding pairs, implant-retained overdentures, and shortened dental arches were positively associated with OHQoL (45, 46, 48, 49), while xerostomia and orofacial pain were negatively related (44). Meanwhile, chewing is considered significantly relevant to talking, comfort, retention and aesthetics, which are crucial factors for improving quality of life (44, 48). Importantly, one review of moderate quality determined that there also exists a bidirectional relationship between oral health and diabetes mellitus, atherosclerosis, and cerebral vascular accidents (45). One meta-analysis of high quality reported a similar association in elderly individuals with Alzheimer's disease (49). Once the 2 meta-analyses of high quality quantitively analyzing the assessment of oral-related quality of life were included (46, 47), the data together showed that regular oral health care and utilizing dentures can greatly increase quality of life for older people. Combined with the quality and results of the included reviews, quality of life should be considered to be closely associated with poor oral health.

Discussion

The aim of this umbrella review was to provide a systematic overview of the impacts of oral health on holistic health among elderly people, and summarize effective approaches for enhancing public oral health. According to the review and systematic synthesis of the included review papers ($N = 35$), the majority focused on multiple physical outcomes ($N = 23$); six papers mainly discussed mental outcomes, and 6 papers explored social outcomes. Correspondingly, clear evidence is available to support diverse outcomes covering physical, mental and social health in elderly individuals and included respiratory diseases, malnutrition, age-related oral changes, frailty, cognitive impairment, depression and poor quality of life. It is worth noting that although there were many commonalities among the reviews included, the perspectives of the papers varied, and none of the current articles provided a systematic summary of the diverse results, which is crucial for providing better health care for elderly individuals as well as reducing the cost of medical resources (28, 42, 50).

Oral factors and global outcomes

Oral health is inseparable from holistic health and wellbeing, and the oral diseases are prevalent worldwide, which considerably placing a huge global burden and reducing the quality of life (65). Crucially, it is necessary to emphasize that this umbrella review showed that the oral health and holistic health of elderly individuals are strongly related. With aging, a decline in the physiology of elderly individuals is accompanied by the weakening of oral function and an increase in oral problems. Specifically, age-related oral changes can be summarized in three main aspects: (i) oral diseases such as dental caries and periodontitis resulting from bacterial colonization, which greatly increase the difficulty of oral cleaning (42, 43); (ii) tooth loss and chewing problems, which are closely associated with the diet of older people (29, 57, 58); and (iii) a decrease in salivary flow rate and oral soft issue function, which, however, have not been verified to affect the lives of the participants (39, 40, 61). Correspondingly, the

changes were considered to physically lead to a range of impacts. As a consensus, microorganisms such as dental caries and periodontal pathogens colonized in saliva and dental plaque are the main potential risk factors for hospitalization and respiratory diseases, which significantly increase the incidence of aspiration pneumonia (13, 50, 55).

On the other hand, a complete lack of functional dentition and decreased masticatory ability can notably affect the selection and intake of food (35), e.g., fruits and vegetables containing various dietary fibers and vitamins, naturally resulting in malnutrition, including low BMI and serum albumin levels, weight loss and protein-energy malnutrition (28, 34–38). Additionally, the number of oral problems is positively related to the severity of malnutrition (37). In the meantime, poor oral health and oral-related physical diseases can directly or indirectly result in a multifaceted and complex condition of general health, i.e., frailty (29, 57, 58). Clearly, oral health is still considered to have a cumulative effect on frailty throughout life, which slowly contributes to the development of additional chronic conditions and leads to the deterioration of general health quickly in old age (57).

Similarly, in addition to physical outcomes, poor oral health can directly or indirectly affect the mental health of elderly individuals. Nangle's review clearly reported that oral health is significantly associated with cognitive conditions, including study, memory, complex attention, and executive function (59). Meanwhile, they also pointed out that there is still a lack of evidence to verify the relationship between poor oral health and the decrease in language and perceptual motor function in elderly individuals. Interestingly, the rest of the included reviews focusing on cognitive impairment mainly analyzed the impacts of oral health on older people with dementia (60–63). On the one hand, the prevalence of diseases of oral hard tissue (including dental caries, periodontitis and orofacial pain) and oral soft tissue (including gingival bleeding, periodontal pockets, stomatitis, mucosal lesions and reduced salivary flow) is significantly higher in elderly individuals with dementia than in people without dementia (60–62). One review also mentioned that some primary studies have found that oral health measures such as number of teeth and periodontal disease were associated with risk of cognitive decline or incident dementia, whereas others did not find an association (63); this needs further research. Importantly, one review of high quality showed a positive correlation between oral diseases and depression among elderly individuals over 65 years of age, probably because missing teeth hinder smiling, laughing or showing teeth without embarrassment (64). In addition, pain and difficulty speaking also leads to embarrassment and a loss of self-esteem contributing to loneliness and social isolation (66).

Finally, as a comprehensive and complex outcome, quality of life is also considered to be associated with oral health. Although there were different assessment criteria used in the included reviews, such as OHQoL, GOHAI, and OHIP (44–49), all the results supported the fact that some specific oral problems significantly impact quality of life. In particular, the number of teeth and chewing function were considered the main issues positively associated with quality of life (44, 45, 48). Moreover, oral problems can also lead to a host of socioeconomic problems; for example, receiving regular dental care or treatment of complications adds to the financial burden of older people, which is reflected by the generally lower OHQoL of socially deprived residents (45). However, a clearer map between diverse oral issues and quality of life requires more relevant research.

To summarize, the present results showed that oral health is significantly associated with holistic health in older people. Intuitively, poor oral condition can directly impact the physical health of elderly individuals and add to their mental burden or aggravate cognitive impairments; moreover, such physical and mental obstruction not only impacts quality of life socioeconomically but also worsens oral health. On the other hand, oral health has always been a neglected topic given low priority in contrast with many other competing health problems worldwide (67). As with most non-communicable diseases, oral conditions are chronic and strongly socially patterned, with elderly individuals being one of the groups affected (68). Therefore, to achieve significant improvements in oral health, effective strategies including oral health policy and guidelines are required to improve oral health of people with special health care needs. Good oral health can be established by early exposure to dental services, risk assessment and check-ups, as well as a meticulous oral health prevention regimen (7, 69).

Solutions and suggestions

To establish a better relationship between oral health and holistic health, improvements can be summarized in the following three main aspects in public oral health.

(i) More rigorous and universal scales are needed. Although multiple outcomes of holistic health have been presented in a range of reviews and primary studies of high quality, it remains difficult to explain the relationship precisely. Moreover, popular scales are not always appropriate and may not fully represent actual oral health problems (49).

(ii) Providing oral hygiene and professional oral health care are important factors. Although evidence has demonstrated that routine oral care can achieve the same positive results (51, 53), professional methods are still considered effective measures to decrease the load of potentially pathogenic microorganisms and reduce the risk of aspiration pneumonia related to poor oral health (13, 15, 56). Especially for elderly individuals with limited mobility living in the community, nursing homes, and ICUs, professional oral health or routine oral hygiene care can not only reduce incidence of aspiration pneumonia and mortality rates due to oral-related diseases but can also result in significant cost savings in light of the economic burden of hospitalization to

improve quality of life (50). Nurses should play a key role in referring elderly individuals to general practitioners or dental care providers (37). Attitudes and knowledge related to the screening, prevention and treatment of oral health problems need to be improved through the training and education of professional caregivers, which are important to eliminate the anxiety-related responses of dental fear among the elderly patients (70).

(iii) Improving self-awareness regarding oral care for elderly individuals is important. Oral problems are considered a cumulative process along with aging (57), and the older adults are generally at higher risk for dental infections and associated complex complications. Therefore, it is important for older people to clean their teeth regularly and use dentures once it becomes difficult to maintain their original dental habits (28, 29, 35, 36, 38, 57, 58). Simultaneously, the neatness and integrity of teeth is considered aesthetically attractive and is related to confidence in elderly individuals, which directly affects their mental and social wellbeing (64). Therefore, the importance of oral care should be emphasized more for elderly individuals during the nursing process.

In the process of screening the literature, we noticed some interesting primary studies verifying the relationship between oral health and other chronic diseases, such as diabetes (71), hypertension and metabolic syndrome; however, there was no corresponding systematic review, or the reviews did not focus on older people and therefore did not meet the screening criteria. In such cases, more cross-sectional and longitudinal research and corresponding systematic reviews should be conducted to help in the evaluation, prevention, intervention, and clinical practice of oral-related holistic health.

Implications and limitations

There has been a rapid increase in research and corresponding systematic reviews on the impact of oral health on diverse chronic or non-chronic diseases in elderly individuals, which indicates the promotion of health awareness among elderly people in society. Accordingly, an umbrella review that qualitatively and quantitatively synthesizes studies by mixed methods provides an effective platform to efficiently extract relevant information for clinical practice and future research. Because the literature search was also systematic, according to the PRISMA guidelines, it gives a more comprehensive overview and a higher-level perspective than a narrative review with a narrow topic. Meanwhile, a convincing result of the umbrella review depends on the quality of the included systematic reviews with or without meta-analyses. Eleven of the 35 included reviews were of high quality.

In terms of the limitations, a more complete map of the final result in this research requires the inclusion of more studies written in languages other than English. Regarding the results of this study, although almost all of the included studies were associated with oral health, only one systematic review with 15 studies focused on depression and mental outcomes, which weakens the integrity of the conclusions. More importantly, it is worth noting that holistic health is a relatively broad concept, which indicates a wider result beyond the 7 exact outcomes in the present study. As a result, we are aware that the whole picture of the relationship between oral health and holistic health still has not been displayed through our analysis of the included papers, and that other symptoms or diseases remain to be further researched.

Conclusion

This umbrella review provided a macro perspective to determine the multiple outcomes of holistic health associated with oral health and summarized intervention measures to improve public oral hygiene. On the basis of the consistent findings, clear evidence is available to show the multidimensional results of holistic health. Evidence indicates that oral health can be mainly divided into two issues: (i) poor oral hygiene, where the multiple pathogenic microorganisms colonizing the oral microbiome are significantly associated with respiratory disease, dental caries and periodontitis, and (ii) tooth loss and chewing problems, with which elderly individuals have a higher risk of malnutrition and frailty. The combination of the two issues can also result in poor mental health, such as cognitive impairment and depression, in older people. Correspondingly, to acquire a higher quality of life, elderly people are encouraged to clean their teeth regularly, to have dentures fitted and to receive timely oral care.

Among the included reviews, the majority provided a precise point of view to illustrate the results, while a few papers, especially those regarding mental and social outcomes, were more conservative in their discussions and argued that more research is needed, although evidence has shown significant correlations. In addition, it is necessary to emphasize that due to the lack of relevant systematic reviews, some other popular chronic oral-related diseases were not included in the present umbrella review. Although there are still some limitations and other different oral-related diseases remain to be studied, this umbrella review is expected to provide a global and effective reference for clinical practice in public health.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author/s.

Author contributions

FL and XH led the current study. FL and SS initiated the study design and drafted the manuscript. FL, SS, and XH searched databases and screened the articles and extracted the data. XY and SH conducted the quality of the studies. XH, JH, and GW reviewed and revised the manuscript. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.1021104/full#supplementary-material

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Longitudinal effects of exercise according to the World Health Organization guidelines on cognitive function in middle-aged and older adults

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Purpose: To investigate the longitudinal effects of adequate exercise, defined as an exercise duration of ≥150 min/week by the World Health Organization (WHO), on cognitive function in middle-aged adults.

Methods: This study was a longitudinal panel analysis using secondary data obtained from the Korean Longitudinal Study of Aging (KLoSA) database, with 4,825 participants registered and comprising five rounds of survey data in 2-year intervals from 2010 to 2018. The participants were divided into the adequate exercise (≥150 min/week), deficient exercise (<150 min/week), and no exercise groups according to the WHO definition, and their cognitive decline over the 8-year period was analyzed. Further, we investigated the longitudinal effects of exercise using a fixed effects model with cognitive function as the dependent variable.

Results: In the dementia group, both deficient (<150 min/week) and adequate (≥150 min/week) exercises had statistically significantly positive effects on cognitive function. However, the coefficient size was not significantly larger in the adequate exercise group than in the deficient exercise group. In the participants with mild cognitive impairment (MCI), an adequate exercise level had significantly positive effects on cognitive function, while a deficient exercise level did not. In the participants with normal cognition, an adequate exercise level was not significantly associated with changes in cognitive function.

Conclusion: Continuous exercise can have a positive influence on cognitive function scores in middle-aged and older adults with MCI or dementia, but the findings cannot substantiate that adequate exercise (≥150 min/week) is more effective compared to deficient exercise (<150 min/week).

KEYWORDS

aged, cognition, mental status and dementia tests, physical activity, longitudinal analysis

Introduction

The prevalence of dementia among older adults aged ≥60 years is reported to be ∼5% globally, but the absolute number of patients with dementia is anticipated to increase as a result of the growing elderly population. In particular, the entire baby boomer generation in Korea will enter the older adulthood stage by 2028, thereby increasing the elderly population to 17.22 million by 2040. In other words, the elderly population is estimated to double in size in ∼20 years from 8.13 million in 2020. Furthermore, with a decreasing fertility rate, the old age dependency ratio is projected to triple from 22.4 in 2020 to 61.6 in 2040, highlighting a looming national elderly caregiving crisis along with escalating health care burden (1, 2).

The currently known non-modifiable dementia risk factors include gene polymorphisms, age, sex, race, and family history, and although age is a potent risk factor, dementia is not considered a normal aging process. Modifiable dementia risk factors include educational level, alcohol use, smoking, malnutrition, reduced physical activity, chronic diseases, such as hypertension, diabetes mellitus, and hypercholesterolemia, obesity, depression, social isolation, and poor cognitive activity (3–6).

Among these factors, physical activity and cognitive function—the focuses of this study—can potentially lower the risk for cardiovascular disease (CVD), hypertension, insulin resistance, and hypercholesterolemia indirectly. According to the frontal aging hypothesis, physical activity delays neuronal destruction by increasing the blood flow to the brain and level of brain-derived neurotrophic factor (BDNF) (7). Further, some studies suggest that physical activity does not influence the entire cognitive function but rather only the cognitive function related to the frontal lobe. The frontal lobe is responsible for the following cognitive functions: short-term memory, concentration, immediate memory, delayed memory, language proficiency, and frontal motor function (8, 9). In particular, studies showed that aerobic exercise is significantly effective by increasing the brain blood flow through the improvement of the cardiovascular functions (9).

Individuals who maintained physical activity in middle adulthood reportedly show a larger brain volume and considerably larger gray matter volume on magnetic resonance imaging (MRI) scans ∼20 years later than those who maintained a sedentary lifestyle (10). This suggests that long-term physical activity can mechanically alter the brain structure and that even short-term exercise is linked to brain activity.

The 2019 WHO Guidelines for Risk Reduction of Cognitive Decline and Dementia recommend physical activity to maintain cognitive function in older adults. However, more specifically, the level of evidence for physical activity preventing cognitive decline in normal older adults was moderate, whereas that among older adults with a diminished cognitive function was low (11). Systematic reviews and meta-analyses reported that physical activity helps individuals maintain their ability to perform the activities of daily living (ADLs) and lowers the psychomotor symptoms of dementia and depression in older adults with mild cognitive impairment (MCI) and dementia; however, the direct effects of exercise on cognitive function remain controversial (12–15). Nevertheless, the WHO guidelines for physical activity in older adults recommend exercising for ≥150 min/week and stress the importance of muscle and aerobic exercises.

However, no study has conducted a longitudinal follow-up to examine the effects of long-term engagement in an adequate level of exercise (≥150 min/week according to the WHO recommendation) on cognitive function and to investigate whether an adequate exercise level serves as a cognitive protective factor by comparing individuals with an adequate exercise level with those without an adequate exercise level (<150 min/week). Research utilizing long-term data is considered as highly significant because the adequate exercise affects the cognitive function, and the effect accumulate over time.

In this context, this study aimed to longitudinally analyze the levels of exercise among middle-aged and older adults with normal cognition, MCI, or dementia in Korea from 2010 to 2018 and identify the effects of an adequate exercise level on cognitive function using a fixed effects model that utilizes the Korean Longitudinal Study of Aging (KLoSA) data.

The present study aimed to (1) longitudinally analyze the levels of exercise in middle-aged and older adults with normal cognition, MCI, or dementia using panel data; (2) examine the longitudinal effects of an adequate exercise level according to the WHO recommendation on cognitive function; and (3) examine the longitudinal effects of an adequate exercise level according to the WHO recommendation on the cognitive function of adults with normal cognition, MCI, and dementia.

Methods

Study design

The present study is a longitudinal panel analysis using secondary data (KLoSA) comprising five rounds of survey data collected in 2-year intervals from 2010 to 2018.

Participants

We downloaded the light version of the KLoSA data and used the five datasets collected for the same parameters in 2-year intervals from 2010 (3rd survey) to 2018 (7th survey). The data used in this study were open access data that do not contain personal information; thus, the present investigation

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TABLE 1 Descriptive analysis of the characteristics of the participants in the 2010 survey (3rd wave).

Variable	Categories	Normal ($N = 3,341$)	MCI ($N = 694$)	Dementia ($N = 250$)
		Mean ± SD or *N* (%)		
	Age	60.14 ± 7.96	65.61 ± 8.08	69.46 ± 9.06
Sex	Male	1,590 (47.59)	289 (41.64)	113 (45.20)
	Female	1,751 (52.41)	405 (58.36)	137 (54.80)
Education	Elementary school	956 (28.62)	405 (58.36)	154 (61.6)
	Middle school	679 (20.33)	124 (17.87)	44 (17.6)
	High school	1,260 (37.72)	138 (19.88)	38 (15.2)
	Above college	445 (13.32)	27 (3.89)	14 (5.6)
Marital state	Not married/not partnered	397 (11.88)	127 (18.30)	74 (29.60)
	Married/partnered	2,944 (88.12)	567 (81.70)	176 (70.40)
Social contact	No one	79 (2.36)	28 (4.03)	16 (6.4)
	Rarely meet	7 (0.21)	1 (0.14)	0 (0)
	1–6/year	218 (6.52)	87 (12.54)	22 (8.8)
	1–2/months	834 (24.96)	108 (15.56)	37 (14.8)
	1/week	812 (24.3)	142 (20.46)	59 (23.6)
	2–3/weeks	454 (13.59)	102 (14.7)	32 (12.8)
	Everyday	937 (28.05)	226 (32.56)	84 (33.6)
	Personal allowance (USD)	173.39 ± 162.57	126.08 ± 154.88	107.31 ± 83.25
	Depression	1.38 ± 1.45	1.61 ± 1.82	1.5 ± 1.92
	MMSE score	28.15 ± 1.85	27.07 ± 2.00	27.37 ± 2.08
Smoking	No smoking	2,239 (67.02)	476 (68.59)	166 (66.4)
	Past smoking	474 (14.19)	104 (14.99)	33 (13.2)
	Current smoking	628 (18.8)	114 (16.43)	51 (20.4)
Alcohol assumption	No drinking	1,590 (47.59)	365 (52.59)	137 (54.8)
	Past drinking	326 (9.76)	80 (11.53)	28 (11.2)
	Current drinking	1,425 (42.65)	249 (35.88)	85 (34)
Exercise	Adequate (More than 150 min/week)	653 (19.55)	125 (18.01)	69 (27.60)
	Deficient (<150 min/week)	686 (20.53)	105 (15.13)	28 (11.20)
	No exercise	2,002 (59.92)	464 (66.86)	153 (61.20)
	ADL	0.01 ± 0.15	0.02 ± 0.28	0.02 ± 0.20
	IADL	0.13 ± 0.61	0.13 ± 0.76	0.18 ± 0.83

USD = 1,118.30 Korean Won, average exchange rate between 2010 and 2018.
MCI, mild cognitive impairment; MMSE, mini mental state examination; ADL, activity of daily living; IADL, instrumental activity of daily living.

is not considered a human study. Accordingly, the study was exempted for review by the Institutional Review Board (IRB) at Gachon University (IRB No. 1044396-202202-HR-040-01). From the data of 5,672 participants matched from the 7th survey to the 3rd survey in reverse order based on the panel ID, the data of 4,825 participants who were determined to have normal cognition based on the Mini Mental State Examination (MMSE) in the 3rd survey (2010) were analyzed.

The KLoSA was first conducted in 2006 by sampling from home-dwelling individuals aged ≥45 years in regions in Korea, excluding Jeju Island. Beginning with the 1st survey in 2006, basic general surveys including the same parameters were repeated every other year, with the 7th survey completed in 2018. First, the study population was stratified by region and living arrangement, and 1,000 sample enumeration districts were extracted. A systematic sampling method was used to extract sample households per the designated sampling rate. The enumerators visited the sample households in order and determined the eligibility of each household, i.e., at least one member of the household was aged ≥45 years. All household members aged ≥45 years were interviewed.

Instruments

Demographic characteristics

In this study, the factors reported to potentially influence cognitive function, namely age, educational level, sex, marital

status, socioeconomic status (SES), depression, and health behaviors were selected as confounders (5, 6, 11, 16–19) to effectively infer the effects of exercise on cognitive changes.

The educational level was determined based on the highest completed educational level and was classified into elementary school, middle school, high school, and college or higher. A higher educational level was given a higher value. For marital status, 0 was coded for unmarried (separated, widowed, and divorced) and 1 was coded for married or living with a partner. SES was determined based on the personal allowance per month (unit: USD), which better reflects the excess resources available for use in daily life, as compared with net worth or debt.

Social contact frequency refers to the frequency of meeting a close social contact, such as friend, neighbor, or relative, in the past year.

Cognitive function

The dependent variable in this study is the presence of cognitive decline, and cognitive function was assessed using the Korean version of the MMSE (K-MMSE), which comprises 30 items for orientation, memory, attention and computation, language, and spatiotemporal aspect. The participants were classified as having suspected dementia (K-MMSE $\leq$ 17), cognitive impairment (K-MMSE 18–23), and normal cognitive function (K-MMSE $\geq$ 24) (4). Further, the participants with normal cognition, cognitive impairment, suspected dementia, and no response or with missing value were coded with 0, 1, 2, and 3, respectively.

Exercise sufficiency

Weekly exercise frequency and duration (minutes) in the 3rd−7th KLoSA database were used. The responses were interpreted for exercise sufficiency in older adults according to the WHO guidelines (11) to code the participants with 0 for no exercise, 1 for deficient exercise frequency or duration, and 2 for adequate exercise frequency or duration as defined as at least 30 min of per session for at least $\geq$5 days/week or at least 150 min/week.

Analysis

First, the data were analyzed using STATA 17.0. The participants were divided into three groups (normal cognition, MCI, and dementia) based on the K-MMSE score in the 7th survey (2018). Missing values were replaced by generating five datasets using multiple imputations, and all variables used in the fixed effects analysis were considered in the multiple imputation model. Furthermore, five datasets were synthesized in the final fixed effect model for analysis (20).

Second, for the demographic characteristics, SES, depression, cognitive function, and health behaviors, categorical variables were expressed as frequencies and percentages, and continuous variables as means and standard deviations. To analyze the exercise status by cognitive function, the between-frequency and between-proportion data for the adequate exercise ($\geq$150 min/week), deficient exercise ($<$150 min/week), and no exercise groups were analyzed. Moreover, the degree of cognitive decline over time was graphed for each group (adequate, deficient, and no exercise groups).

Third, we examined the longitudinal effects of adequate exercise on cognitive function by setting the cognitive function as the dependent variable and entering the demographic factors and other confounders into a fixed effects model using panel data. The fit of the fixed and random effects models were compared using the Hausman test. The fixed effects model was chosen, because the null hypothesis was rejected. A fixed effects model shows whether an dependent variable can be altered by changing the independent variable included in the model; if the independent variables do not have fixed effects on the dependent variable, it is highly likely to be due to inter-individual heterogeneity not observed in the study. Therefore, if an adequate exercise level has significant fixed effects on cognitive function in a model, we can infer that an increase in an individual's exercise level affects cognitive function over time even after controlling for the effect of innately lower cognitive function compared with other individuals (21).

Therefore, this enables a clearer inference of the causal effects of alterations of the independent variable on the dependent variable over time, in contrast to the regression analysis performed in cross-sectional studies.

Results

General characteristics of the participants

Table 1 shows the general characteristics of the participants stratified by their level of cognition (normal cognition, MCI, and dementia groups). The mean age was 60.14 $\pm$ 7.96, 65.61 $\pm$ 8.08, and 69.46 $\pm$ 9.06 years in the normal cognition, MCI, and dementia groups, respectively. Given that cognitive decline occurs in ages $\geq$65 years, the MCI and dementia groups were older than the normal cognition group in the 7th survey.

Regarding social contact, 79 (2.36%), 28 (4.03%), and 16 (6.4%) in the normal cognition, MCI, and dementia groups, respectively, stated that they have no close social contacts. The percentage of individuals who have social contacts whom they regularly meet from once a year to 2–3 times a week was higher in the normal cognition group than in the dementia and MCI groups. However, the percentage of individuals who meet a social contact every day was the highest in the dementia

TABLE 2 Exercise status of middle-aged and older adults stratified according to their cognitive function.

Category		Overall *n* (%)	Between *n* (%)	Within *n* (%)
Total	1	13,291 (62.0)	3,811 (88.9)	69.8
	2	3,827 (17.9)	2,044 (47.7)	37.5
	3	4,307 (20.1)	2,061 (48.1)	41.8
Normal ($N = 3,341$)	1	9,591 (59.7)	2,799 (87.2)	68.5
	2	3,129 (19.5)	1,626 (50.6)	38.5
	3	3,335 (20.8)	1,567 (48.8)	42.6
MCI ($N = 694$)	1	2,286 (67.9)	632 (93.9)	72.3
	2	466 (13.9)	279 (41.5)	33.4
	3	613 (18.2)	312 (46.4)	39.3
Dementia ($N = 250$)	1	857 (74.5)	223 (97.0)	76.9
	2	92 (8.0)	65 (28.3)	28.3
	3	201 (17.5)	101 (43.9)	39.8

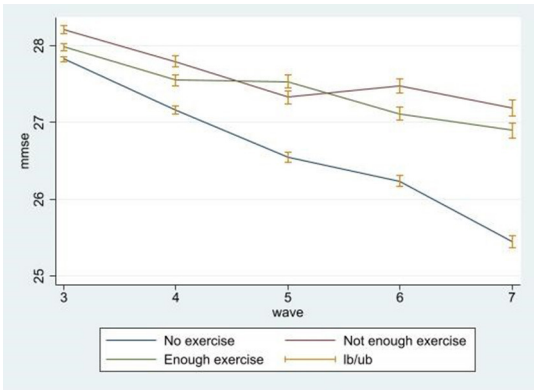

FIGURE 1
Longitudinal trends of cognitive function by exercise group.

group, with 84 (33.6%), 226 (32.56%), and 937 (28.05%) in the dementia, MCI, and normal cognition groups, respectively.

The number of individuals with college education or higher was 445 (13.32%), 27 (3.89%), and 14 (5.6%) in the normal cognition, MCI, and dementia groups, respectively. Regarding marital status, the number of people living alone due to bereavement or divorce was 74 (29.60%), 127 (18.30%), and 397 (11.88%) in the dementia, MCI, and normal cognition groups, respectively.

Personal allowance was the highest in the normal cognition group, with 173.39 ± 162.57 USD, 126.08 ± 154.88 USD, and 107.31 ± 83.25 USD in the normal cognition, MCI, and dementia groups, respectively. Depression score was 1.38 ± 1.45, 1.61 ± 1.82, and 1.5 ± 1.92 in the normal cognition, MCI, and dementia groups, respectively. As the participants with normal cognitive function in the 3rd survey was selected, the cognitive function scores in the 3rd survey did not significantly vary among the normal cognition g (28.15 ± 1.85), MCI (27.07 ± 2.00), and dementia (27.37 ± 2.08) groups.

Exercise status of middle-aged and older adults by cognitive function

Table 2 shows the results of a longitudinal analysis of the exercise status of the cognitive function group based on the 2018 assessment. The within percent of the entire study sample was 41.80%; that is, the individuals who claimed to engage in adequate exercise maintained an adequate level of exercise for ∼41.80% (3 years) of the 8-year period. By cognitive function group, the normal cognition group maintained an adequate level of exercise for 42.57% of the 8-year period, while the percentages were shorter at 39.29 and 39.8% in the MCI and dementia groups, respectively. The dementia group did not exercise at all for 76.86% of the period, which is relatively longer than that of the MCI (72.34%) and normal cognition (68.53%) groups.

Figure 1 illustrates the changes in cognitive function scores over the 8-year period from the 3rd wave to the 7th wave. The green line is the cognitive function score of the adequate exercise group, and the red line represents the cognitive function score of the deficient exercise group. The blue line represents the cognitive function score of the no exercise group. The cognitive function score tended to decline in all groups, and although the graph does not present causality, the cognitive function score decreases more dramatically in the no exercise group, as compared to the other two groups

Fixed effects model for cognitive score according to WHO-defined adequate exercise

Table 3 shows the results of a fixed effects model analysis of the effects of an adequate exercise level according to the WHO definition on the changes in cognitive function in the entire study sample. We investigated the effects of each factor identified in previous studies to affect cognitive function, namely demographic characteristics, personal allowance, depression, and health behaviors. This model was statistically significant ($F = 108.15$, $p < 0.001$).

A fixed effects model was used to estimate the effects of changes of an independent variable on the changes of the dependent variable. As known thus far, old age is the most powerful predictor of cognitive decline, and low educational level, female sex, unmarried status compared to married status or living with a partner, and low social contact frequency

TABLE 3 Effects of exercise on cognition by a fixed effects linear regression analysis of panel data obtained from 2010 to 2018 KLoSA.

Independent variables		Dependent variable: MMSE score					
		B	SE	*t*	*p*	[95% confidence interval]	
Age		−0.112	0.004	−30.250	<0.001***	−0.120	−0.105
Sex (reference: male)		–	–	–	–	–	–
Education		0.438	0.035	12.440	<0.001***	0.369	0.507
Marital state (reference: not married)		0.312	0.081	3.840	<0.001***	0.152	0.471
Social contact		0.116	0.015	7.990	<0.001***	0.087	0.144
Personal allowance		0.002	0.002	1.000	0.316	−0.002	0.005
Depression		−0.176	0.013	−13.110	<0.001***	−0.203	−0.150
Smoking		0.030	0.053	0.560	0.578	−0.075	0.134
Alcohol assumption		0.034	0.039	0.880	0.381	−0.043	0.111
Exercise sufficiency (reference: no exercise)	Not enough	0.289	0.057	5.040	<0.001***	0.177	0.402
	Enough	0.366	0.056	6.550	<0.001***	0.256	0.475
ADL		−0.549	0.061	−8.940	<0.001***	−0.672	−0.425
IADL		−0.793	0.026	−30.120	<0.001***	−0.845	−0.742
Wave (reference: 3rd wave)	4	−0.376	0.055	−6.790	<0.001***	−0.485	−0.268
	5	−0.509	0.058	−8.800	<0.001***	−0.623	−0.396
	6	−0.540	0.061	−8.870	<0.001***	−0.660	−0.421
	7	−0.892	0.065	−13.680	<0.001***	−1.020	−0.764
Constant		33.158	0.367	90.430	<0.001***	32.439	33.876

Sex is omitted due to collinearity.
***p < 0.001, **p < 0.01, and *p < 0.05.

were identified as statistically significant predictors of cognitive decline ($p < 0.001$). Contrarily, smoking and alcohol-related factors were not significant predictive factors ($p > 0.05$). In addition, increasing depression and strong dependence when performing ADL and IADL were found to have adverse effects on cognitive decline ($p < 0.001$). Personal allowance was not significantly associated with cognitive changes.

Regarding exercise adequacy, the primary outcome of this study, deficient exercise had statistically significant effects on the cognitive function score ($B = 0.289$, $p < 0.001$); similar results were observed for adequate exercise with no exercise as the reference. The coefficient size was larger with adequate exercise than with deficient exercise ($B = 0.366$, $p < 0.001$).

Table 4 shows the fixed effects estimations for each of the cognitive function groups as assessed in the final 7th survey. As we used a fixed effects model, and sex is an invariant factor, the regression coefficient was not computed. Educational level had significant effects on the changes in cognitive function among those assessed to have a normal cognitive function in the last assessment but did not have significant effects in the dementia or MCI group. Age had significant negative effects on cognitive function in all groups. Marital status can be changed over the 8-year period, and the married status had positive effects on cognitive function compared to the unmarried status in the dementia group but not in the MCI and normal cognition groups. Social contact frequency did not have significant effects on the longitudinal cognitive decline in the normal cognition group (although this group had the highest social contact frequency) but had statistically significantly positive effects in the MCI and dementia groups, although the coefficients were not large. Smoking and alcohol consumption did not have statistically significant effects on longitudinal cognitive decline over the 8-year period. Depression had statistically significant effects in all groups, with the dementia group having the largest coefficient in the final assessment. One interesting finding was that ADL was not significantly associated with cognitive changes in the dementia and MCI groups. Increased dependence for ADL was linked to cognitive decline in the normal cognition group. However, increasing dependence for IADL was associated with cognitive decline in all groups. Increased personal allowance was not significantly associated with cognitive decline over time.

Regarding exercise adequacy, the study's primary outcome, adequate and deficient exercise had statistically significantly more positive effects on cognitive function, as compared to no exercise. However, the coefficient size was not larger in the adequate exercise group than in the deficient exercise group. In the MCI group, with no exercise as the reference, adequate exercise had significantly positive effects. However, deficient exercise did not have significant effects. In the normal cognition group, exercise adequacy did not have significant effects on cognitive changes.

TABLE 4 Effects of exercise on cognition using fixed effects linear regression by cognitive group.

MMSE	Normal						MCI						Dementia					
	Coefficient	Std. err.	*t*	*P* > |*t*|	[95% conf. interval]		Coefficient	Std. err.	*t*	*P* > |*t*|	[95% conf. interval]		Coefficient	Std. err.	*t*	*P* > |*t*|	[95% conf. interval]	
Sex	−0.039	0.019	−2.05	0.04*	−0.075	−0.002	−0.241	0.055	−4.35	<0.001***	−0.350	−0.133	−0.208	0.147	−1.42	0.155	−0.496	0.079
Education	0.378	0.028	13.27	<0.001***	0.322	0.434	0.141	0.089	1.58	0.114	−0.034	0.315	0.169	0.252	0.67	0.504	−0.326	0.663
Age	−0.032	0.003	−10.29	<0.001***	−0.038	−0.026	−0.175	0.009	−18.98	<0.001***	−0.194	−0.157	−0.188	0.023	−8.1	<0.001***	−0.233	−0.143
Marital state	−0.053	0.070	−0.76	0.447	−0.191	0.084	0.273	0.179	1.52	0.128	−0.078	0.624	1.260	0.456	2.76	0.006**	0.367	2.154
Social contact	0.015	0.013	1.2	0.229	−0.010	0.040	0.214	0.034	6.23	<0.001***	0.147	0.281	0.435	0.090	4.83	<0.001***	0.259	0.612
Smoking	0.094	0.044	2.14	0.032	0.008	0.180	−0.018	0.132	−0.14	0.890	−0.277	0.240	0.126	0.363	0.35	0.729	−0.586	0.838
Alcohol assumption	−0.002	0.032	−0.07	0.945	−0.064	0.060	−0.038	0.097	−0.39	0.698	−0.228	0.152	0.029	0.281	0.1	0.918	−0.521	0.579
Depression	−0.119	0.012	−9.58	<0.001***	−0.143	−0.095	−0.179	0.032	−5.6	<0.001***	−0.242	−0.116	−0.260	0.077	−3.36	0.001**	−0.412	−0.108
ADL	−0.562	0.076	−7.36	<0.001***	−0.712	−0.412	−0.326	0.170	−1.92	0.057	−0.663	0.010	−0.084	0.173	−0.48	0.629	−0.424	0.256
IADL	−0.172	0.031	−5.5	<0.001***	−0.234	−0.111	−0.355	0.065	−5.46	<0.001***	−0.482	−0.228	−1.227	0.085	−14.47	<0.001***	−1.393	−1.061
Personal allowance (USD)	0.000	0.001	<0.001	0.996	−0.002	0.002	−0.006	0.005	−1.17	0.240	−0.015	0.004	−0.024	0.020	−1.2	0.231	−0.063	0.015
Exercise sufficiency (reference: no exercise)	0.083	0.047	1.78	0.075	−0.008	0.175	0.183	0.173	1.06	0.290	−0.156	0.522	2.914	0.608	4.79	<0.001***	1.723	4.105
	0.048	0.047	1.02	0.307	−0.044	0.141	0.376	0.158	2.39	0.017*	0.067	0.686	2.803	0.450	6.23	<0.001***	1.921	3.685
Constant	29.325	0.300	97.89	<0.001***	28.737	29.912	36.510	0.913	39.99	<0.001***	34.721	38.299	33.958	2.369	14.33	<0.001***	29.315	38.602
F (*p*-value)	403.09 (<0.001***)						467.07 (<0.001***)						72.17 (<0.001***)					

***p < 0.001, **p < 0.01, *p < 0.05.

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Discussion

This study longitudinally analyzed the levels of exercise among middle-aged and older adults with normal cognition, MCI, or dementia in Korea from 2010 to 2018 and investigated the effects of an adequate exercise level on cognitive function using a fixed effects model. The neuropathological complexity of dementia is a barrier to dementia prevention, and the effects of lifestyle modification in delaying cognitive decline remain unclear with inconsistent findings. This study broadly has three implications: 1) for adults with a gene specific for dementia onset, continuous exercise helps in slowing the cognitive decline over time, 2) exercise has significant positive effects on cognitive function in the MCI and dementia groups; however, there is low evidence on the effectiveness of exercise in older adults with normal cognition, and 3) according to the WHO guidelines, adequate exercise and deficient exercise exert different effects in preventing cognitive decline in each of the cognitive function groups.

First, the results of the fixed effects model used in this study are significant, in that they control for the unique individual characteristics that crucially contribute to cognitive decline and dementia onset, such as genetic factors (related to beta-amyloid accumulation). On the basis of our findings, even those with a gene specific for dementia onset, continuous exercise helps slow the cognitive decline over time, as compared to no exercise at all. Therefore, we can infer that an adequate exercise level is a significant protective factor against cognitive decline over time even after controlling for unique individual characteristics. One supportive evidence recently published reported that patients with Alzheimer's disease did not develop dementia symptoms, supporting the fact that cognitive function has resilience (22–24). It is hypothesized that a healthy lifestyle delays the onset of dementia and its symptoms by increasing the brain's resilience. Duzel et al. (25) shed light on the existence of exercise-related neuroplasticity and showed that continuous exercise can boost brain functions, prevent hippocampal atrophy, and induce structural and neurochemical changes of the brain area involved in memory using MRI scans.

Second, the WHO currently recommends moderate exercise for older adults with normal cognition; however, it suggests that there is low evidence on the effectiveness of exercise in older adults with a cognitive decline (11). However, our findings showed that exercise did not have statistically significant effects on cognitive decline over time, regardless of the exercise duration in older adults with a normal cognitive function, whereas educational level, depression, ADL, and IADL were actually associated with cognitive decline over time. Contrarily, exercise had significantly positive effects on cognitive function in the MCI and dementia groups. The Cochrane review, which meta-analyzed the effect of aerobic exercise on cognitive function in normal elderly without cognitive impairment, showed that some individuals had delayed memory function and attention skills; however, 9 out of 11 cognitive function areas showed no statistically significant positive effects compared with the no intervention group (24, 26). In this study, the sub-domains of cognitive function could not be identified, so comparison with previous studies was not possible. The studies included in the Cochrane review were RCTs, but the follow-up period was short (8–26 weeks). In this study, 8-year follow-up of a large panel survey was used to improve such aspects, but the overall improvements in cognitive function could not be confirmed.

Further, the coefficient size was larger and significant at $p < 0.001$ in the MCI group than in the dementia group. These results highlight the need for continuous exercise intervention in older adults with MCI or dementia. Moreover, our study findings would serve as fundamental data for prospective systematic reviews and meta-analyses of studies relating to exercise interventions for older adults with MCI and dementia.

Third, this study analyzed whether adequate and deficient exercise according to the WHO guidelines differ in their effects in preventing cognitive decline in each of the cognitive function groups. We reviewed the existing studies but could not identify studies that compared adequate and deficient exercises. A recent systematic review did not also find a dose–response association due to the large heterogeneity in the frequency, duration, and type of exercise interventions (19, 27). According to our results, adequate exercise—regardless of the exercise type—served as a protective factor against MCI and dementia, as compared to no exercise at all. However, one finding that complicates our interpretation on the exercise duration is that the effects of deficient exercise (<150 min/week) did not statistically significantly differ with those of no exercise in the MCI group. The study results pertaining to exercise interventions for older adults with MCI remain controversial. A systematic review showed that 92% of the 14 included studies reported statistically non-significant effects and that exercise does not improve memory (28, 29). In a well-designed study included in a systematic review on MCI, 1-year follow-up of the moderate aerobic exercise and sedentary groups showed no significant differences in terms of cognitive functions; however, more poorly designed studies reported mixed findings (28). Based on our findings, in the dementia group, both adequate and deficient exercises were effective as compared with no exercise (Deficient exercise: $B = 2.914$, $p < 0.001$; Adequate exercise: $B = 2.803$, $p < 0.001$). As in previous studies, this finding may support the hypothesis that exercise intensity rather than exercise duration will help maintain and improve cognitive function (30, 31).

Based on the abovementioned results, exercise may have varying effects on the cognitive function among the normal cognition, MCI, and dementia groups, and appropriate exercise intensity and degree may differ among these groups. Overall, scientific evidence for the association between exercise and cognitive function is still insufficient, but our results suggest

that continuous exercise has positive effects on cognitive function longitudinally, as compared to not exercising at all. As prevention is the best treatment, it is important to manage modifiable risk factors and to continuously implement exercise interventions not only in older adults with normal cognitive function but also in those with MCI and dementia (6).

The main limitations of this study are the absences of exercise type consideration and the exercise evaluative numerical measurement such as VO2max (Maximal oxygen consumption) or METs (Metabolic equivalent of task) values. In the future, longitudinal follow-up of a large population with parameters that enable the determination of exercise intensity specifically for different exercise types, such as resistance and aerobic exercises (e.g., metabolic equivalents) would facilitate the development of evidence-based guidelines for physical activities that enhance cognitive functions in older adults.

Conclusion

This study showed that the adequacy of exercise longitudinally over an 8-year period could have positive effects on the cognitive function scores in older adults with dementia. Further, our result showing that the coefficient size of the effect was larger in the dementia and MCI groups than in the normal cognition group highlights the importance of implementing regular exercise interventions in cognitively impaired older adults. However, exercising for $\geq$150 min/week was not found to be more effective than that for <150 min/week; thus, we could not determine the benefits of exercise durations that meet or exceed the WHO guidelines. Since we only examined the total weekly exercise duration without considering the exercise type, we recommend that large-scale longitudinal studies that take exercise intensity and type into consideration should be conducted in the future.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: Korean Longitudinal Study of Aging (KLoSA). https://survey.keis.or.kr/eng/klosa/klosa01.jsp.

Author contributions

DK and YK contributed to conception and design of the study. DK organized the database, performed the statistical analysis, and wrote the first draft of the manuscript. DK, YK, and AJ wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Visual quality analysis using the Chinese Catquest-9SF scale following different spherical aberration IOL implantation

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Purpose: Based on the Chinese version of the Catquest-9SF scale, the contrast sensitivity meter and wavefront aberrometer were used to evaluate the visual quality of cataract patients implanted with different spherical aberrations IOL.

Design: Retrospective Observational Study.

Methods: Patients who had the lens implantation in our department from January 2020 to December 2021 were enrolled. All patients underwent uncorrected visual acuity, best corrected visual acuity and slit lamp microscope, high-order aberrations and contrast sensitivity test. The KR-1W wavefront analyzer (Topcon Medical System, Tokyo, Japan) was used to measure wavefront aberrations post-operation. The Chinese Catquest-9SF scale was used to score the postoperative visual satisfaction of the patients.

Results: 145 patients were screened according to the exclusion criteria, including 51 patients in the zero aspherical IOL (SOFTEC HD) group, 42 patients in the negative aspherical IOL (ZCB00) group, and a total of 52 patients in the spherical IOL (HQ-201HEP) group. The score was the highest in the zero spherical aberration group, followed by the negative spherical aberration group with the lowest scores in the spherical IOL group. Higher-order aberrations are relatively low in eyes implanted with the zero spherical aberration group. Contrast sensitivity with spherical lenses under glare-free and glare conditions was lower than those with aspheric lenses, and at higher frequencies the zero-aberration aspheric lens performed the best.

Conclusion: The Chinese Catquest-9SF scale provides an indication of visual quality after aspheric IOL implantation.

KEYWORDS

visual quality, the Chinese Catquest-9SF scale, spherical aberration, aspheric IOL, contrast sensitivity

Highlights

- There is disagreement on the extent to which reduced spherical aberration can optimize the patient's postoperative visual satisfaction.
- The present study uses the Chinese version of the Catquest-9SF scale to compare contrast sensitivity and ocular aberrations to evaluate the visual quality of cataract patients after surgery with three different IOL.
- Contrast sensitivity with spherical lenses under glare-free and glare conditions was lower than with aspheric lenses, and at higher frequencies the zero-aberration aspheric lens performed best.
- In regard to the evaluation of the visual quality. The Chinese Catquest-9SF scale provides an indication of visual quality after aspheric IOL implantation.

Introduction

The implantation of an aspheric IOL with modified spherical aberration can reduce the postoperative global aberration to some extent and increase the contrast sensitivity in dark and light environment, thereby improving postoperative visual quality (1–5). There is disagreement on the extent to which reduced spherical aberration can optimize the patient's postoperative visual satisfaction. Some researchers assert that zero residual spherical aberration can improve the postoperative contrast sensitivity of patients, thus improving postoperative vision quality, while others point out that limited postoperative depth of focus means that some spherical aberration remains after the surgery (6–11). Previous research has used higher-order aberrations or contrast sensitivity to evaluate the patient's postoperative visual quality, but these are not complete indicators of patients' postoperative overall visual satisfaction. In recent years, vision-related quality of life scales have been widely used in clinics for subjective evaluation. A variety of scales are applied in clinical practice, including the VF-14 scale, Activities of Daily Vision Scale questionnaire (ADVS), and Vision-Related Quality of Life and Visual Function questionnaire (NEI-VFQ25) (12–18). However, the above scales and questionnaires were not validated in the Chinese population, so their applicability in this population is unknown. The Catquest-9SF scale, for subjective evaluation of postoperative visual quality, is derived from Catquest quantitative performance. It has been translated into various languages, which have been accepted by the International Consortium for Health Outcomes Measurement (ICHOM) to assess the recovery of visual function after cataract surgery (19–23). Our previous research has shown that the Chinese version of the Catquest-9SF scale has good one-dimensionality and effectiveness (24).

Therefore, the present study uses the Chinese version of the Catquest-9SF scale to compare contrast sensitivity and ocular aberrations to evaluate the visual quality of cataract patients with three different IOL.

Materials and methods

Study design

This is a retrospective study. Data were collected between January 2020 to December 2021. The trial was conducted in accordance with the principles of the Declaration of Helsinki.

The study population consisted of 145 subjects who underwent cataract phacoemulsification and IOL implantation in our department. All patients underwent tests of uncorrected visual acuity, best corrected visual acuity, higher-order aberrations, contrast sensitivity, and slit lamp microscopy after cataract surgery. Patients were included if they fulfilled the following criteria: (1) simple phacoemulsification + IOL implantation; (2) no intraoperative or postoperative eye complications; (3) no irregular corneal astigmatism; (4) normal pupil responses and dilated pupil diameter >5 mm. Patients meeting any of the following criteria were excluded: (1) Other diseases of the eye, such as corneal disease, glaucoma, uveitis, retinopathy, or high refractive error; (2) serious cardiopulmonary diseases or diabetes; (3) fundus lesions that affect visual quality, such as macular epiretinal membranes or age-related macular degeneration; (4) severe postoperative complication; (5) significant tilt or eccentricity of IOL after surgery.

We compared the postoperative visual quality of a zero spherical aberration aspherical IOL (Softec HD), a negative aspherical IOL (ZCB00), and a spherical IOL (HQ-201HEP). The Softec HD^{TM} posterior chamber IOL (Lenstec Inc., St. Petersburg, FL, USA) is an ultraviolet (UV)-absorbing, single-piece modified "C" loop IOL (IOL) with a symmetrical anterior and posterior surface aspheric design (zero aberration). It is manufactured completely from a medical-grade copolymer of hydrophilic acrylic hydroxyethyl methacrylate (HEMA, 26% water content) and a polymerizable UV blocker. The overall length of the lens is 12.0 mm. The 5.5-mm-long lens optic has a 360° square edge design, designed for placement in the capsular bag. This lens is offered in power options in 0.25-D steps across the +18 to +25 D range, allowing more precise power correction. Tecnis ZCB00 is a one-piece 6.0 mm biconvex hydrophobic acrylic lens with anterior aspheric surface that resulted in a negative SA of −0.27 μm and frosted continuous 360° posterior square edge. This lens is offered in power options in 0.5-D steps across the +5 to +34 D range. It is an UV-blocking hydrophobic acrylic, single-piece modified "C" loop IOL (IOL) with a ProTEC frosted, continuous 360° posterior square edge. The HQ-201HEP (HexaVision, Inc.) is a conventional spheric IOL with a positive SA (Table 1).

TABLE 1 Comparison of three IOL.

IOL type	SOFTEC HD	ZCB00	HQ-201 HEP
IOL spherical Aberration	0 μm	−0.27 μm	>0 μm
IOL design	Aspherical IOL	Aspherical IOL	Spherical IOL
IOL material	Hydrophilic-PMMA	Hydrophobic-PMMA	Hydrophilic-PMMA
IOL diameter (mm)	12	13	12.5
Pupil diameter (mm)	5.75	6.0	6.0
Constant-A	118	119.3	118.2
IOL refractive power (D; Mean, SD)	+15.25 D∼24.7 D	+5.0 D ∼+34.0 D	+4.0 D∼ +34.0 D

D, diopters.

Outcome measurements

Uncorrected distance visual quality (UDVA) and best corrected visual acuity (BCVA) were accessed using a log MAR chart. BCVA was measured following refraction. Prior to acuity measurement, an autorefractor (NIDEK AOS-1500, Japan) was used to measure refractive error. Patients were required to blink to exclude the effect of tear film instability and then measurements were taken following the instrument specifications. These objective data were used as a basis for subjective refraction, which was worn to record monocular best corrected visual acuity.

The CSV-1000 contrast sensitivity test (Vector Vision, Ohio, USA) was used to measure monocular contrast sensitivities. Mean luminance of the display was 85 cd/m² and was constant during the test, minimizing pupil size changes. The patient adjusted to dark room light levels for 5 mins, seated at a distance of 2.5 m from the display, and contrast sensitivity values of each eye were recorded with and without glare (45 cd/m²).

The KR-1W wavefront analyzer (Topcon Medical System, Tokyo, Japan) was used to measure wavefront aberrations post-surgery. The Chinese Catquest-9SF scale score was used to measure visual quality (Table 2).

TABLE 2 Version of the Chinese Catquest-9SF.

Item	Chinese Catquest-9SF
Q1	Vision difficulty in everyday life
Q2	Vision satisfaction in general
Q3	Reading text in the newspaper
Q4	Recognizing the faces of people around you
Q5	Seeing prices of goods when shopping, or descriptions on medicine bottles or bank receipts, electricity bill, water account, etc.
Q6	Seeing to walk on uneven ground.
Q7	Reading text on TV or in movie or on advertising board
Q8	Seeing to do delicate work (needlework, handiwork, carpentry, etc.)
Q9	Seeing to carry on an activity/hobby you are interested in, such as photography, calligraphy, Mah-jongg playing

The Chinese Catquest-9SF questionnaire contains 9 questions. The response options are as follows: 1 = very great difficulty; 2 = great difficulty; 3 = some difficulty; 4 = no difficulty; and 5 = cannot decide. There is also one global question about general satisfaction. The response options are as follows: 1 = very dissatisfied; 2 = rather dissatisfied; 3 = fairly satisfied; 4 = very satisfied; and 5 = cannot decide. The response category "cannot decide" is treated as missing data in the analysis.

Statistical analysis

The data were processed and analyzed statistically using SPSS version 23.0 (IBM Corporation, Chicago, IL, USA). The sample size was chosen to achieve a statistical power of 80% for group comparisons at a 5% significance level. The age, Chinese Catquest-9SF scores, contrast sensitivity, higher-order aberrations and visual acuity measurements of patients with each of the three types of aspheric IOL were expressed in the form of mean ± standard deviation. The correlation between the Chinese Catquest-9SF scale score and visual acuity was expressed by a simple linear regression equation. Contrast sensitivity, higher-order aberrations and scale scores were compared between the three lenses using non-parametric tests (Kruskal-Wallis test). The range of the best spherical aberration was confirmed according to the score result of the scale using non-parametric test. $P < 0.05$ was considered significant.

Results

Patient assignment and baseline characteristics

A total of 145 eyes of 145 people were included in the study (56 males, 89 females). Fifty-one eyes were implanted with SOFTEC HD IOL, 42 eyes were implanted with ZCB00, and 52 eyes were implanted with HQ-201HEP. Mean age of patients with each type of lens was 73.31 (±8.74), 72.64 (±8.95) and 74.13 (±8.20) years, respectively. No significant difference in age was found between the three groups ($P > 0.05$) (Table 3).

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Correlation between Chinese Catquest-9SF score and visual acuity

Figure 1 shows that UCVA and BCVA are significantly negatively correlated with the Chinese Catquest-9SF scale score.

Comparison of contrast sensitivity between groups

Contrast sensitivity at the full range of spatial frequencies was significantly lower in the spherical group (HQ-201HEP) than in the aspheric groups (SOFTEC HD, ZCB00; $P < 0.05$). Within the aspheric group in medium, non-glare and glare lighting conditions, contrast sensitivity at low spatial frequencies [3 cycles per degree (c/d) and 6 c/d] was higher in the negative spherical aberration aspheric IOL group (ZCB00) than the zero spherical aberration aspheric IOL group (SOFTEC HD), while at higher spatial frequencies (12 c/d and 18 c/d) the converse was true (Tables 4, 5).

TABLE 3 Baseline patient characteristics.

Characteristics	Total group	SOFTEC HD group	ZCB00 group	HQ-201HEP
Eye	145	51	42	52
Age	73.41 ± 8.58	73.31 ± 8.74	72.64 ± 8.95	74.13 ± 8.20
HOA (μm)	0.31 ± 0.24	0.24 ± 0.12	0.26 ± 0.19	0.42 ± 0.31
TOA (μm)	0.21 ± 0.13	0.21 ± 0.12	0.24 ± 0.18	0.19 ± 0.08
FOA (μm)	0.12 ± 0.08	0.11 ± 0.48	0.09 ± 0.09	0.16 ± 0.08
CA (μm)	0.12 ± 0.09	0.12 ± 0.07	0.14 ± 0.12	0.11 ± 0.06
SA (μm)	0.10 ± 0.13	0.08 ± 0.04	0.02 ± 0.06	0.18 ± 0.17
Score	32.51 ± 3.10	34.49 ± 1.46	32.93 ± 2.23	30.23 ± 3.42
UCVA	0.75 ± 0.22	0.81 ± 0.21	0.75 ± 0.21	0.68 ± 0.23
BCVA	0.88 ± 0.21	0.96 ± 0.21	0.89 ± 0.18	0.79 ± 0.20

HOA, higher-order aberrations; TOA, third-order aberrations; FOA, fourth-order aberrations; CA, coma; SA, spherical aberration; UCVA and BCVA, uncorrected and best corrected visual acuity, respectively.

Comparison of different aberrations between groups

The overall higher-order aberration was significantly lower in the zero spherical aberration aspheric IOL group (SOFTEC HD; 0.24 ± 0.1 μm) and in the negative spherical aberration aspheric IOL group (ZCB00; 0.26 ± 0.19 μm) than in the spheric IOL group (HQ-201HEP; 0.42 ± 0.31 μm) ($P = 0.0078$ and 0.0151, respectively). No significant difference was found between the three groups in third-order aberration or coma. The fourth-order aberration was significantly lower in the zero spherical aberration aspheric IOL group (SOFTEC HD; 0.11 ± 0.48 μm) and in the negative spherical aberration aspheric IOL group (ZCB00; 0.09 ± 0.09 μm) than in the HQ-201HEP group (0.16 ± 0.08 μm; $P = 0.0447$ and 0.0001, respectively), and significantly lower in the negative spherical aberration aspheric IOL group (ZCB00; 0.09 ± 0.09 μm) than in the zero spherical aberration aspheric IOL group (SOFTEC HD; 0.11 ± 0.48 μm; $P = 0.0321$). Overall spherical aberration was significantly lower in the zero spherical aberration aspheric IOL group (SOFTEC HD; 0.08 ± 0.04 μm) and the negative spherical aberration aspheric IOL group (ZCB00; 0.02 ± 0.06 μm) than in the spheric IOL group (HQ-201HEP; 0.18 ± 0.17 μm; $P = 0.0146$ and <0.0001 respectively), and was significantly lower in the negative spherical aberration aspheric IOL group (ZCB00; 0.02 ± 0.06 μm) than in the zero spherical aberration aspheric IOL group (SOFTEC HD; 0.08 ± 0.04 μm) (Table 6).

Comparison of scale scores between groups

The scale scores were significantly different between all three groups. The scores of the zero spherical aberration aspheric IOL

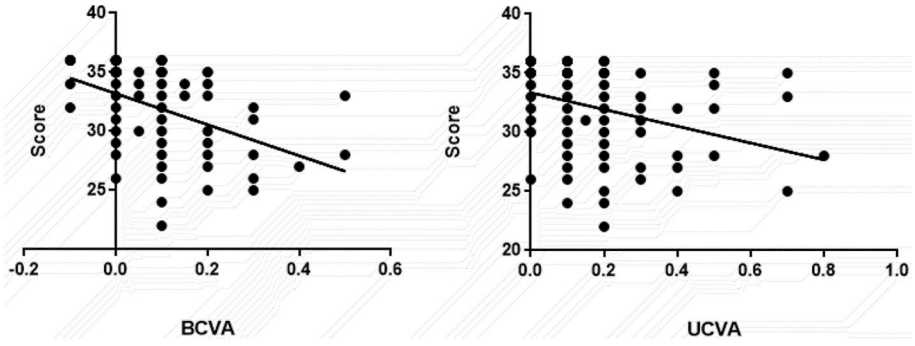

FIGURE 1
Correlation between uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) and scale scores.

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TABLE 4 Contrast sensitivity in non-glare state (mean ± SD).

Spatial frequency (c/d)	SOFTEC HD	ZCB00	HQ
3	1.31 ± 0.43	1.34 ± 0.40	1.17 ± 0.50
6	1.54 ± 0.40	1.60 ± 0.40	1.40 ± 0.47
12	1.10 ± 0.51	1.08 ± 0.48	0.95 ± 0.52
18	0.65 ± 0.46	0.61 ± 0.49	0.52 ± 0.49

TABLE 5 Contrast sensitivity in glare state (mean ± SD).

Spatial frequency (c/d)	SOFTEC HD	ZCB00	HQ
3	1.40 ± 0.28	1.40 ± 0.33	0.98 ± 0.48
6	1.54 ± 0.38	1.57 ± 0.36	1.27 ± 1.32
12	1.22 ± 0.43	1.19 ± 0.43	0.78 ± 0.46
18	0.67 ± 0.39	0.66 ± 0.44	0.35 ± 0.45

TABLE 6 Comparison of higher-order aberrations, fourth-order aberrations and spherical aberrations of three intraocular lenses (mean ± SD).

Groups	SOFTEC HD	ZCB00	HQ	*P*
High-order	0.24 ± 0.12	0.26 ± 0.19	–	>0.9999
aberration (μm)	0.24 ± 0.12	–	0.42 ± 0.31	0.0078*
	–	0.26 ± 0.19	0.42 ± 0.31	0.0151*
Fourth-order	0.11 ± 0.48	0.09 ± 0.09	–	0.0321*
aberration (μm)	0.11 ± 0.48	–	0.16 ± 0.08	0.0447*
		0.09 ± 0.09	0.16 ± 0.08	<0.0001*
Spherical	0.08 ± 0.04	0.02 ± 0.06	–	<0.0001*
aberration (μm)	0.08 ± 0.04	–	0.18 ± 0.17	0.0146*
	–	0.02 ± 0.06	0.18 ± 0.17	<0.0001*

*stands for $P < 0.05$.

group (SOFTEC HD; 34.49 ± 1.46) and the negative spherical aberration aspheric IOL group (ZCB00; 32.93 ± 2.23) were higher than the spheric IOL group (HQ-201HEP; 30.23 ± 3.42) ($P < 0.0001$ and $P = 0.0018$, respectively) and the score in the zero spherical aberration aspheric IOL group (SOFTCE HD) was higher than that of the negative spherical aberration aspheric IOL group (ZCB00; $P = 0.0036$) (Figure 2).

The range of the best spherical aberration based on the score of the scale

One-sample rank sum test was performed on the overall spherical aberration after surgery in the zero spherical aberration aspheric IOL group. According to the score of the scale using non-parametric test, the 95% confidence interval of the overall spherical aberration after surgery was between 0.06616 and 0.08772 μm, $P < 0.0001$ (Figure 3). So, the range of the best spherical aberration is 0.06616–0.08772 μm.

Discussion

The use of aspherical rather than spherical IOL may reduce spherical aberrations and increase contrast sensitivity, but the impact of this improvement on overall visual quality is not well understood. Most previous studies have evaluated visual quality in postoperative patients using a single subjective or objective measure (25–29). Our research combined the Chinese Catquest-9SF scale score with residual spherical aberration of the eye after surgery to evaluate postoperative visual quality from subjective and objective viewpoints. The results of our study revealed that when the residual spherical aberration of the eye was 0.06616–0.08772 μm, the postoperative visual quality was excellent.

We compared the postoperative visual quality of a zero spherical aberration aspherical IOL, a negative aspherical IOL, and a spherical IOL. Consistent with previous studies (30, 31), contrast sensitivity and postoperative scale scores are higher and spherical aberration lower with aspheric than with spherical IOLs. Different scholars have different views about the extent to which residual spherical aberration can affect postoperative visual satisfaction. Garcin et al. (32) used the optical quality analysis system (OQAS) visual quality assessment system to study the postoperative visual quality with zero spherical aberration IOL. The authors reported that the best corrected visual acuity and contrast sensitivity were significantly improved after surgery. Zhang et al. demonstrated that (33) an aspheric IOL with a low negative or zero primary spherical aberration is recommended for cataract patients with high myopia. Hervella et al. (34) found that negative values of spherical aberration extend the depth of focus in different ways depending on each patient. Tzamalis et al. (35) revealed that Bioline yellow IOL indicated lower contrast sensitivity under mesopic conditions when glare was applied but resulted in less trefoil aberrations after uneventful cataract surgery. Although the above assessments are based on objective data comparing postoperative residual global aberration and visual quality, they all have some limitations.

Many related visual function scales exist, including the VA-14, ADVS and the NEI-VFQ25 (12–18) but their content is complex. In 1995, the Swedish National Cataract Registry Center used the Catquest questionnaire to collect data on visual function in cataract patients before and after surgery (22). The questionnaire has since been subjected to Rasch analysis, reduced from 12 to nine questions, and named the Catquest-9SF scale (19). The Catquest-9SF scale has been translated into different languages and has been endorsed by the ICHOM agency for the evaluation of visual function

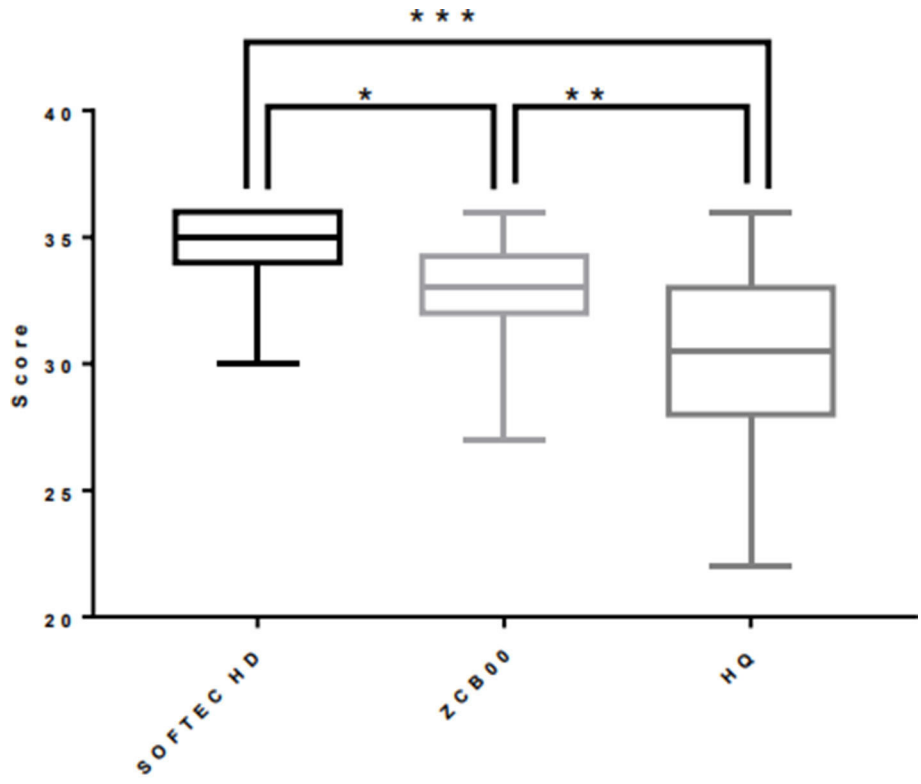

FIGURE 2
Comparison of scale scores between groups. *$P = 0.0036$; **$P = 0.0018$; *** $P < 0.0001$.

after cataract surgery. Recently, Xu et al. (24) applied Rasch model analysis to develop and verify the Chinese version of the Catquest-9SF scale. In the present study, the Chinese version of the Catquest-9SF was used to analyze scores among patients with three different IOL types including two aspheric lenses with different levels of spherical aberration and one spherical lens. Our research revealed that the score was the highest in the zero spherical aberration group, followed by the negative spherical aberration IOL group, and the lowest scores in the spherical IOL group. Linear regression analysis showed a significant positive correlation between the scale score and both uncorrected and best corrected visual acuities, in broad agreement with previous work (21, 25). In addition, our study revealed a significant difference between the two aspherical IOL scores. It is probable that difference levels of aberration with these two lens types in our study led to levels of difficulty in understanding the questions, which leads to differences in scores.

We found that contrast sensitivity with spherical lenses under glare-free and glare conditions was lower than with aspheric lenses, and at higher frequencies the zero-aberration aspheric lens performed the best. Our research shows that higher-order aberrations are relatively low in eyes implanted with zero spherical aberration aspheric IOL. For total spherical aberration, the negative spherical aberration aspheric IOL group is lower than the zero spherical aberration aspheric IOL group. Caporossi et al. (36) implanted one of three types of aspherical IOL or one type of spherical IOL in 250 eyes of 125 patients and demonstrated that the mean total spherical aberration was statistically lower in dominant eyes with aspheric IOLs compared with eyes with spherical IOLs. Lee et al. (37) randomly implanted three types of IOL with different spheric aberrations, and found no statistically significant difference between the best corrected visual acuity or refractive errors, and higher-order aberrations of zero spherical aberration aspheric IOL group after surgery were relatively lower than the other type of aspheric IOL. Zhao et al. (38) concluded that the aspherical acrylic IOL can reduce the higher-order aberrations (especially the spherical aberration) and increase the contrast sensitivity to improve the visual performance. Our research results are consistent with these findings.

Third-order aberration and coma mainly reflect the tilt and eccentricity of the IOL. In the present study, no significant difference in these types of aberration was found between the three IOL, suggesting

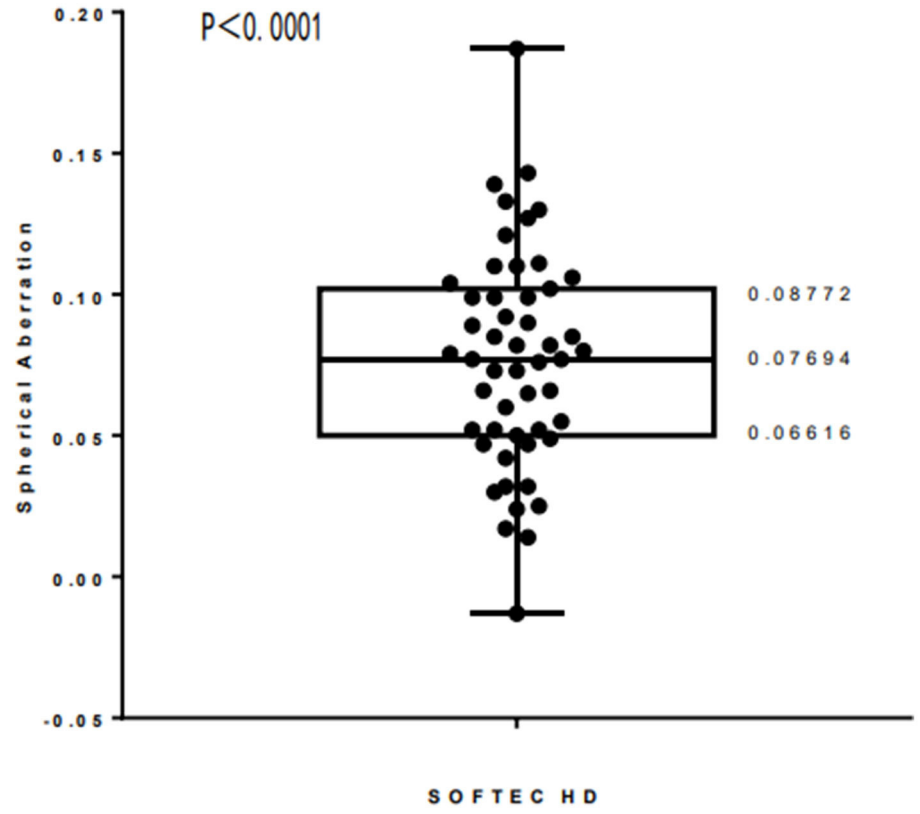

FIGURE 3
The range of the best spherical aberration based on the scale score results.

that any tilt or eccentricity was similar in the three IOL.

Numerous studies have shown that higher-order aberrations on the anterior surface of the cornea of cataract patients vary greatly among individuals, and that corneal spherical aberration has the greatest impact on postoperative visual quality. This type of aberration is rotationally symmetric, making it the only high-order aberration that can be corrected using IOLs. Inter-individual differences in corneal spherical aberration mean that to optimize postoperative visual acuity it is vital to implant an aspheric IOL based on corneal spherical aberration. Studies on non-Chinese populations indicate that the average corneal spherical aberration of the human eye is 0.27 μm (39, 40) whereas the average in Chinese is 0.312 (±0.114) μm (41). Therefore, implantation of aspherical IOL based on non-Chinese corneal spherical aberration data may produce errors. Notably, personalized implantation of aspherical IOL should be based on the different ethnic groups.

Studies by Zhang et al. (42) have shown that higher-order aberrations of the corneal anterior surface may also depend on age. Young people have greater corneal spherical aberrations and less coma and with increasing age, the coma and trefoil gradually increase and corneal spherical aberration gradually decreases. The present study included an elderly population with total spherical aberration of 0.08 (± 0.04) μm after implantation of aspherical IOL. This study used the Chinese Catquest-9SF scale to analyze the correlation between visual quality and the spherical aberration of the eye after implantation of two types of aspheric IOL with different spherical aberration values and one type of spherical IOL. The post-surgery scale score was highest with zero-spherical aberration lenses. The range of the best spherical aberration is confirmed according to the score result of the scale using non-parametric test. Therefore, we believe that the total aberration after aspheric IOL implantation is within this range, and the postoperative visual quality is better.

This study has some limitations. Firstly, recent study (41) has shown that there is a certain correlation between the depth of focus and the higher-order aberrations, so how to balance the relationship between the two factors to obtain the best visual quality needs to be investigated in our further research. Secondly, the sample size was limited. Further research with larger sample size is desirable to studying the visual quality of various intraocular lenses including multifocal intraocular lens implantation. In

addition, the total postoperative global aberration measured in this study included only the anterior corneal and IOL spherical aberrations, and not the posterior corneal spherical aberration, so further studies should take into account the other higher-order aberrations that may affect visual quality.

To conclude, the Chinese Catquest-9SF scale provides an indication of visual quality after aspheric IOL implantation.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee of Shanghai Sixth People's Hospital. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Conceptualization: DW and WQ. Methodology: DW, HY, and LW. Formal analysis and investigation: DW, LW, and XZ. Writing—original draft preparation: DW. Writing—review and editing: DW and HY. Resources: WQ and JL. Supervision: WQ. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Disease burden and risk factors of ischemic heart disease in China during 1990–2019 based on the Global Burden of Disease 2019 report: A systematic analysis

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Objective: The aim of this study was to identify the disease burden and risk factors of ischemic heart disease (IHD) in China, during 1990–2019, through a systematic analysis using the Global Burden of Disease (GBD) 2019 report in order to provide first-hand information for primary and secondary prevention of IHD in China.

Methods: Data on the rates of incidence, death, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs) of IHD were obtained from GBD2019 to determine the disease burden and risk factors of IHD in China.

Results: The rates of incidence, death, YLLs, YLDs, and DALYs of IHD in China increased at different levels during 1990–2019. The annual rate of change in incidence, death, YLLs, YLDs, and DALYs of IHD were 1.31%, 1.57%, 0.93%, 1.14%, and 0.94%, respectively. In 2019, the YLDs of IHD in Chinese women were higher, while the rates of incidence and death, YLLs, and DALYs were lower in Chinese women than in Chinese men. The disease burden of IHD had significant age differences, and people aged ≥70 years had the highest disease burden. A total of 24 risk factors were associated with the rates of death and DALYs of IHD, and the five most significant risk factors were high systolic blood pressure, high LDL cholesterol (LDL-C), smoking, ambient particulate matter pollution, and intake of a high-sodium diet. From 1990 to 2019, a high annual rate of change in IHD-related deaths and DALYs was observed due to ambient particulate matter pollution, high body mass index (BMI), and intake of a diet high in processed meat.

Conclusion: The results of the study revealed that the disease burden of IHD in China was on the rise, especially in people aged ≥70 years. The main disease burden of IHD in male patients was premature death and that in female patients was disability. Environmental, behavioral, and metabolic factors were considered the three main risks of the disease burden of IHD, with metabolic factors having the greatest impact. Therefore, periodic health check-ups and high-risk factor interventions for key populations should be strengthened from the grassroots level, which are conducive to further reducing the disease burden of IHD in China.

KEYWORDS

ischemic heart disease, China, disease burden, risk factors, Global Burden of Disease

Introduction

Ischemic heart disease (IHD), also referred to as coronary atherosclerotic heart disease, is a major chronic and fatal non-communicable disease, but the preferred management approach for this disease has not been well-defined (1, 2). Ischemic heart disease is one of the major contributors to cardiovascular disease (CVD)-related disease burden, which has been proven to be the leading cause of death in both developed and developing countries (3). Based on the Global Burden of Disease (GBD) 2019 report, the total number of deaths due to IHD reached 9.14 million in 2019 worldwide, accounting for 49.2% of CVD-related deaths (4). Except for life metrics such as disability-adjusted life years (DALYs), IHD has an enormous impact on productive life years (PLYs). Researchers projected that, by 2030, 8,100 people aged 45–64 years will be out of the labor force due to IHD in Australia, and there will be a 35% increase in government's welfare payments (5).

Currently, IHD has become a serious public health problem in China (6–8). In China, from 1990 to 2019, with the rapid development of the economy and social background, food consumption patterns, and lifestyles of people have changed dramatically. The most common feature is that the plant-based Eastern diet is gradually replaced by the unhealthy Western type of diet characterized by animal-based foods and foods with high added sugar (9). It has been reported that many known controllable risk factors contribute to IHD, such as hypertension, smoking, high LDL cholesterol (LDL-C), excessive sodium intake, and insufficient intake of nuts and seeds (3). Moreover, a survey conducted in the Hexi Corridor, Northwest China, showed that sandstorm weather is a risk factor for mortality in patients with IHD (10). In pursuit of better primary and secondary prevention of IHD, in this study, the current status and changing trends for the disease burden and risk factors of IHD in China were analyzed by using the GBD2019 data. The IHD-related rates of death and DALYs attributed to environmental, behavioral, and metabolic risk factors were assessed to propose more targeted strategies for IHD prevention in China.

Methods

Data sources

As a retrospective study, data were obtained from GBD2019, including the disease burden and risk factors of IHD in China. The GBD2019 database (http://ghdx.healthdata.org/gbdresults-tool) is created by the Institute for Health Measurement and Evaluation and the University of Washington, covering a total of 86,249 standardized data sources worldwide. The death data of various diseases were evaluated by coding the diseases according to the 10th edition of the International Classification of Diseases (ICD-10), and the coding range of IHD was I20–I25 (11). The death data of IHD in China were mainly derived from Disease Surveillance Points (DSPs), the Maternal and Child Surveillance System, and the Chinese Centers for Disease Control and Prevention's (CDC) cause-of-death-reporting system (12). Data on risk factors and disability disease burden were mainly derived from relevant monitoring and surveys over the years, as well as through a systematic review of relevant literature. Population data are mainly obtained from previous censuses (13). All the aforementioned data can be queried from the GBD Global Health Data Exchange Index (http://ghdx.healthdata.org/gbd-2019/data-input-sources; https://www.healthdata.org/).

Risk factor classification

According to GBD2019, risk factors can be divided into environmental, behavioral, and metabolic risk factors. Environmental risk factors include ambient particulate matter pollution, household air pollution from solid fuels, and lead exposure. Behavioral risk factors include smoking; secondhand smoke; intake of a diet low in whole grains, vegetables, fruits, legumes, fiber, nuts and seeds, seafood omega-3 fatty acids, and polyunsaturated fatty acids; and intake of a diet high in processed meat, sugar-sweetened beverages, trans fatty acids, and sodium, as well as low physical activity and alcohol use. Metabolic risk factors include high systolic blood pressure, high fasting plasma glucose, high LDL-C, high body-mass index (BMI), and kidney dysfunction (14).

Statistics

First, the rates of incidence, death, years of life lost (YLLs), years lived with disability (YLDs), and DALYs were used to describe the disease burden of IHD in different gender and age groups in China. Second, the death rate and DALYs attributed to 24 controllable risk factors for IHD were also analyzed. Finally, the changing trends in IHD-related risk factors from 1990 to 2019 were assessed with the annual rate of change caused by death and DALYs. Statistical analysis has been explained in detail in previous studies (15).

The rate of incidence can be defined as the frequency of new cases of a disease in a specified population within a given period. The rate of incidence can be used to reflect the effect of this disease on the population, which can be represented as follows: rate of incidence = the number of new cases/the number of exposures during the same period. The death rate is the ratio of the number of dead individuals in a specified period (usually 1 year) in a given region to the average population size during the same period represented as follows: Death rate = the number of dead individuals per unit time/average population size per unit time × 1,000%. YLLs represent years of life lost due to premature

TABLE 1 Disease burden of IHD in various age-groups in China, in 2019 (1/100,000).

Age (years)	Incidence	Death	YLLs	YLDs	DALYs
<20	0.86 (0.16–1.93)	0.26 (0.22–0.31)	18.61 (15.43–22.29)	0.07 (0.03–0.15)	18.68 (15.51–22.36)
20–54	80.93 (65.17–99.33)	19.59 (16.14–23.58)	845.47 (698.09–1016.56)	47.84 (29.38–73.73)	893.31 (743.15–21062.71)
55–59	298.50 (205.71–409.16)	82.74 (68.04–99.86)	2682.20 (2205.69–3232.27)	192.43 (118.59–301.76)	2874.63 (2382.08–3435.54)
60–64	412.90 (319.82–523.79)	141.96 (118.01–167.92)	3950.34 (3283.65–4673.16)	278.96 (170.87–430.06)	4229.30 (3549.57–4971.77)
65–69	550.11 (398.74–709.96)	242.19 (204.88–282.77)	5644.85 (4775.18–6591.11)	406.07 (254.71–590.58)	6050.92 (5178.83–6993.22)
70–74	844.76 (670.85–1013.78)	478.36 (411.70–551.14)	9122.24 (7850.92–10508.92)	552.05 (351.14–795.75)	9674.29 (8361.26–11032.98)
75–79	1299.53 (942.76–1780.48)	894.94 (768.15–1018.89)	13491.69 (11576.89–15363.33)	708.70 (441.80–1036.23)	14200.39 (12311.03–16045.1)
≥80	3592.57 (2931.42–4404.11)	2860.87 (2465.16–3205.22)	27314.99 (23602.02–30715.79)	1002.59 (643.34–1457.40)	28317.57 (24571.57–31660.46)
Total	246.09 (216.97–276.97)	131.75 (113.34–149.88)	2309.58 (1974.13–2653.03)	129.05 (85.74–183.36)	2438.63 (2106.15–2786.90)

YLLs, years of life lost; YLDs, years lived with disability; DALYs, disability-adjusted life years.

mortality, which is expressed as follows: YLLs = the longest possible life expectancy for a person in that age-group – the age at death. Years of life lost can also be described as years lived with any short- or long-term health loss, which can be expressed as follows: YLDs = prevalence × disability weights. Disability weights are derived from public surveys to reflect the severity of different cases. Disability-adjusted life years (DALYs) is the sum of YLLs and YLDs, and it is also a comprehensive indicator response to the number of lives and quality of life measured in time.

Results

Disease burden and risk factors of Chinese IHD in 2019

In 2019, the rates of incidence, death, YLLs, YLDs, and DALYs of IHD in the Chinese population were 246.06/100,000 [95% uncertainty interval (UI) 216.97–276.97], 131.75/100,000 (95% UI 113.34–149.88), 2309.58/100,000 (95% UI 2249.30–3392.04), 129.05/100,000 (95% UI 85.74–183.36), and 2438.63/100,000 (95% UI 2106.15–2786.90), respectively (Table 1 and Figure 1A). All index values increased with age, with an increase in people aged ≥70 years and a peak reached in people aged ≥80 years. The rates of incidence, death, YLLs, YLDs, and DALYs in people aged ≥80 years were 3592.57/100,000 (95% UI 2931.42–4404.11), 2860.87/100,000 (95% UI 2465.16–3205.22), 27314.99/100,000 (95% UI 23602.02–30715.79), 1002.59/100,000 (95% UI 643.34–1457.40), and 28317.57/100,000 (95% UI 24571.57–31660.46), respectively (Table 1 and Figure 1B).

In 2019, the rate of YLDs of IHD in Chinese women [132.08/100,000 (95% UI 87.75–186.90)] were higher than those in their male counterparts [126.12/100,000 (95% UI 83.29–182.24)], while the rate of incidence [227.03/100,000 (95% UI 200.23–256.23)], the rate of death [121.64/100,000 (95% UI 98.60–145.14)], YLLs [1823.52/100,000 (95% UI 1471.67–2216.15)], and the rate of DALYs [1955.61/100,000 (95% UI 1601.81–2336.10)] in women were lower than those in their male counterparts (Table 2 and Figure 1A).

Among the controllable risk factors for IHD in 2019, the metabolic risk was the primary risk factor leading to IHD-related death [103.34/100,000 (95% UI 86.41–120.40)] and DALYs [1972.50/100,000 (95% UI 1668.85–2292.02)] in China. However, the impact of environmental and behavioral risk factors on IHD also cannot be ignored. The death rates of IHD caused by environmental and behavioral risk factors were [45.79/100,000 (95% UI 37.90–53.52)] and [87.17/100,000 (95% UI 72.46–102.61)] in China. The rate of DALYs of IHD caused by both environmental and behavioral risk factors were [926.40/100,000 (95% UI 775.96–1088.77)] and [1741.03/100,000 (95% UI 1464.22–2059.41)]. Compared with the global trend, the death rates of the three risk factors have increased in China. For DALYs of IHD, China had a higher impact on environmental and behavioral risk factors but a lower impact on the metabolic risk factors than the global trend (Table 3). Gender and age differences in controllable risk factors were explored in China. The impact of the controllable risk factors on the IHD-related death rate and DALYs in men was higher than that in women, with an age-dependent overall increase (Table 3).

As shown in Figure 2A, the five most important risk factors associated with the death of IHD in China were high systolic blood pressure [68.14/100,000 (95% UI 52.15–85.57)], high LDL-C [51.56/100,000 (95% UI 36.62–69.06)], smoking [28.97/100,000 (95% UI 24.25–34.63)], ambient particulate matter pollution [26.29/100,000 (95% UI 21.20–31.82)], and high fasting blood glucose [24.02/100,000 (95% UI 13.62–39.23)]. The five most important risk factors influencing DALYs of IHD in China were high systolic blood pressure [1304.37/100,000 (95% UI 1036.44–1590.95)], high LDL-C [1081.75/100,000 (95% UI 838.09–1359.48)], smoking [692.44/100,000 (95% UI 577.89–833.66)], ambient particulate

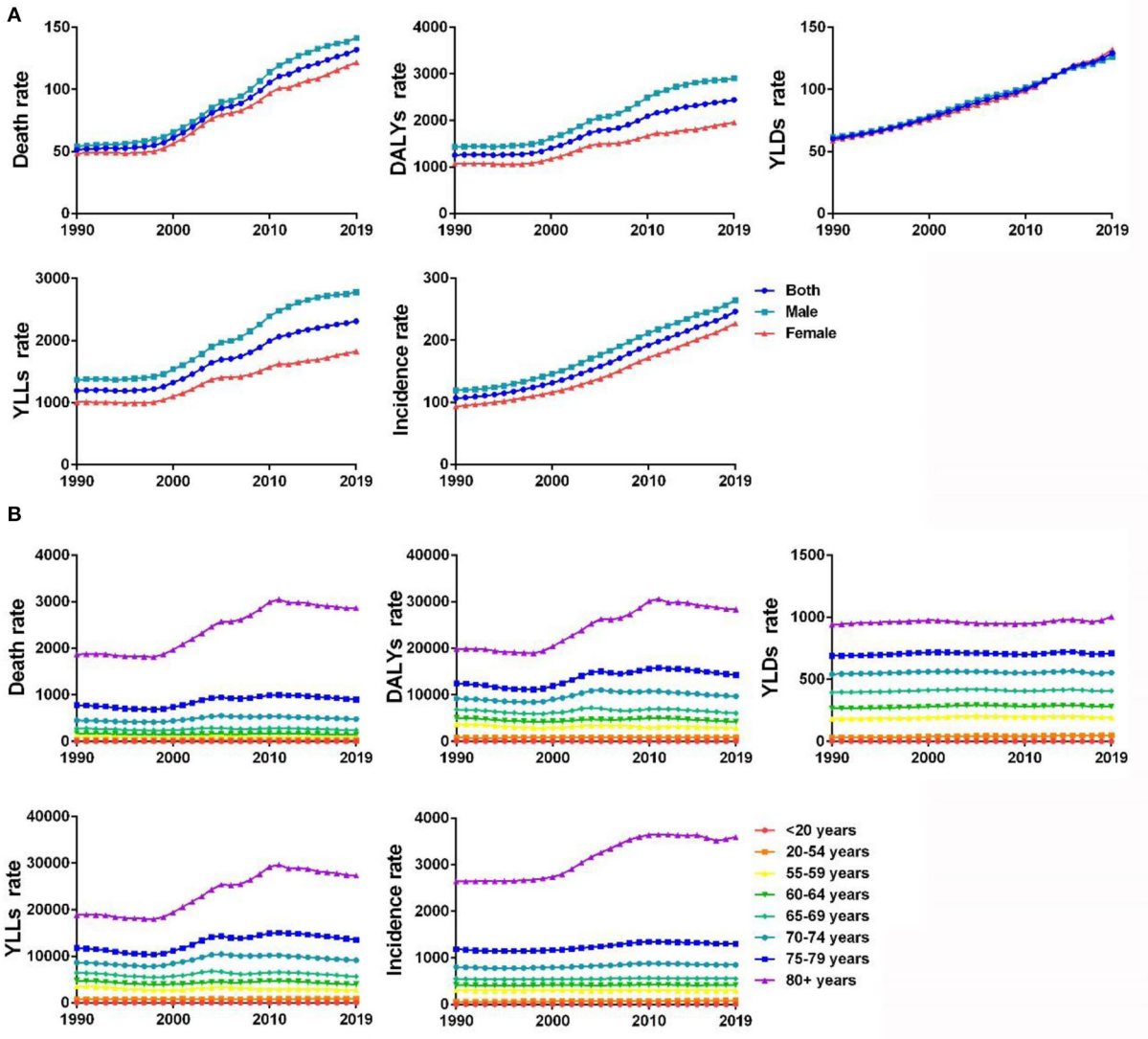

FIGURE 1
(A) Gender differences in disease burden of IHD in China from 1990 to 2019 (1/100,000). **(B)** Disease burden of IHD in different age-groups in China from 1990 to 2019 (1/100,000).

matter pollution [569.47/100,000 (95% UI 458.46–692.84)], and intake of a high-sodium diet [495.28/100,000 (95% UI 222.49–35.22)] (Figure 2B).

Change trends of disease burden and risk factors of IHD in China from 1990 to 2019

From 1990 to 2019, the rates of incidence, death, YLLs, YLDs, and DALYs of IHD in China increased at different levels. The rate of incidence increased from 106.64/100,000 (95% UI 93.87–120.06) in 1990 to 246.09/100,000 (95% UI 216.97–276.97) in 2019, with an annual rate of change of 1.31% (95% UI 1.22–1.40%). The rate of death increased from 51.34/100,000 (95% UI 45.31–257.34) in 1990 to 131.75/100,000 (95% UI 113.34–149.88) in 2019, with an annual rate of change of 1.57% (95% UI 1.16–2.06%). The rate of YLLs increased from 1193.91/100,000 (95% UI 1042.86–1350.43) in 1990 to 2309.58/100,000 (95% UI 2249.30–3392.04) in 2019, with an annual rate of change of 0.93% (95% UI 0.59–1.37%). The rate of YLDs increased from 60.18/100,000 (95% UI 40.04–85.99) in 1990 to 129.05/100,000 (95% UI 85.74–183.36) in 2019, with an annual rate of change of 1.14% (95% UI 1.09–1.20%). The rate

TABLE 2 Gender differences in disease burden of IHD in China in 2019 (1/100,000).

Age (years)	Incidence	Death	YLLs	YLDs	DALYs
Male	264.44 (233.12–297.94)	141.49 (116.82–168.64)	2777.33 (2249.30–3392.04)	126.12 (83.29–182.24)	2903.46 (2378.47–3523.90)
Female	227.03 (200.23–256.23)	121.64 (98.60–145.14)	1823.52 (1471.67–2216.15)	132.08 (87.75–186.90)	1955.61 (1601.81–2336.10)
Total	246.09 (216.97–276.97)	131.75 (113.34–149.88)	2309.58 (1974.13–2653.03)	129.05 (85.74–183.36)	2438.63 (2106.15–2786.90)

of DALYs increased from 1254.09/100,000 (95% UI 1096.61–1408.23) in 1990 to 2438.63/100,000 (95% UI 2106.15–2786.90) in 2019, with an annual rate of change of 0.94% (95% UI 0.62–1.36%) (Table 4). From 1990 to 2019, the rates of incidence, death, YLLs, YLDs, and DALYs of IHD in men and women showed an increasing trend. The annual rate of change for IHD-related death [1.43% (95% UI 1.34–1.54%)] and YLDs [1.25% (95% UI 1.19–1.31%)] in women were higher than those in men [1.22% (95% UI 1.13–1.32%) and 1.05% (95% UI 0.98–1.12%), respectively] (Table 5). The rates of death, DALYs, and YLLs of IHD in the Chinese population aged 20–54 years and ≥70 years, as well as the incidence rate of IHD in people aged 20–54 years and ≥65 years and the rate of YLDs of IHD in people aged ≥20 years, were higher in 2019 than in 1990 (Figure 1B).

As shown in Figure 2A, from 1990 to 2019 in China, the annual rate of change of five metabolic risk factors for IHD-related death in China increased, with high BMI (3.3%), high systolic blood pressure (2.03%), and high fasting blood glucose (1.99%) showing a higher annual rate of change. As for the 16 behavioral risk factors for death caused by IHD, the annual rate of change due to intake of a diet low in vegetables (−0.77%) and fiber (−0.08%) decreased, whereas the remaining 14 behavioral risk factors led to an increase in the annual rate of change and an intake of a diet high in processed meat (2.39%), low physical activity (1.96%), and intake of a diet low in seafood omega-3 fatty acids (1.36%) should be of particular concern. With regard to environmental risk factors for IHD-related death, household air pollution from solid fuels (−0.46%) led to a decrease in the annual rate of change, inconsistent with ambient particulate matter pollution and lead exposure, and the focus should be given on ambient particulate matter pollution (4.08%) with a relatively large change.

Analysis of the annual rate of change for IHD-related DALYs in China during 1990–2019 showed the annual rate of change due to the five controllable metabolic risk factors has increased, with high BMI (2.57%), high systolic blood pressure (1.44%), and high fasting blood glucose (1.42%) showing a greater annual rate of change. As for the 16 controllable behavioral risk factors for IHD-related DALYs, the annual rate of change for intake of a diet low in vegetables (−0.86%) and fiber (−0.29%), alcohol use (−0.20%), and intake of a diet low in nuts and seeds (−0.02%) has declined, whereas the opposite trend was reported for the 12 remaining behavioral risk factors. A diet high in processed meat (1.79%), low physical activity (1.29%), and smoking (0.90%) had the most significant increases in the annual rate of change. We finally analyzed three controllable environmental risk factors of IHD-related DALYs. The annual rate of change due to household air pollution from solid fuels (−0.57) has decreased, but the annual rate of change due to ambient particulate matter pollution and lead exposure has increased, and the annual rate of change due to ambient particulate matter pollution (3.06%) should be of particular concern (Figure 2B).

Discussion

Ischemic heart disease refers to the stenosis or occlusion of the coronary artery caused by atherosclerosis, resulting in myocardial hypoxia or necrosis-induced heart disease, which seriously endangers human health. In 2019, 61.00% of the health burden of cardiovascular disease in China was found to be caused by atherosclerotic cardiovascular disease (ASCVD), in which IHD ranked second after ischemic stroke (13). In 2019, the rate of YLLs of IHD was 2309.58/100,000, which was 17.89 times higher than the rate of YLDs, indicating that premature death was the main cause of the disease burden of IHD in China.

In this report, gender differences were found in the disease burden of IHD in China. The rates of incidence, death, and DALYs of IHD in Chinese men were higher than those in women, but the annual rate of change of IHD in death and YLDs in were higher in women than in men. DALYs of IHD was mainly caused by premature death in male patients, but disability in female patients. In addition, the impact of the controllable risk factors on IHD-related death rate and DALYs in men was higher than that in women. The reasons for the higher disease burden of IHD in Chinese men than women may be heavy social responsibilities and great mental/psychological pressure faced by men, making them prone to developing unhealthy living habits such as staying up late, smoking, excessive drinking, and intake of a high-fat diet. Compared with women, men are more likely to ignore their health problems and fail to seek medical treatment in time. Moreover, the protective effect of estrogen in women can prevent diabetes, protect blood vessels, and delay atherosclerosis; however, the extent of the protective effect needs to be supported by further evidence (16).

With the growth of the population and the intensification of population aging, the absolute number of IHD deaths is continuously increasing. Furthermore, the incidence of chronic

TABLE 3 Death rate and DALYs of risk factor-related IHD in China and worldwide in 2019 (1/100,000).

Risk factors		China		Global	
		Death	DALYs	Death	DALYs
Environmental factors	Total	45.79 (37.90–53.52)	926.40 (775.96–1088.77)	33.81 (29.68–37.99)	767.50 (674.44–860.76)
Behavioral factors	Total	87.17 (72.46–102.61)	1741.03 (1464.22–2059.41)	76.21 (66.82–85.71)	1627.07 (1448.62–1803.59)
Metabolic factors	Total	103.34 (86.41–120.40)	1972.50 (1668.85–2292.02)	97.28 (86.04–107.42)	1979.10 (1793.06–2155.69)
Sex					
Environmental factors	Male	51.88 (41.53–62.59)	1149.33 (914.00–1403.05)	39.13 (34.01–44.22)	966.33 (845.18–1090.32)
	Female	39.46 (31.43–48.55)	694.75 (553.91–853.57)	28.46 (23.95–32.83)	567.41 (486.56–643.70)
Behavioral factors	Male	101.90 (82.99–123.36)	2239.89 (1821.70–2735.89)	88.49 (78.55–98.48)	2094.56 (1877.80–2317.86)
	Female	71.86 (54.89–89.83)	1222.66 (945.00–1534.67)	63.85 (53.99–74.20)	1156.62 (996.21–1322.36)
Metabolic factors	Male	110.98 (89.13–134.20)	2353.89 (1884.46–2855.03)	105.41 (94.22–116.20)	2404.18 (2171.13–2635.87)
	Female	95.40 (75.29–117.03)	1576.19 (1263.85–1916.14)	89.10 (76.60–100.59)	1551.32 (1374.42–1716.45)
Age					
Environmental factors	<20	0.02 (0.01–0.03)	1.50 (1.00–2.04)	0.02 (0.01–0.03)	1.37 (0.76–1.84)
	20–54	9.22 (7.39–11.29)	418.27 (340.85–502.39)	11.33 (9.79–12.93)	504.00 (436.89–571.40)
	55–59	36.54 (28.61–45.62)	1259.01 (993.80–1562.09)	55.64 (46.34–65.57)	1847.85 (1536.83–2177.29)
	60–64	59.41 (46.54–73.58)	1754.29 (1390.26–2145.18)	81.97 (67.83–96.36)	2341.73 (1929.60–2754.58)
	65–69	96.31 (76.50–116.97)	2382.86 (1908.88–2878.55)	116.58 (97.59–135.44)	2808.52 (2352.93–3270.92)
	70–74	178.84 (142.76–217.00)	3583.98 (2878.80–4327.81)	172.02 (142.29–203.32)	3391.24 (2819.32–4008.56)
	75–79	310.22 (252.03–371.44)	4879.70 (3977.65–5853.99)	256.28 (211.42–300.34)	3988.22 (3298.89–4684.98)
	≥80	835.39 (687.47–981.87)	8352.89 (6883.06–9843.81)	520.71 (426.34–616.40)	5075.26 (4187.78–5985.60)
Behavioral factors	<20	−0.00 (−0.01 to −0.00)	−0.27 (−0.49 to −0.08)	−0.00 (−0.01 to −0.00)	−0.23 (−0.37 to −0.07)
	20–54	16.78 (13.76–20.39)	757.96 (628.84–915.57)	21.81 (19.63–23.96)	962.37 (866.02–1056.68)
	55–59	68.03 (54.67–82.91)	2355.04 (1914.90–2867.23)	114.18 (102.37–125.78)	3802.13 (3414.35–4190.16)
	60–64	112.97 (92.81–137.03)	3354.40 (2767.52–4037.35)	175.85 (157.73–193.91)	5040.73 (4522.85–5563.22)
	65–69	179.54 (147.24–213.89)	4471.68 (3698.05–5321.90)	245.30 (217.45–273.11)	5941.17 (5251.17–6636.79)
	70–74	334.06 (274.75–398.55)	6737.98 (5556.98–7961.62)	368.35 (325.38–412.65)	7312.17 (6453.34–8183.30)
	75–79	565.94 (465.34–675.20)	8960.71 (7319.75–10611.32)	550.02 (476.85–622.63)	8624.70 (7480.91–9793.45)
	≥80	1659.36 (1341.78–1970.60)	16548.56 (13508.20–19651.93)	1393.07 (1140.31–1623.50)	13325.98 (11099.37–15460. 29)
Metabolic factors	<20	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.00 (0.00–0.00)
	20–54	17.46 (14.24–21.16)	793.61 (653.05–946.70)	24.06 (21.67–26.47)	1064.74 (958.99–1173.32)
	55–59	72.19 (57.99–87.64)	2508.35 (2027.43–3007.77)	132.56 (120.31–144.15)	4416.04 (4004.15–4796.73)
	60–64	120.03 (97.38–145.29)	3576.29 (2924.14–4296.55)	207.25 (189.61–225.58)	5942.72 (5447.08–6464.11)
	65–69	195.13 (157.90–234.64)	4875.19 (4002.01–5800.24)	298.69 (269.19–328.98)	7235.87 (6501.62–7995.35)
	70–74	370.95 (298.10–447.04)	7501.90 (6061.51–9050.98)	456.40 (402.95–510.01)	9064.12 (8044.83–10122.94)
	75–79	696.70 (579.80–821.19)	11055.04 (9264.58–12968.45)	751.17 (665.73–828.34)	11786.17 (10432.58–13007.21)
	≥80	2147.08 (1691.02–2566.07)	21248.32 (16919.75–25216.83)	1941.91 (1561.35–2256.69)	18442.87 (15020.66–21345.93)

diseases such as hypertension and diabetes are on the rise. The improvement of the healthcare level has shown to prolong the survival period of patients with heart disease. It can be inferred from the aforementioned results that the incidence and severity of IHD increase with age (17). Our study also found age differences in the disease burden of IHD in China, and the overall trend of the disease burden of IHD due to controllable risk factors increases with age. This study showed that from 1990 to 2019, the disease burden of IHD in Chinese people aged ≥70 years has significantly increased, with a peak in people aged ≥80 years. The death rate and DALYs of IHD in the Chinese population aged 20–54 years were higher in 2019 than in 1990, which is consistent with previous research findings that the rates of IHD incidence and death in China show an increasing trend in younger people (18, 19) as a result of overweight, smoking, abnormal lipid metabolism, high blood uric acid, inflammatory response, and impaired vascular endothelial function in young and middle-aged people (20).

In addition to the influence of gender and age, controllable factors such as hypertension, dyslipidemia, diabetes, smoking,

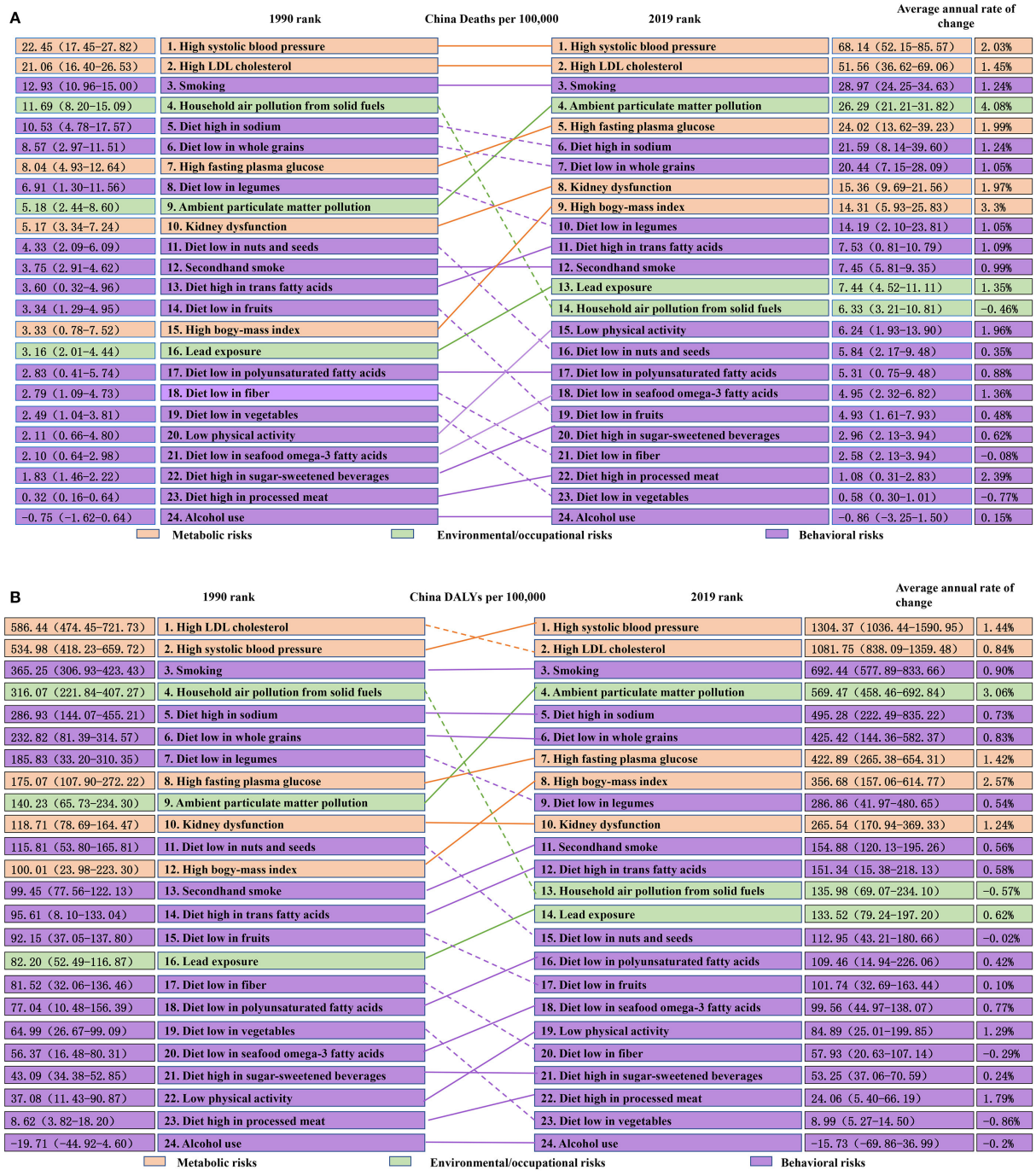

FIGURE 2
(A) Death rate of risk factor-related IHD in China in 1990 and 2019 (1/100,000). **(B)** DALYs of risk factor-related IHD in China in 1990 and 2019 (1/100,000).

and obesity are also closely related to the disease burden of IHD (21). In this study, GBD2019 data were used to estimate the changing trends of 24 risk factors attributable to IHD in the Chinese population, which were divided into three categories: environmental, behavioral, and metabolic factors. Our results showed that metabolic risk factors had the greatest impact on IHD death rate and DALYs in China, followed by environmental and behavioral risk factors. Compared with the global trends, the three major risk factors had a higher impact on the death rate of IHD in China. The impact of environmental and

TABLE 4 Disease burden (1/100,000) and annual rate of change of IHD in China from 1990 to 2019.

Year	Incidence	Death	YLLs	YLDs	DALYs
1990	106.64 (93.87–120.06)	51.34 (45.31–257.34)	1193.91 (1042.86–1350.43)	60.18 (40.04–85.99)	1254.09 (1096.61–1408.23)
2019	246.09 (216.97–276.97)	131.75 (113.34–149.88)	2309.58 (2249.30–3392.04)	129.05 (85.74–183.36)	2438.63 (2106.15–2786.90)
1990–2019	1.31% (1.22–1.40%)	1.57% (1.16–2.06%)	0.93% (0.59–1.37%)	1.14% (1.09–1.20%)	0.94% (0.62–1.36%)

TABLE 5 Annual rate of change of gender-specific disease burden of IHD in China from 1990 to 2019.

Sex	Incidence	Death	YLLs	YLDs	DALYs
Male	1.22% (1.13–1.32%)	1.62% (1.06–2.38%)	1.03 (0.54–1.17%)	1.05% (0.98–1.12%)	1.03% (0.56–1.68%)
Female	1.43% (1.34–1.54%)	1.51% (0.95–2.17%)	0.81% (0.38–1.34%)	1.25% (1.19–1.31%)	0.83% (0.43–1.33%)

behavioral risk factors on DALYs of IHD in China was higher and that of metabolic risk factors was lower than the global trend. China is a country with a large population and is a developing country, with a relatively low economy. Moreover, in China, the rapid development of the economy has resulted in environmental damage, and the unbalanced development of education has resulted in the insufficient awareness of diseases and behavioral restraint. Furthermore, with the development of the economy, the diet structure of Chinese people has changed, characterized by increased intake of protein and fat and insufficient intake of cereals and vegetables, which resulted in a higher death rate of IHD in China than globally. However, the diet structure of people in developed countries is more inclined to high-fat and high-protein diets, so the DALYs of IHD caused by metabolic risk factors in China is slightly lower than that globally. This study reported that among the 24 controllable risk factors, the five most influencing factors were high systolic blood pressure, high LDL-C, smoking, ambient particulate matter pollution, and intake of a high-sodium diet. Blood pressure is significantly related to the progression of IHD. The higher the blood pressure, the longer the course of the disease, and the easier it is to develop multivessel, diffuse, and complex coronary vascular disease (22). High LDL-C can damage the endothelial cell structure and lead to lipid infiltration and the formation of atherosclerosis. The rupture of atherosclerotic plaques can lead to the formation of microthrombi, which is a risk factor for IHD (23). Smoking can damage the vascular endothelium, promote platelet adhesion and aggregation, increase thrombosis, narrow the arterial lumen, block arterial blood flow, and eventually lead to a variety of cardiovascular and cerebrovascular diseases (24). Studies have shown that there is a correlation between ambient particulate matter pollution and IHD deaths (25). A high-sodium diet can cause water and sodium retention, predispose to high blood pressure, and increase the risk of IHD. In this study, from 1990 to 2019, five controllable metabolic risk factors have led to an increase in the annual rate of change of IHD-related death and DALYs, with high BMI, high systolic blood pressure, and high fasting blood glucose showing the highest change. In the 16 controllable behavioral risk factors for IHD-related death, the annual rate of change caused by intake of a diet low in vegetables and fiber decreased, whereas that of the remaining 14 behavioral risk factors showed increased, with high intake of processed meat, low physical activity, and intake of seafood low in omega-3 fatty acids showing the most obvious change. The annual rates of change in DALYs for intake of a diet low in vegetables, fiber, and nuts and seeds, and alcohol use were decreased, whereas those of the remaining 12 behavioral risk factors increased, with intake of a diet high in processed meat, low physical activity, and smoking showing the largest annual changes. The improved lifestyle and accelerated life rhythm changed Chinese diet structure. Being overweight is a consequence of preferring a diet high in processed meat diet and lack of physical activity. Being overweight and smoking increased the incidence of IHD, which can further lead to high risk for recurrent events of kidney dysfunction (26). Moreover, in China, the rapid development of economy has inevitably aggravated environmental damage. For the three controllable environmental risk factors for IHD-related death rate and DALYs, the annual rate of change caused by household air pollution from solid fuels decreased in contrary to the other two environmental risk factors. Among them, the annual rate of change in the disease burden of IHD caused by ambient particulate matter pollution was relatively large (24). However, with the improvement of living standards and educational levels, Chinese people pay more attention to their health and also increase the intake of vegetables and fiber. In addition, the using of natural gas and central heating reduce the environmental pollution caused by the household air pollution from solid fuels. The aforementioned positive changes may have a positive

impact on the primary and secondary prevention of IHD in China.

Conclusion

Given that China is a country with a large aging population and that its medical resources are in short supply, periodic health check-ups and high-risk factor interventions for key populations should be reinforced from the grassroot level. Based on GBD2019 data, the burden and risk factors of IHD in China were analyzed, which not only provide a reference for IHD prevention formulated by public policymakers but also alert patients by increasing health education. According to our analytical data, the following healthy lifestyles can help strengthen IHD management and prevention: health lectures, spreading awareness of the danger of smoking, 150 min of aerobic exercise per week, improvement of the unreasonable diet structure, and promoting trams and bicycles to reduce environmental pollution. Moreover, due to the increase in the incidence of IHD in young and middle-aged people, health education for these populations could help improve patient compliance with treatment, such as informing about reasonable diet, exercise, and weight loss, limiting smoking and alcohol, and reducing the disease burden of IHD in China.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

YL conceived the idea of the study, drafted the manuscript, and drew the figures. JZ reviewed and approved the submitted manuscript version. Both authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The interrelationship between physical activity intensity, cardiorespiratory fitness, and executive function in middle-aged adults: An observational study of office workers

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Background: Previous evidence supports a beneficial effect of physical activity on executive function across the whole lifespan. Yet, the interrelationships of the intensities of physical activity, cardiorespiratory fitness, and executive function require further investigation in adults.

Aim: Using unfiltered accelerometry data and high-resolution intensity classification, we sought to estimate the associations of physical activity with cardiorespiratory fitness and executive function in adult office workers.

Methods: We included 343 full-time office workers (mean age: 42.41 years, range of age: 36–49 years). Executive function was assessed using Stroop, Trail making tests (part-B), and 2-back tests, and a composite score was produced to reflect the general executive function performance. Physical activity was assessed using the Actigraph GT3X+-monitor, worn by each participant for seven days at the hip. Raw accelerometry data were processed by the 10 Hz frequency extended method and divided into 22 intensity bins and sleep time. Cardiorespiratory fitness was estimated using the submaximal Ekblom-Bak cycle ergometer test. Data were analyzed using partial least squares regressions.

Results: In adults, cardiorespiratory fitness was closely correlated with a wide range of absolute physical activity intensity patterns. A higher level of executive function in adults was associated with both higher absolute physical activity intensities and cardiorespiratory fitness, which was independent of age, sex, and education levels. A very weak association between intensities,

fitness, and executive function was observed in high-fit adults. Among low-fit adults, although a positive association started already toward the upper end of moderate intensity, there still appeared to be an association between intensities, cardiorespiratory fitness, and executive function. That is, cardiorespiratory fitness may mediate the association between absolute physical activity intensities and executive function up to a certain level.

Conclusion: The maintenance of executive function in adulthood was related to both physical activity intensities and cardiorespiratory fitness, while their interrelationship was not equal across fitness levels. It is highly recommended to consider the cardiorespiratory fitness level in future studies that focus on executive functions in aging as well when designing individualized physical activity training programs.

KEYWORDS

physical activity intensities, cardiorespiratory fitness, executive function, office workers, active aging

Background

Executive function, as a set of cognitive processes, is related to higher-order of cognitive processes (e.g., planning, working memory, and inhibiting) and goal-directed behaviors (1, 2). Aging preferentially affects certain cognitive domains more than others, and a decline in executive function is one of the hallmarks of cognitive aging (3, 4). Although the decline in executive function is partly attributable to the anatomical changes of the brain areas (e.g., frontal lobe atrophy), it remains unclear why individual differences exist in executive function, especially in relation to the aging process (4–6).

The beneficial effect of physical activity on cognition, including executive function, has been recognized in early and late periods of lifespan, as well as in certain populations characterized by cognitive deficits, e.g., Alzheimer's disease (7–13). Yet, a limited body of evidence supports the link between physical activity and executive functioning in young to middle-aged adults (14). A recent systematic review displays that among sedentary adults without cognitive impairment, aerobic physical activity interventions may preserve executive function with a small amount of effect (15). Considering that the selection criteria of participants in physical activity interventions may be strict in certain groups, observational studies are thus necessary to explore the link between physical activity intensity levels and executive function among adults in a deeper manner (9).

Both chronic and acute effect on executive function from physical activity has been presented previously. For instance, acute bouts of moderate-to-vigorous physical activity exhibit a temporal benefit on executive function during the post-recovery period following exercise, which is shown mostly in studies with children (16–18). The chronic effect is indicated by the greater effectiveness of physical activity intervention on cognitive outcomes seen in studies with longer intervention lengths (19). It is uncertain how the intensity of physical activity is linked to executive function across adulthood. Firstly, physiological reactions to physical exercise vary foremost with its intensity, such as increases over resting values in the cerebral circulation, lactate concentration, and secretion of neurotrophines (20, 21). Evidence is lacking to draw a holistic picture between a wide spectrum of physical activity intensity and executive functioning in adults. Secondly, the magnitude of the physiological reactions to physical activity, especially to acute exercise, is normally relative to the maximally tolerated work capacity (termed as cardiorespiratory fitness) (22). It differs greatly between individuals, with a 2–3-fold variation in the mixed populations (23, 24). Individuals with higher levels of physical exercise and cardiorespiratory fitness during midlife have displayed better-preserved cognition in late life, (25) but little is known about the interrelationship among the three domains in earlier lifespan.

In the current study, our working model hypothesized that different physical activity intensities may show association to various degrees of slower cognitive aging, in the subdomain of executive function, from middle age through late life. Physical activity of sufficient intensity may preserve executive functioning in middle age through its effect on cardiorespiratory fitness or other neuroprotective pathways. Moreover, we theorized that cardiorespiratory fitness may moderate the association between specific physical activity intensity patterns and executive function (Figure 1). In this study of middle-aged office workers, we aim to thoroughly investigate the interrelationships between physical activity intensity spectrum, cardiorespiratory fitness, and executive function, *via* applying device-based physical activity measurements with more than 20 intensity classes.

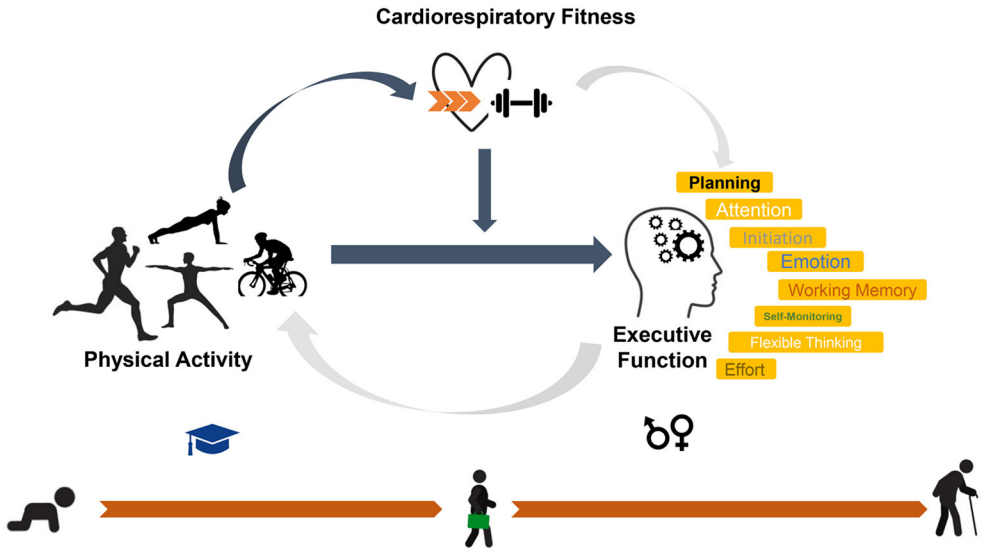

FIGURE 1
Theoretical model of a lifelong interrelationship between physical activity, cardiorespiratory fitness, and executive function. The working model hypothesized that different physical activity intensities may slow cognitive aging in the subdomain of executive function, from middle age through late life. Sufficient physical activity intensity may preserve executive functioning in middle age through its effect on cardiorespiratory fitness or other neuroprotective pathways. Moreover, we theorized that cardiorespiratory fitness may moderate the association between specific physical activity intensity patterns and executive function. We will investigate thoroughly the interrelationship between physical activity intensities, cardiorespiratory fitness, and executive function by following the pathways pointed by dark arrows in this figure. The gray arrows indicate (1) possible pathways from cardiorespiratory fitness to executive function, such as cerebral perfusion and cardiovascular health, (2) reverse pathways from executive function to physical activity intensities, such as making exercise plans.

Methods

Participants

The data in this study were retrieved from a larger project with a cross-sectional design called Physical Activity and Healthy Brain Functions (data collection: Jan 2016—Dec 2017) (26). Study participants were selected from the office-based employees at three workplaces in Stockholm and Gothenburg. In total, 2024 employees were invited to participate in this study and to respond to a self-reported web-based questionnaire. Approximately 1 week after the online survey has been completed, participants were invited to take part in an assessment of executive function using computer-based and pen-and-paper-based tests as well as starting their week-long physical activity assessment. The Stockholm regional ethical review board approved the project (Dnr 2016/1840-32) and all participants signed a written informed consent form.

Executive functions testing

A comprehensive cognitive test battery (9 tests: 6 were computerized tests and 3 were with pen and paper) was administered at the workplaces during office hours (test duration: ~45 min) by trained test leaders. We applied E-Prime 2.0 (Psychology Software Tools) for computerized tests. All cognitive tests were conducted in a specific order, which have shown good validity and reliability for measurement of the respective cognitive domains. Details of these cognitive tests were described previously (26).

Executive functions were measured by Trail Making Test-B (TMT-B, shifting), 2-back (updating), and the Stroop test (inhibition) (27). TMT-B had 25 encircled, but with digits and letters that were to be connected in alternating order (1-A-2-B-3-C, etc.). The outcome score for 2-back was accuracy for 4 blocks of 20-digit sequences. The Stroop paper test consisted of 50 incongruent printed color words (5 rows with 10 words, e.g., the word blue printed in red color). A practice of 10 words was completed prior to the test. During the test, the test leader commented on errors, and participants needed to say the correct color (not read the word) for all targets until the test ended. The outcome score was the completion time.

The reverse scores of TMT-B and Stroop were estimated by calculating the distance between the maximum value and individual scores. A standardized score was further calculated for TMT-B reverse score, Stroop reverse score, and 2-back accuracy score, respectively. We calculated the average score of the three standardized scores as a composite score of executive function, with a higher score indicating a better function.

Physical activity assessments

Device-based data collection

After executive function testing, participants were equipped with an activity monitor (ActiGraph GT3X, Pensacola, FL, USA) and received a diary logbook. The participants were asked to wear the activity monitor during all waking time (except for water-based activities) and noted the time points for when they went to bed and woke up, for seven consecutive days. The accelerometer was worn on the right hip with an elastic band. Accelerometers were set to record at a sampling frequency of 30 Hz. To be considered valid and included in the analyses, recordings were required to cover at least 600 min per day on at least four separate days (28).

Analysis/processing of device-based physical activity data

We applied a filter with a frequency range of 0.29–10 Hz to process the raw accelerometry data on physical activity intensity (29, 30). We defined the non-wearing time as a continuous zero output for at least 60 min with an allowance of up to 2 min of output above zero but below the sedentary cut-point. Time to bed or sleep time was identified according to the daily diary records from the participants during the measurement period. When there are missing records, the standard time in and out of bed was replaced as 23:00 and 06:00, respectively. The physical activity intensity of the time defined as sensor worn and out of bed was divided into specific intensity levels—it is based on accelerometry output cut-points in two ways (as described below). To describe the activity patterns, worn time was divided into sedentary, light-, moderate-, vigorous- and very-vigorous physical activity, using counts-based physical activity data, referring to 1.5, 3, 6, and 9 metabolic equivalents of tasks (METs), respectively. To provide more detailed analyses of the physical activity intensity range, it was divided into a spectrum of 22 smaller bins, using filtered raw acceleration data (expressed in milli-gravity units, mg). The width of the bins was chosen to ensure (1) having enough detail at low intensity with the MET cut-points, and (2) avoiding extreme detail at high intensities. The bin edges were 0, 40, 80, 160, 240 mg, and so forth, increasing with 80 mg (30). The physical activity intensity level of time out of bed and sensor not worn on valid days was extrapolated assuming an equal distribution as the time the sensor was worn. Accelerometry data processing was performed in MATLAB R2020a (MathWorks, Natick, MA, USA).

Fitness testing

The submaximal Ekblom-Bak cycle ergometer test was performed to collect the data on estimated cardiorespiratory fitness (31). During a sub-maximal cycle ergometer test, the heart rates that responded to different sub-maximal rates of work were recorded using telemetry (Polar Oy, Tampere, Finland). We estimated cardiorespiratory fitness, or maximal oxygen consumption, using the sex-specific equations based on the difference in heart rate response between two different sub-maximal rates of work, i.e., a standardized work rate and a higher, individually set rate of work. In our analysis, fitness was expressed as a relative value (milliliters per minute per body mass). It was calculated using a revised algorithm which has been shown to give a valid and reliable estimate of the directly measured maximal oxygen consumption ($r = 0.90$) in adults (32).

Statistics

Characteristics of subjects were described by gender using either mean (standard deviation, SD) or median (interquartile range, IQR) for continuous variables, and frequecies (percentage) for categorical variables. We compared differences in characteristics between men and women using a two-sample *t*-test or Mann-Whitney U-test for continuous variables, and a chi-square test for categorical variables. We standardized the intensity of the physical activity spectrum and sleep to z-scores for further data analysis.

Three steps of analysis were carried out to investigate the interrelationships between physical activity intensity, cardiorespiratory fitness, and executive function. In the first step of the analysis, we aim to determine the association between physical activity intensity and cardiorespiratory fitness. In the second step, we aim to verify the combined contribution of physical activity intensity and cardiorespiratory fitness to executive function. In the third step of the analysis, we aim to determine whether the link between physical activity intensity pattern and executive function varies by cardiorespiratory levels.

Because the data on the physical activity spectrum are highly correlated with each other (correlations up to 0.97), in the first and second steps of analysis, we applied partial least squares (PLS) regression to explore the association between the spectrum of physical activity, cardiorespiratory fitness, and executive function. Briefly, PLS regressions estimate the associations between the components of independent variables (intensity of physical activity/cardiorespiratory fitness) and response variable (cardiorespiratory fitness/executive function). The number of components was chosen by the smallest value of Root Mean Square Error (RMSE) in the cross-validation. We applied permutation tests to reflect the importance of the selected PLS model, and an alpha value was reported. If the alpha value is quite small, it suggests that the covariance for unpermuted data should be larger than the covariance for permuted data, indicating a probability that the given model is significantly different from one built under the same conditions but on random data. The β-coefficients and

TABLE 1 Characteristics of study participants ($n = 343$).

	Total ($n = 343$)	Gender		
		Women ($n = 233$)	Men ($n = 110$)	*P*-value
Age (years), mean/SD	42.4 (9.0)	41.8 (9.3)	43.41 (8.4)	0.159
Education (years)[a], mean/SD	14.4 (2.3)	14.2 (2.3)	14.85 (2.2)	0.012
Cardiorespiratory fitness (mL/kg×min)[a], mean/SD	39.9 (8.4)	37.7 (7.8)	44.56 (7.7)	<0.001
Executive function[a], mean/SD	0.01 (0.7)	0.03 (0.8)	−0.03 (0.7)	0.535
Accelerometry data, median (IQR)				
Valid days	8.0 (7.0–8.0)	8.0 (7.0–8.0)	8.0 (7.0–8.0)	0.839
Average wear time per day (minutes)	960.81 (926.9–988.8)	960,0 (927.5–985.0)	968.6 (926.9–1010.6)	0.078
Average sleep time (minutes)	479.2 (451.3–513.1)	480.0 (455.0–512.5)	471.4 (429.4–513.1)	0.078
Average time spent sedentary (minutes)	751.2 (716.4–798.0)	745.4 (716.2–788.8)	762.9 (721.5–819.4)	0.039
Average time spent in low-intensity PA (minutes)	116.7 (99.4–137.2)	115.2 (99.5–137.5)	120.0 (99.4–135.6)	0.68
Average time spent in moderate intensity PA (minutes)	76.1 (65.3–92.1)	79.2 (67.2–94.4)	72.7 (59.1–81.5)	<0.01
Average time spent in vigorous intensity PA (minutes)	1.4 (0.6–3.8)	1.5 (0.7–3.9)	1.1 (0.5–3.3)	0.12
Average time spent in very vigorous intensity PA (minutes)	0.1 (0.0–0.4)	0.1 (0.0–0.3)	0.1 (0.0–0.7)	0.70

[a]There were two missing values for education, 5 for cardiorespiratory fitness level, 51 for executive function score.
SD, Standard Deviation; IQR, Interquartile range; PA, Physical Activity.

their 95% confidence intervals (CI) of independent variables in each PLS regression model were reported to reflect the contribution of predictors to the shared components as well as the associations between independent variables and response variables. To fully understand the relationship of physical activity patterns and cardiorespiratory fitness with executive functions in the second step of the analysis, we performed different PLS models to consider the confounding effects of other factors (i.e., age, gender, education). We first ran a PLS model using executive function as the outcome, and physical activity intensity and cardiorespiratory fitness as predictors. The second model was conducted using the same predictors, but we removed the effect of age, gender, and education status from the outcome of executive function. This was done using the residuals from a multiple linear regression with age, gender, and education as independent variables and the executive function as the dependent variable (33).

In the third step of the analysis, to entirely understand whether certain patterns of physical activity intensity are associated with executive function and whether the patterns are independent of cardiorespiratory fitness, PLS-regression models were performed (predictor: physical activity intensities, outcome: executive function), stratifying by gender-specific low- and high-fitness groups.

To further understand the interrelationships between physical activity intensity, cardiorespiratory fitness, and executive function, in the additional analyses, we divided our study participants into four groups according to their joint executive function and cardiorespiratory fitness— (1) low-fit and low executive function, (2) low-fit and high executive function, (3) high-fit and low executive function, and (4) high-fit and high executive function. We described the average level of weekly time spent on different activities in the four groups.

Our analysis was performed using R 4.0.5 software and STATA 16.0 (STATA Corporation, College Station, TX).

Results

Characteristics of study participants

In total, 343 participants (233 women and 110 men) with available physical activity data, were included in the analyses (Table 1). The average age of study participants was 42.4 ± 9.0 years and the average length of education was 14.4 years. Compared with women, men showed higher levels in education year, cardiorespiratory fitness, and sedentary time, whereas less time was spent on moderate intensity physical activity. No significant differences were detected between men and women regarding age, executive function, wear time, low-intensity physical activity, vigorous-intensity physical activity, and very vigorous intensity physical activity.

Association between physical activity intensity and cardiorespiratory fitness

Based on the smallest RMSE value (see Supplementary Figure 1A), we selected one component in the PLS regression (18.39% of variance explained in the cross-validation) to associate cardiorespiratory fitness (response variable) with the

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physical activity spectrum. Permutation test showed that the PLS model linking physical activity intensity to cardiorespiratory fitness in all participants was significant (alpha value<0.001). This, together with the β-coefficients (95% CI) of the physical activity spectrum from the PLS regression (Figure 2A), indicated that cardiorespiratory fitness was associated with a physically active lifestyle pattern (i.e., limited sedentary time and more time spent in activities with a wide range of intensity levels). We further applied the gender-specific median value of cardiorespiratory fitness (44.4 mL/kg × min for men and 37.40 mL/kg × min for women) to categorize our participants into high-fit and low-fit groups. The associations between cardiorespiratory fitness and physical activity intensity spectrum seemed to vary by the fitness levels. When the stratification analyses (Figures 2B,C) were carried out by the fitness groups, we found that the PLS regression was significant among low-fit adults (alpha value = 0.04) but not among high-fit adults (alpha value = 0.09).

The contribution of physical activity intensity and cardiorespiratory fitness to executive function

When we linked physical activity intensity and fitness to executive function, both unadjusted and adjusted models suggest the PLS regression model with one component (16.3% of the variance was explained in the unadjusted model, and 15.4% of the variance was explained in the age, sex, and education adjusted model, see Supplementary Figures 1B,C). Results in the unadjusted PLS regression model (Figure 3, Model 1) displayed that higher executive functions were associated with both more time spent in vigorous and very vigorous physical activity as well as a high level of cardiorespiratory fitness, although the PLS model was not significant (alpha value = 0.13). A similar weekly activity pattern was demonstrated in the adjusted PLS regression model (Figure 3, Model 2).

The link between physical activity intensity and executive function by cardiorespiratory fitness levels

To understand whether the association between physical activity intensity and executive function was independent of cardiorespiratory fitness level, we further conducted the stratified PLS regression model by cardiorespiratory fitness levels. Supplementary Figures 1D,E showed the RMSE values for the selected PLS regression model in high-fit adults and low-fit adults, respectively. Although permutation tests suggested that PLS models in both high-fit and low-fit adults were not significant (alpha value $_{\text{high-fit}}$ = 0.95 and alpha value $_{\text{low-fit}}$ = 0.39), Figure 4 displayed

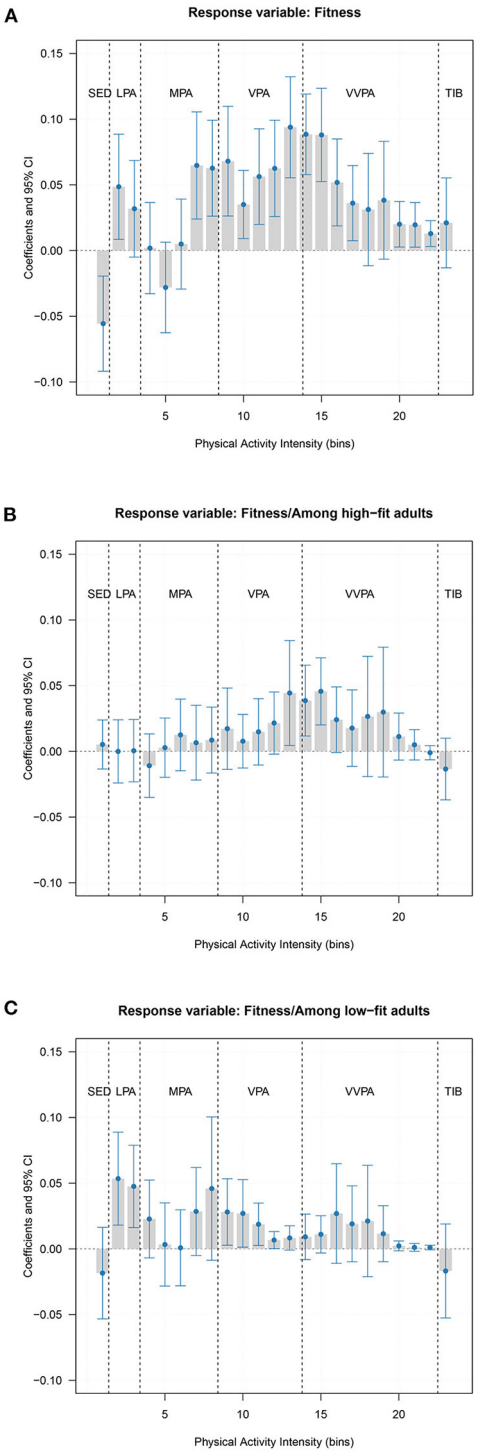

FIGURE 2
Association between physical activity intensity and cardiorespiratory fitness. A positive bar indicates more time spent at that activity intensity is associated with a higher level of cardiorespiratory fitness, while a negative bar indicates more time spent at that activity is associated with a lower level of fitness. SED, Sedentary; LPA, Light physical activity; MPA, Moderate physical activity; VPA, Vigorous physical activity; VVPA, Very vigorous physical activity; TIB, Time in bed/sleep time. **(A)** Displays the results in all analytical sample, **(B)** shows the results in the high-fit adults, and **(C)** presents the results in the low-fit adults.

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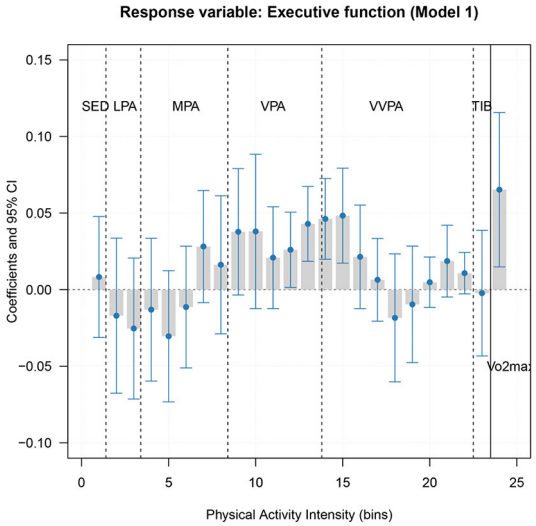


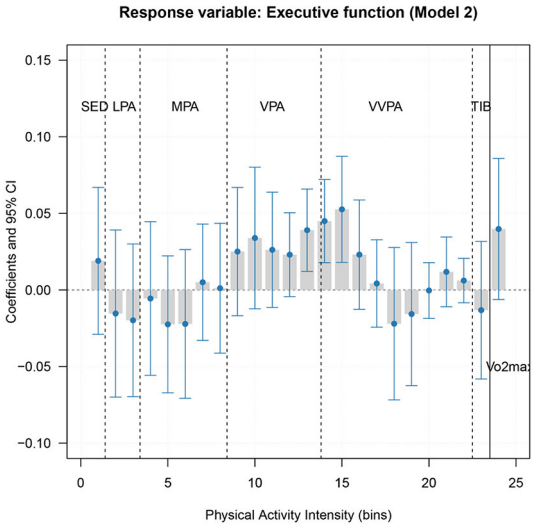
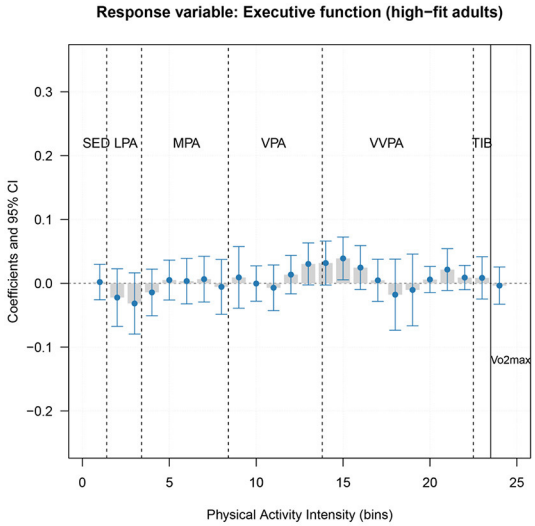


FIGURE 3
Association of physical activity intensity variable (bin) and cardiorespiratory fitness with the executive function composite score. A positive bar indicates more time spent at that intensity is associated with higher executive function, while a negative bar indicates more time spent at that activity is associated with lower executive function. The last bar marked with Vo2max reflects the association between cardiorespiratory fitness and executive function. Model 1 is unadjusted model, and Model 2 was additionally adjusted for the influence of age, sex, and education level. SED, Sedentary; LPA, Light physical activity; MPA, Moderate physical activity; VPA, Vigorous physical activity; VVPA, Very vigorous physical activity; TIB, Time in bed/sleep time.



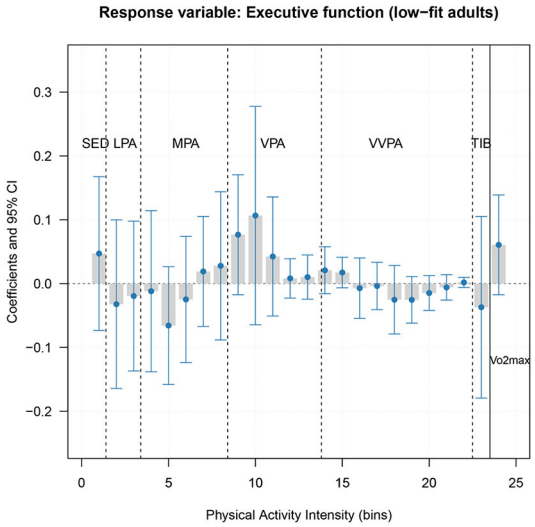


FIGURE 4
Association of physical activity intensity variable (bin) and cardiorespiratory fitness with the executive function composite score by fitness level. The last bar marked with Vo2max reflects the association between cardiorespiratory fitness and executive function. We applied gender-specific cut-off value of cardiorespiratory fitness to categorize our participants into high-fit (men: Vo2max>44.56 mL/kg×min; women: Vo2max>37.69 mL/kg×min; $n = 143$) and low-fit (men: Vo2max≤44.56 mL/kg/min; women: Vo2max≤37.69 mL/kg/min; $n = 145$) groups. SED, Sedentary; LPA, Light physical activity; MPA, Moderate physical activity; VPA, Vigorous physical activity; VVPA, Very vigorous physical activity; TIB, Time in bed/sleep time.

that the relationships of physical activity intensity and cardiorespiratory fitness with executive function may differ between high-fit and low-fit adults. Among high-fit adults ($n = 143$), only weak associations were observed between physical activity, cardiorespiratory fitness, and executive function. Yet, among low-fit adults ($n = 145$), a higher executive function tended to relate to more time spent sedentary, and in vigorous physical activity (although a positive association started already toward the upper end of moderate intensity), as well as a higher level of cardiorespiratory fitness. The same results were obtained when we excluded

cardiorespiratory fitness in the PLS model (Supplementary Figure 2).

Additional analyses

Results in the additional analyses showed that there were no substantial differences in light-to-moderate physical activity intensities between the four joint groups. Yet, compared to low-fit adults, high-fit adults presented less sedentary time and more time in bed/sleep time, which was regardless of executive function level. More differences between the four joint groups were displayed in the high levels of physical activity intensities. That is, the group with low-fit and low executive function demonstrated the least time spent in vigorous to very vigorous physical activity, whereas the group with high-fit and high executive function appeared to show the most time spent on these activities.

Discussion

Main findings

Findings from the current study can be summarized as (1) absolute physical activity intensity and cardiorespiratory fitness may have an interdependent effect on mid-life executive function; (2) the joint effect of absolute physical activity intensity and cardiorespiratory fitness on executive function among adults may be largely diluted when cardiorespiratory reached to certain level.

In comparison with other studies

Previous research only shows a general relation between physical activity and executive functions, especially in children (34). One possible reason for the lack of detailed physical activity intensity data is that only a few previous studies have applied sensor-based measurements of physical activity, as self-reported data lack precision and temporal resolution. In most studies that engaged sensor-based physical activity measurements, physical activity data is often processed into three or four intensity classes using the cut-point of ActiGraph counts-based energy expenditure, with a class width span normally varying between 1.5 METs and infinity for sedentary behavior, 1–1.5 METs for light-intensity physical activity, 1.5–3 METs for moderate-intensity physical activity, and 3–6 METs for vigorous physical activity, 6–9 METs for very vigorous physical activity (35). This may narrow down the physical activity intensity spectrum and loss much information regarding the accelerometry data (30). Further, in the most frequently used monitor, the ActiGraph GT3X, a frequency filter, has been applied. This may limit the investigations of activities inducing high frequent accelerations, and thus hinder detailed investigations on the relation between vigorous physical activity and executive functions.

Most previous studies that investigated the association between physical activity and executive function did not take variations of cardiorespiratory fitness into account. This may be of importance, as health effects are associated with relative intensity, not absolute physical activity intensity. It may, therefore, well obscure relations between activities of different intensities and cognitive performance. Thus, taking fitness into account, for example *via* stratified analyses, is an important step in expanding our understanding of the relations between physical activity and cognitive abilities. In our stratified analyses, different patterns were observed between high-fit and low-fit adults regarding the association of physical activity intensity and cardiorespiratory fitness with executive function. Notely, accelerometry data capture absolute intensity of physical activity but the output measurement is often expressed in relative terms (i.e., time spent in moderate or vigorous physical activity). Relative physical activity intensity is dependent on individual levels of fitness, which itself might be influenced by multiple factors, e.g., genes and health conditions. Thus, the relationships between relative activity intensities and executive function may actually show similar patterns between high-fit and low-fit adults, though the patterns of absolute physical activity differ. More research is required to further explore the connections between relative physical activity intensities, fitness, and executive function. In addition, the unsignificant PLS models and β-coefficients in the stratified analyses might be attributable to the fact that stratifications remove a lot of the variation and leaves less statistical power to locate significant associations.

Although the beneficial effect of physical activity on cardiorespiratory fitness measured by VO_2max has been well documented by previous studies, (36, 37) findings remain inconclusive regarding the association of physical activity intensities with cardiorespiratory fitness, especially in adults. Studies based on self-reported physical activity data have provided a general link between physical activity and VO_2max. For example, a study involving adolescents who were followed for 23 years untill adulthood revealed that self-reported physical activity level is weakly related to VO2max (38). A study involving German women showed that a self-reported high level of leisure time activity, was associated with high VO_2max (39). Studies based on device-based physical activity measurements have mostly been focusing on certain physical activity patterns, such as the association of VO_2max with moderate-to-vigorous physical activity (40). Our findings, although from a cross-sectional design, suggest that physical activity of lower absolute intensities was sufficient to improve cardiorespiratory fitness even in low-fit adults, which differed from high-fit adults where physical activity of higher intensities was required.

The interrelationship between physical activity, cardiorespiratory fitness, and cognitive performance has been investigated essentially in children and older adults, (41, 42) but is understudied in observational studies involving healthy adults. A recent study involving young adults has provided the first neural evidence that cardiorespiratory fitness levels modify the effect of acute exercise on executive function (43). To the best of our knowledge, this is the first work that thoroughly examined the interrelationship between absolute physical activity intensity, cardiorespiratory fitness, and executive function in healthy adults. Our findings have highlighted that the relation between different absolute physical activity intensities and executive functions through adulthood varied with fitness levels.

Mechanisms and interpretations

Although habitual high-intensity exercise generally increases aerobic fitness, this investigation could not confirm that fitness is independently linked to higher executive functions. Nevertheless, cardiorespiratory fitness level may serve as a mediator or moderator to explain enhanced cognitive performance through different levels of intensity training. In general, moderate and vigorous intensity exercises can raise VO2max levels, increase oxygen delivery to the working muscles, and facilitate higher oxygen extraction in the muscles. Yet, the individual fitness level does influence the optimum absolute intensity needed for sufficient stimulus. Our findings are in line with previous studies showing that compared to low-fit adults, well-trained adults require higher absolute intensities to gain improvements in their cardiorespiratory fitness (44). The finding that cardiorespiratory fitness moderated the associations between absolute physical activity intensities and executive function so that higher absolute intensities related to executive function in higher fit as compared to lower fit individuals, supports the notion that the intensity of exercise prescribed to improve executive functions should be set relative to the fitness of the individual. Besides the moderating role, cardiorespiratory fitness may act as a mediator linking physical activity to executive function. The influence of cardiorespiratory fitness on cognition may be through cerebral blood flow regulation or a molecular pathway beyond vascularization, such as N-acetyl aspartate (45, 46). Further, a threshold of VO2max may exist with no further effect of physical activity on executive function, as indicated by our stratified analyses with only weak association in high-fit individuals but with stronger associations in low-fit individuals. However, additional research is required to confirm our non-significant findings and to explore other pathways between physical activity intensities and executive function that are moderated but not mediated by fitness.

Strength and limitations

Several strengths are included in the current study. Firstly, calibration research has revealed that the ActiGraph counts become insensible at higher physical activity intensities, such as vigorous physical activities, in comparison with walking (47). With the improvement of accelerometry raw data processing, we have applied a wider frequency filter, which has been shown to better capture the variations in physical activity and movement patterns (29). Secondly, to avoid the limitation of cut points, we divided the intensity spectrum into many blocks or bins, which keeps much more accelerometry information and improves the knowledge about the association pattern of physical activity. Thirdly, applying multivariate analysis, i.e., PLS regression, can handle well the collinear nature of the intensity spectrum of physical activity variables as shown by large proportion of high correlation. We applied PLS regression to identify the potential relations between a matrix of physical activity variables, cardiorespiratory fitness, and executive function, which were assessed by the explained variance, the magnitude of coefficients, and model fitness. Fourth, applying device-based measurements in this study (i.e., physical activity and cardiorespiratory fitness) can overcome the reporting bias that often exists in epidemiological studies with questionnaire data. Several limitations likewise remain in our study. With the cross-sectional design, the bidirectional association between physical activity pattern and cardiorespiratory fitness makes it difficult to distinguish the long-term influence of physical activity pattern on fitness and executive function as well as the causal effects. Lacking relative intensity measurements, we were unable to compare the patterns between relative and absolute intensities in relation to both fitness and executive function. Large variation may exist in physical activity data regarding the investigated intensity levels. The habitual physical activity pattern may not be captured entirely using a 7-day of physical activity measurement (48). There might be a small effect of valid day and wearing time on our study results, although previous research did not observe much difference (30). In this study, we included 343 participants, 338 were with available data on cardiorespiratory fitness and 292 were with available data on executive function. Results in the permutation tests showed that only the PLS model linking physical activity intensity and cardiorespiratory fitness in all participants ($n = 338$) was significant (alpha value<0.001). This indicates that the PLS analysis of physical activity patterns and executive function is plausible to have an insufficient power of estimation owing to the limited number of available participants. In addition, volunteered participants in our study are more likely to show a profile of well-educated, highly motivated, and active office workers. Although tendencies of association between low-intensity of physical activity pattern, fitness, and executive function were observed in our results, cautions are needed when generalizing the findings to other populations. Another limitation of the current study is lacking objective measures of

cardiovascular health and lung function. The interrelationships between physical activity intensities, cardiorespiratory fitness, and cognition may differ by these factors.

Conclusion

The maintenance of executive function in adulthood is related to both physical activity intensities and cardiorespiratory fitness, while their interrelationship may be fluctuated by the cardiorespiratory fitness. Firstly, to increase or maintain cardiorespiratory fitness in adults, training programs should be adapted to the cardiorespiratory fitness level, such as the absolute physical activity intensity level should be gradually increased to enhance cardiorespiratory fitness. In this way, less fit individuals are able to achieve a higher fitness level with less (absolute) intensity work. Secondly, cardiorespiratory fitness may mediate the effect of physical activity on executive function up to a certain level. Future research that focuses on exercise-related cognitive boosting in aging thus is recommended to take cardiorespiratory fitness level into account. More investigations are necessary to explore other pathways linking physical activity intensities to cognitive maintenance, such as neuroplasticity.

Data availability statement

Derived and raw data supporting the findings of this study are available from the corresponding author on request.

Ethics statement

The studies involving human participants were reviewed and approved by the Stockholm Regional Ethical Review Board approved the project (Dnr 2016/1840-32) and all participants signed a written informed consent form. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

RW and ÖE: conceptualization. RW, ME, DA, JF, MB, and ÖE: methodology and writing–review and editing. RW: formal analysis and writing–original draft preparation. ME, DA, JF, MB, and ÖE: resources. ÖE and ME: funding acquisition. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.1035521/full#supplementary-material

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The role of health-related quality of life in risk prediction for developing cardiovascular disease, dementia and all-cause death among general older adults

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KEYWORDS

health-related quality of life, cardiovascular disease, dementia, cognitive decline, mortality, older people

The world is experiencing rapid growth in the aging population (1). Such a notable increase in human longevity is one of humanity's novel accomplishments of this century which reflects public health initiatives and healthcare improvement. In 2020, approximately 9% of the global population were aged ≥65 years representing 727 million and this proportion is expected to reach about 16% representing 2 billion in 2050 (1). On the other hand, aging also increases the risk of developing chronic age-related diseases such as diabetes, hypertension, osteoporosis, cardiovascular disease (CVD), and dementia (2). Among these age-related diseases, CVD and dementia are two of the leading causes of global disease burden, long-term disability claims and death in older people (3). Thus, the continued rapid growth in the aging population comes with an increased global disease burden, which places pressure on the healthcare resources as well as the society.

In this 21st century, a patient-centric paradigm shift has occurred in healthcare and patient-centredness, which is respectful of an individual patient's values and preferences, is now widely considered a basic principle underpinning the provision of high-quality healthcare (4). Hence, the use of patient-reported outcome measures (PROMs) has gained increasing interest since they can capture not only an individual's perception of their health condition but also insights related to the improvements in functional capacity which are the ultimate goal of both healthcare providers and patients in seeking healthcare service (4).

The subjective health-related quality of life (HRQoL) is one of the most widely used PROMs in clinical research and public health surveillance. HRQoL consists of a broad multidimensional concept that includes physical, mental, emotional, and social health functioning domains (5). It captures the impact of an individual's health condition on their own daily activities (5). Therefore, together with the current patient-centric movement, HRQoL has received increasing attention in healthcare settings, particularly as a patient's HRQoL can be monitored to evaluate the recovery progress of the patient following a specific medical treatment such as surgery (4). Further, there is evidence that

lower HRQoL predicts worse prognosis, rehospitalization, and overall survival in people with chronic diseases including CVD (6, 7). Thus, HRQoL has been considered a novel prognostic indicator in the patient population, including among CVD patients.

In the context of non-clinical settings, we recently conducted the prospective analyses using five-year longitudinal data of the ASPREE (ASPirin in Reducing Events in the Elderly) cohort including 19,106 community-dwelling individuals aged ≥70 years (all others) or ≥65 years (United States minority i.e., African American and Hispanic groups only) who had no prior CVD events, diagnosed dementia or persistent physical disability at the time of study entry (8–11). Therefore, our ASPREE study participants who were "free" of major health events at baseline could be employed to address the predictive value of HRQoL for the development of chronic health outcomes. Furthermore, our study cohort had a good diversity in gender (56.4%, women), educational level (54.8%, ≥12 years of education), and baseline health-related behaviors (44.7%, former/current smoker; 52.8%, current low-risk alcohol consumption) (8–10). Although our unique ASPREE cohort was initially "healthy" at the time of study entry, the study participants also had other chronic diseases such as hypertension (74.3%) and dyslipidaemia (65.2%) which are usually found in community-dwelling older adults (8–10). Therefore, this sample could perhaps be representative of relatively "healthy" community-dwelling older people in primary care settings. In Australia, the postcode for the area of residence was additionally recorded and we estimated a macro-level socioeconomic position (Socio-Economic Indexes for Areas Index of Relative Socio-economic Advantage and Disadvantage (SEIFA-IRSAD), divided into quintiles) (12). Our Australian sample, which represents 87.4% of the cohort overall, was evenly distributed across all socioeconomic quintiles (12). In our prospective analyses, we found that the self-reported 12-item short form HRQoL assessment (SF-12, version-2) can predict the future risk of CVD, cognitive decline, dementia, and all-cause mortality in older adults, even when adjusting for sociodemographic

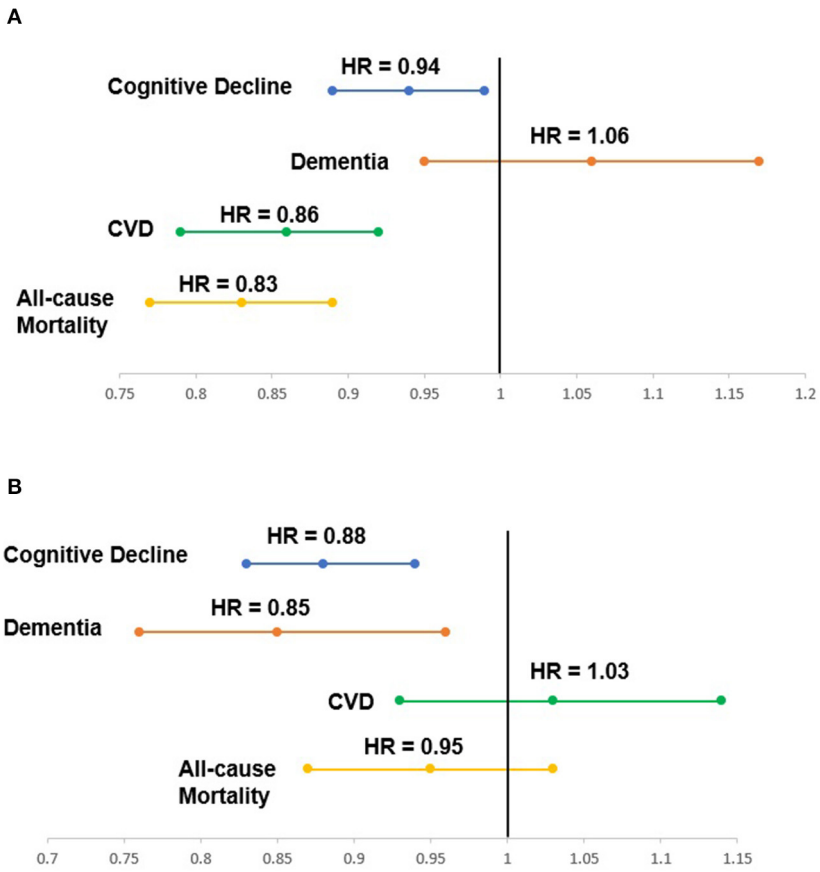

FIGURE 1
(A) Association between physical health-related quality of life at baseline and the risk of health outcomes over a median of 4.7 years; **(B)** Association between mental health-related quality of life at baseline and the risk of health outcomes over a median of 4.7 years.

factors, health-related behaviors and clinical measures (8–10). Specifically, over a median of 4.7 years, a 10-unit higher physical HRQoL at baseline was associated with a lower risk of incident CVD by 14%, cognitive decline by 6%, and all-cause mortality by 17% (Figure 1) (8–10). A 10-unit higher mental HRQoL was associated, with a 12% lower risk of cognitive decline and 15% lower risk of dementia, but was not associated with incident CVD or all-cause mortality (Figure 1) (8–10). Next, we assessed whether changes in physical HRQoL (i.e. trajectories) over a median of 4.7 years among the same ASPREE cohort (11). We found that older individuals in the declining physical HRQoL trajectory (i.e., about 9 units decrease over a median of 4.7 years follow-up) had approximately 50% higher subsequent risk of incident CVD in the next 2 years compared to those in the high physical HRQoL trajectory group (11).

In this manner, poor HRQoL has also been shown to increase the risks of adverse health outcomes in community-dwelling older adults. These recent findings reflect the importance of an individual's perception of their health status (i.e., HRQoL) in primary care settings. Additionally, our findings support the Australian Commission on Safety and Quality in Health Care's government recommendations that PROMs, including HRQoL, be incorporated into the health system as a policy goal (13). One limitation for the integration of the HRQoL measure into the routine clinical practice is how to score the HRQoL as the HRQoL has a multi-step calculation to derive the summarized component scores of physical and mental HRQoL. Thus, future efforts should be made on developing an automatic scoring system, providing a superior option for clinicians to implement routine HRQoL measurements in primary care settings.

Notably, our findings are independent of traditional risk factors for developing age-related diseases such as age, gender, lifestyle factors, co-morbidities, and objective clinical measures - body mass index, blood pressure and total cholesterol level, which are all included in existing risk prediction models. This demonstrates that in addition to our known modifiable and non-modifiable risk factors, HRQoL can predict future risk of CVD, cognitive decline, dementia and all-cause death in community-dwelling older people. To the best of our knowledge, an individual's subjective perception of health status is yet to be incorporated into disease risk scores. Our preliminary findings suggest that there is considerable potential to expand the use of an inexpensive HRQoL measure in chronic disease risk assessments, especially for older people. In this approach, earlier identification of older individuals at a higher risk of chronic diseases could increase the efficacy of healthcare resources for the aging population by focusing primary prevention on those who need it the most. Overall, based on our emerging evidence and prior research, we, as HRQoL researchers, call for healthcare professionals to appraise the insight of an individual's perception of their health conditions (i.e., self-reported HRQoL) in the risk assessment for developing CVD, dementia, and all-cause deaths among general older people in this patient-centric era.

Author contributions

AZZP wrote the initial manuscript draft and undertook revisions. JR and RF-P provided critical comments and suggestions. All authors approved the final version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The physiological mechanism and effect of resistance exercise on cognitive function in the elderly people

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Background: As brain function declines and cognitive ability declines, the benefits of resistance exercise to the brain of older people are gradually gaining attention.

Objective: The purpose of this review is to explore the mechanism and relationship between physiological factors such as vascular and neuronal degeneration and cognitive decline, and to categorize the differences in the effects of an acute and chronic resistance exercise intervention on cognitive function in healthy elderly people and the possible regulators of cognitive effects.

Methods: Using PubMed, Elsevier, Web of Science, X-MOL, CNKI, and Taiwan academic literature database, the research papers published in relevant journals at home and abroad until April 2022 were searched with Chinese and English keywords such as Resistance exercise, the elderly, hippocampus, memory performance, neurons, cognitive function. Pedro scale was used to check the quality of various documents, and the relevant research documents were obtained with the resistance exercise elements as the main axis for comprehensive analysis.

Results and conclusion: (1) Resistance exercise can have a beneficial effect on the brain function of the elderly through blood flow changes, stimulate nerve conduction substances and endocrine metabolism, promote cerebrovascular regeneration and gray matter volume of the brain, and prevent or delay the cognitive function degradation such as memory and attention of the elderly; (2) Acute resistance can temporarily stimulate hormone secretion *in vivo* and significantly improve the effect of short-term memory test, but it has little effect on the cognitive performance of the elderly; (3) Moderate-high intensity resistance exercise (50–80%1RM, 1–3 times/week, 2–3 groups/time) lasting for at least 6 months is more prominent for the improvement of cognitive function of the elderly, while the parameters such as resistance exercise intensity, exercise amount, duration, evaluation test time and differences of subjects may have different degrees of influence on cognitive benefits.

KEYWORDS

Alzheimer's disease, elderly, cognitive health, physiological function, resistance exercise

Introduction

According to the official demographic forecast, China's elderly population will reach 480 million in 2050 (1). With the increase of age, physical abilities (such as muscle strength) and cognitive functions (such as attention, memory, and central executive control capability) will gradually decline (2). The structure and function of the organic system (i.e., brain) may be negatively affected, leading to a decline in individual abilities (e.g., cognitive ability), and ultimately leading to Alzheimer's disease (AD). Cellular and molecular biological studies have shown that brain-derived neurotrophic factor (BDNF) and cortisol (COR) have an impact on the neurogenesis of the brain of all mammalian species (including humans), which directly change the basic structure and morphology of the brain (3). In addition, the study found that cerebrovascular dysfunction, neuronal plasticity, neurogenesis, and stress hormone levels are all related to the etiology of AD or cognitive and emotional disorders (4).

Notably, resistance exercise (RE) can stimulate a variety of neurochemicals, such as lactate, cortisol (COR), brain-derived neurotrophic factor (BDNF), serum insulin-like growth factor-1(IGF-1), vascular endothelial growth factor (VEGF), acetylcholine, dopamine, norepinephrine, and serotonin (5). These specific neurochemicals interact with each other through other regulatory factors, triggering complex neurobiological processes (6–8), and making elastic changes in cognitive control through environmental changes. They can also inject more attention resources to adjust behavioral performance after reaction errors or conflicts (9, 10). At the same time, it can also fight against different types of body and brain-related health problems, such as angiogenesis, which can enhance blood perfusion, learning-related hippocampus, and chronic memory (11).

Given that there is currently no cure for cognitive decline, and that the health and economic burden of a general decline in people's cognition has seriously affected social life. Therefore, establishing prevention methods is critical to delaying the occurrence of cognitive decline. However, structured resistance exercise has been shown to improve memory, attention, spatial awareness, reaction time, planning, and information processing capabilities in middle-aged and older adults (12). To date, there is evidence to support the close relationship between neurodegenerative diseases and progressive cognitive decline during aging, but its exact physiological mechanism is still unclear. And there is limited information about the different benefits of acute resistance or chronic resistance intervention on the cognitive health of the elderly. Therefore, the primary end-point of the review is to explore the mechanisms and relationships between physiological factors such as vascular and neuronal degeneration and cognitive decline. Furthermore, we also discuss the difference in the effectiveness of acute and long-term resistance exercise intervention on the cognitive function of healthy elderly people, to provide an important reference for future academic research or training practice.

Methods

Search strategy

We conducted a comprehensive literature search in databases including PubMed, Elsevier, Web of Science, X-MOL, CNKI, and Taiwan academic literature for reports published from inception through the date of search (initial search conducted on November 3, 2021, with an updated search conducted on April 7, 2022). Searches were specific to literature published in English and Chinese but were not limited to any age or publication date ranges.

Literature selection

We identified 3,502 studies from the different searched databases based on "elderly" and "cognitive function," and from these 3,502 studies identified 1827 studies based on the keyword "resistance exercise" or "resistance training." Then, a total of 257 studies were further identified by the relevant terms, including specifically "acute resistance" or "chronic resistance" and terms related to cognition in older adults (atherosclerosis, hippocampus, memory performance, neurons) and "Alzheimer's disease." Among the 257 pieces of related literature established, 184 records were retained by removing duplicate records. Two reviewers (AC, HL) carefully read the abstracts and contents of the remaining articles, and then excluded the articles irrelevant to the subject ($n = 56$), ineligible study design (such as review, protocol, case report, $n = 27$), and cannot get full text ($n = 2$). Disagreements were resolved through consensus or with the help of a third reviewer (JL). Pedro Scale was used to check and judge the literature quality, and finally, 99 pieces of literature were obtained. The details of our study selection process are reported in Figure 1.

Data extraction and analysis

One reviewer (AC) used a specially designed form to extract data from the included research, and it was verified by another reviewer (HX). The extracted data contained basic information about the publication (article title, author, year of publication, journal name, etc.), design (randomization, allocation concealment, etc.), characteristics of subjects (number, age, sex, etc.), intervention measures (intervention type, frequency, intensity and duration of each group) and outcomes (measurement tools, drop-out, etc.) were extracted from each included study. Among them, 13 items

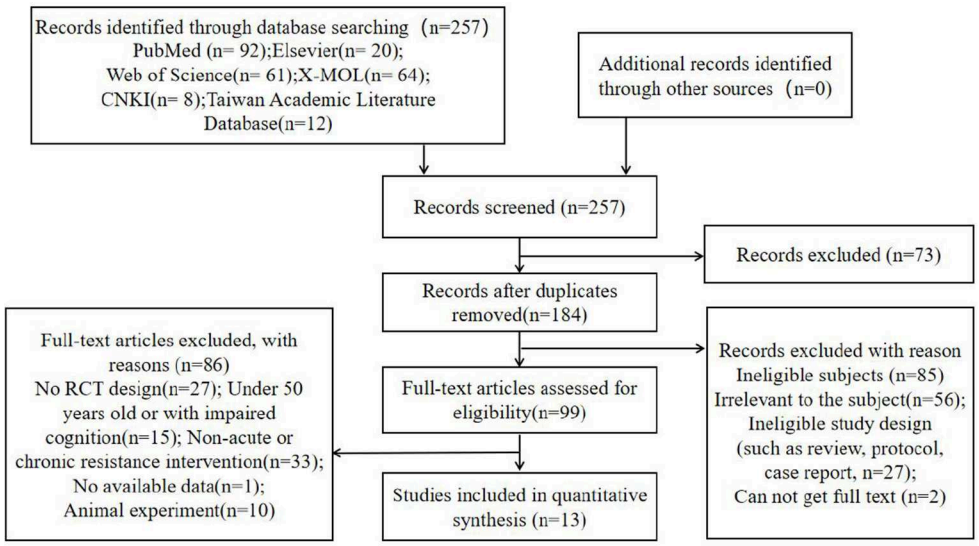

FIGURE 1
Flow chart with information about the search, screening, and selection processes.

(5 acute resistance and 8 chronic resistance) were included in the quantitative comprehensive analysis, and the remaining 86 articles were excluded for the following reasons: (1) No RCT design ($n = 27$); (2) Under 50 years old or with impaired cognition ($n = 15$); (3) Non-acute or chronic resistance intervention ($n = 33$); (4) No available data ($n = 1$); (5) Animal experiment ($n = 10$).

Cochrane Review Manager (RevMan 5.4) was used to perform the data analysis. Mean difference (MD) or standardized MD (SMD) with 95% confidence intervals (95%CIs) were employed to measure trial outcomes of continuous data. If the data are available and the heterogeneity test does not find significant heterogeneity among the included studies, the fixed effect model is used to estimate the merger effect; Otherwise, the random effect model is used.

Risk of bias assessment

Two evaluators independently evaluated the research quality by using Cochrane Collaboration's Risk of Bias Tool. The evaluation criteria of this tool are divided into seven items, and the bias risk rating of each item is "low," "high" or "unclear" to judge and divide the research quality (13). Any differences in bias risk assessment are resolved through discussions between evaluators or with the third author when necessary. The evaluation results are reported in Figures 2, 3.

It was found that in the blind field of Random sequence generation, Allocation concealment, incomplete outcome data, and Selective reporting, most studies are rated as low bias risk or unclear bias risk. The reviewed studies are considered to have ambiguous bias risks in these areas because they are not described in sufficient detail (such as allocation concealment). However, there are high-performance bias risks in the other three blind areas, which is inevitable.

Mechanism of aging and neurodegenerative diseases on cognitive health

Cerebral-vascular dysfunction

Atherosclerosis, cerebral blood flow

Atherosclerosis (AS) is a vascular disease with the hardening of blood vessels, internal thickening, and inhibition of vascular tension (14). It is characterized by the formation of atherosclerotic plaque or fibrous plaque in the intima, and it is one of the most common and dangerous diseases (15). After developing AS the atherosclerotic carotid and cerebral arteries attenuate cerebral blood flow (CBF) (16) over time. The decrease in cerebral blood flow is related to insufficient cerebral perfusion, reduced nutrient transport, low metabolism, and cognitive ability, and it decreases by 1% in healthy adults every year (17). The Rotterdam study (18) showed that a patient with severe atherosclerosis has three times the probability of developing AD compared with normal people. In the process of AS formation, under the condition of a high-fat diet (high cholesterol and saturated fat), extracellular lipids and white blood cells accumulate in the intima, and endothelial cells produce relatively reduced shear stress at the proximal arterial

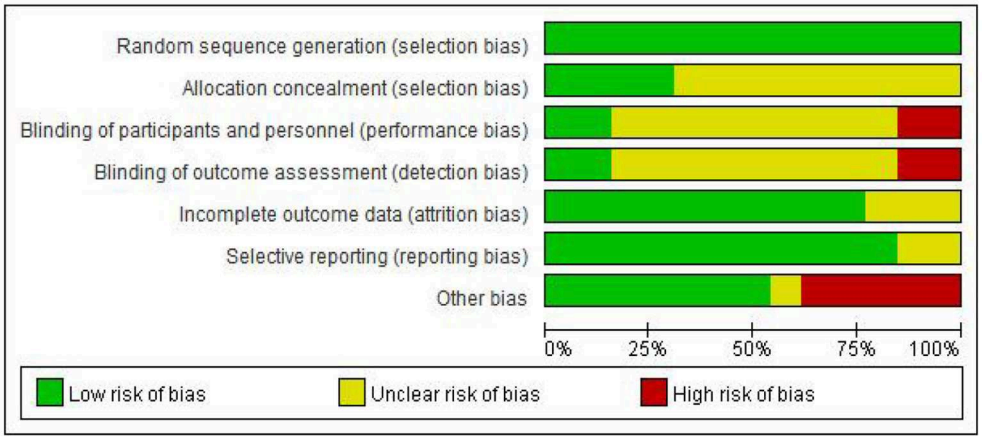

FIGURE 2
Risk of randomized control studies bias graph.

blood flow shunt (19), which leads to abnormal hemodynamics and increased blood viscosity. It is found that atherosclerosis is positively correlated with blood viscosity (20). Compared with people with normal blood viscosity, older men with higher blood viscosity have poorer cognitive performance (21). Importantly, blood viscosity increases with age (22), and is affected by erythrocyte aggregation, leukocyte count, plasma fibrinogen, immunoglobulin, and erythrocyte rigidity (23). In the presence of cognitive impairment, these age-related rheological changes will be more obvious (24). For example, fibrinogen concentration increases with age, and it is related to the cognitive decline of individuals with mild cognitive impairment (RP = 0.17, $p < 0.05$) (25). Lucas et al. (26) pointed out that the increase in blood viscosity and the decrease of CBF related to age reflect brain atrophy because less active nerve mass requires less oxygen and nutrition (i.e., low metabolism), so it is speculated that low metabolism may be one of the reasons for the decrease of CBF. In addition, the change in blood pressure is speculated to be one of the key factors to reduce CBF. At present, the relationship between hypotension and cognition is unclear, but hypertension can indirectly reduce CBF by destroying the brain's self-regulation, promoting harmful vascular remodeling, oxidative stress, and inflammatory response (27), and paving the way for white matter degeneration.

In addition, inflammatory factors (such as apolipoprotein B-lipoprotein (apoB-LPs), interleukin IL-1, IL-6, tumor necrosis factor-α, etc.), embryonic phenotype smooth muscle cells (SMC), and arterial extracellular matrix (ECM) in AS lesions exacerbate the plaque inflammation and calcification (28). Calcification not only causes the dysfunction of the blood-brain barrier (BBB) but also accelerates the deposition of amyloid-β(Aβ) in and around cerebral arteries. This condition is called cerebral amyloid angiopathy (CAA), and its severity is related to the accelerated decline of perception speed, situational memory, and semantic memory of the elderly (29). Generally, Aβ is a landmark feature observed in the brains of AD patients and is considered to be the main cause of neuron degeneration (30). In the pathogenesis of AD, Aβ is strongly supported by the rare gene mutations of transmembrane protein amyloid-β, presenilin 1, and 2, which directly lead to the overproduction of Aβ (31). Due to the unbalanced production and discharge, toxic Aβ peptide is accumulated, which promotes cerebral atherosclerosis (32), and causes vascular dysfunction and permanent circulation accumulation of Aβ (33) (Figure 4). To remove Aβ from the brain, it is necessary to rely on the special way that interstitial fluid (ISF) and cerebrospinal fluid (CSF) are excluded from the cell through BBB and gelatinous lymph (colloid and lymph) system (34, 35). In this process, gelatinous lymphatic drainage occurs along the basilar membrane (perivascular pathway) of arteries and capillaries (36), and the adjacent smooth muscle carrying water channel (34). It is assumed that the movement of ISF and CSF along the perivascular, and the channel depends on arterial pulsation (34, 37). In this model, the space around the blood vessel is compressed during each pulse period, and the resultant pressure wave can remove solutes such as Aβ (38). On the contrary, if the elasticity-dependent arterial pulsation is damaged in AS and aging blood vessels, it is likely that the excretion will decrease and toxic Aβ will accumulate more (34, 35, 39) with time, which will accelerate cognitive decline.

Neuroplasticity, neurogenesis, neurotrophic growth factors

Brain-derived neurotrophic factor

Neuroplasticity is the primary process of remodeling brain structure and function in response to neuron activity, injury, death, and growth (40). As a process of neuroplasticity, neurogenesis is the process of forming neurons from neural

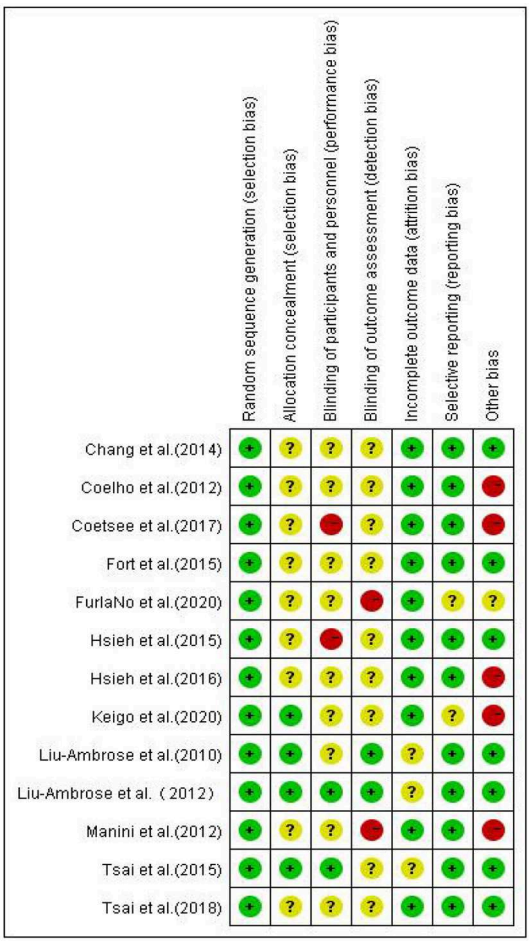

FIGURE 3
Risk of randomized control studies bias summary.

stem cells and neural precursor cells. It occurs in three regions of the adult mammalian brain: the subventricular area of the lateral ventricle (for interneuronogenesis), the basolateral region of the amygdala, and the hippocampal dentate gyrus (41, 42). Hippocampal neurogenesis is the way of memory formation, and it is one of the earliest brain regions affected by severe atrophy in AD (43). It exists in the hippocampus and cerebral cortex with a high concentration of brain-derived neurotrophic factor (BDNF). BDNF is the most widely distributed neurotrophic factor in neurogenesis and synaptic plasticity. Through its high-affinity tropomyosin-associated kinase B(TRK-B) receptor (44), BDNF may have a bidirectional transport function across BBB (45), increasing the number of synapses in the brain and the branches of the axonal in the cortex (46). BDNF and IGF-1 are known as the key factors of learning and memory, which are responsible for the generation, proliferation, survival, and maintenance of neurons (such as neurons in the hippocampus, cortex, and root ganglion cells) (47), making the brain operate more efficiently and improving the learning process and memory ability. In addition, *in vivo*, and *in vitro* evidence also shows that BDNF-mediated neuroprotection can inhibit Aβ toxicity in rats (48).

The basic peripheral level of BDNF in healthy individuals varies from 1.5 to 30.9 $ng{\cdot}mL^{-1}$ (49). Lommatzsch et al. (50) observed that the decrease in plasma BDNF was negatively correlated with the increase in age ($rs = -0.20$, $p < 0.05$). In AD patients, the serum BDNF level rises in the early stage of the disease (about 21%), which may be a compensatory response to mild neurodegeneration (51, 52). In late AD, BDNF has obvious transcription defects in several cortical areas (13), and the level of BDNF protein in serum is 31% lower than that of early AD patients (51). The brain tissue of AD patients after death showed that BDNF mRNA decreased in the crucial areas of memory formation and learning (hippocampus and cortex) (13). In addition, some gene polymorphisms will also harm BDNF. There is a common single nucleotide polymorphism (SNP) in BDNF. At codon 66, the amino acid valine (Val), which is responsible for correctly coding BDNF, is replaced by methionine (Met), a sulfur-containing amino acid (Val66Met SNP). Met substitution damages the activity-dependent secretion and intracellular distribution of BDNF in hippocampal neurons (53). Compared with Val carriers, Met carriers have worse episodic memory and hippocampal function, and the gray matter volume of the prefrontal lobe and temporal lobe is smaller (54).

Insulin growth factor (IGF) and growth hormone (GH)

Aging is a dynamic and gradual process, which will decrease the function of the nerve conduction system, reduce the release of nerve substances (such as IGF-1 and GH) (55), and then make cognitive performance decline, reducing the ability of individuals to adapt to the environment. Growth hormone (GH) is the master of all hormones, and it is also the key element for all brain and body cells to grow into adulthood. It can not only control energy allocation but also counteract the natural aging of cells (56). GH mostly exists in the hippocampus, inferior hypothalamus, putamen, and choroid plexus in the brain. However, aging will significantly reduce GH values in these parts of the brain (57). Vitiello et al. (58) speculated that GH was closely related to cognitive function, and GH supplementation could improve the cognitive decline of elderly or AD patients. Insulin-like growth factor 1 (IGF-1) is a hormone produced by GH stimulation, which is secreted by the anterior pituitary gland. After GH secretion, it can promote the synthesis and secretion of IGF-1 by hepatocytes within a few minutes (59). Its main function is the growth and maintenance of skeletal muscle, especially in the developmental stage of life (60). IGF-1 plays an important role in neurogenesis and angiogenesis of the brain. For example, during the transport of IGF-1, it

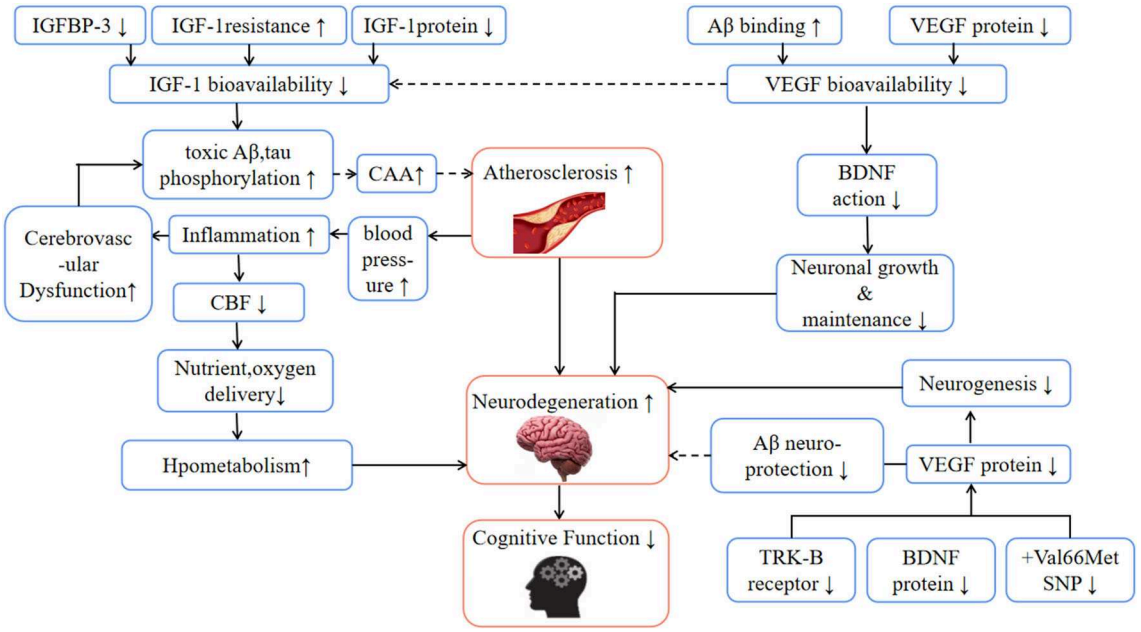

FIGURE 4
The effects of aging and neurodegenerative diseases on physiological mechanisms related to cognitive health. Aβ, amyloid β; BDNF, brain-derived nerve factor; CAA, cerebral amyloid angiopathy; CBF, cerebral blood flow; IGF-1, insulin-like growth factor 1; IGFBP-3, insulin-like growth factor binding protein 3; TRK-B, tropomyosin-related kinase b; SNP, single nucleotide polymorphism; VEGF, vascular endothelial growth factor; Hypothetical pathways are marked "—".

is easy to interact with the target tissue through BBB, which binds insulin-like growth factor protein 3(IGFBP-3) with its high affinity, to produce neuromodulation effects, including assisting in the production of glial cells, myelin sheath, and neurons (61). In addition, IGF-1 may also play an important role in the pathogenesis and chronic neuroprotection of AD. For example, IGF-1 can regulate lipoprotein albumin and thyroxine carrier protein carried by amyloid, and when IGF-1 is inhibited, it will destroy this amyloid regulatory pathway (13). Importantly, a sufficient level of IGF-1 in blood circulation is a necessary condition for pre-BDNF (an immature precursor) (62), which leads to more mature BDNF production. Therefore, IGF-1 is called the intermediary for improving cognitive function after resistance exercise, and it plays a key role in the central nervous system.

Angiogenesis and vascular endothelial growth factor

Angiogenesis refers to the stimulated growth of capillaries and requires endothelial cell division, basement membrane degradation, and endothelial cell migration to form new blood vessels from the original ones (63, 64). Angiogenesis is physiologically regulated by hypoxia, muscle contraction, fluid shear force, and metabolic changes (65). With the increase of age, the cerebrovascular formation and CBF decrease, the responsiveness to hypoxia decreases, and the expression of vascular endothelial growth factor decreases (66), which leads to vascular dementia. In addition, similar to AD patients, the decrease of angiogenesis in patients with vascular dementia is related to cerebral vasoconstriction, vascular degeneration, and CAA (67).

Vascular endothelial growth factor (VEGF), also known as vascular permeability factor or angiopoietin, is a powerful stimulator of endothelial cell proliferation, germination, and vascular survival, and has the effects of promoting vascular growth and osmotic regulation (68). In addition, VEGF, as a highly specific mitogen, can act on vascular endothelial cells, promote cell proliferation, inhibit their apoptosis, and induce angiogenesis. In AD patients, the serum concentration of VEGF may decrease by 30% (69), and it tends to directly bind to Aβ plaque, which may reduce the bioavailability and brain perfusion of VEGF (70). In the VEGF family (VEGF A-F and placental growth factor), VEGF-A is strongly related to angiogenesis, neurogenesis, and nerve maintenance. For example, angiogenesis induced by VEGF-A (41) can promote nerve regeneration in local tissues of blood vessels. In addition, it was found that VEGF-A stimulated blood vessels can promote the release of BDNF while reducing toxic Aβ deposition and hyperphosphorylation of tau (70). Importantly, the inhibition of VEGF-A will lead to the interruption of neurogenesis,

TABLE 1 Effect of acute resistance exercise on the cognitive function of the elderly.

Researcher	Research objects	Resistance exercise program		Research results	
		Training content	Training design	Physiology	Cognition
Tsai et al. (74)	$N = 66$ Age:65.3 ± 7 year Sex:28M, 38F Condition:MCI	Biceps bending, triceps stretching, bench pushing, leg pushing, foreleg stretching, butterfly machine pinching. 3:RT, AE, CON	Number of groups: 2 Strength: 75%1RM Repetitions: 10 Rest: 90s Acute	BDNF↑[a] IGF-1↑[b] VEGF⇔ FGF-1Δ	Reaction time ↓[b]
Manini et al. (75)	$N = 20$ Age:67.4 ± 4.6 year ($N = 10$); 28.0 ± 7.8 year ($N = 10$) Sex:20M Condition: Health	Knee flexion and extension 2:RT (L), RT (H)	Number of groups: 4 Strength:20%1RM,80%1RM Repetitions: exercise fatigue Rest: 120s Acute	IGF-1⇔ GH↑[a]	NS
Chang et al. (76)	$N = 30$ Age:58.1 ± 3.0 year Sex:15F, 15M Condition: Health	Biceps left and right bend, high pull-down, bird, bench press, leg bend, leg push. 2:RT, CON	Number of groups: 2 Strength: 70%1RM Repetitions: 10 Rest: 30s, 60s Acute	NS	Expressive force ↑[a]
Hsieh et al. (77)	$N = 40$ Age:21–30 year ($N = 20$); 65–72 ($N = 20$) Sex:40M Condition: Health	Lying push, leg extension, high pull-down, leg bending, rowing, leg pressing, shoulder pushing, and biceps bending. 2:RT (1), RT (2)	Number of groups: 2 Strength: 70%10RM Repetitions: 10 Rest: 30s, 90s Acute	NS	Working memory ↑[b] Processing speed ↑[b]

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TABLE 1 (Continued)

Researcher	Research objects	Resistance exercise program		Research results	
		Training content	Training design	Physiology	Cognition
Hsieh et al. (78)	$N = 35$ Age:23.9 ± 2.3 year ($N = 18$); 66.4 ± 1.2 ($N = 17$) Sex:35M Condition: Health	Lying push, leg extension, high pull-down, leg bending, rowing, leg pressing, shoulder pushing, and biceps bending. 2:RT (1), RT (2)	Number of groups: 2 Strength: 70%10RM Repetitions: 10 Rest: NS Acute	NS	Attention ↑[a] Reaction time ↑[a]

N, the number of subjects; H, high load; L, low load; RT, resistance exercise group; HIIT, High-intensity aerobic interval training group; MCT, moderate-intensity continuous aerobic training group; CON, control group; RM, the maximum number of repetitions; BDNF, Brain-derived neurotrophic factor; IGF-1, insulin growth factor-1; FGF-1, fibroblast growth factor-1; MCI, mild cognitive impairment; RM, the maximum number of repetitions; VEGF, vascular endothelial growth factor; a, between-group differences; b, within-group differences; *, significant; NS, not specified.
Intra-group differences: *: Remarkable; NS: Not specified.

cognitive function, and capillary growth (66). In skeletal muscle, muscle cells are released after stimulation mediated by muscle contraction, and more extracellular VEGF expression depends on the content of interstitial adenosine. Adenosine infusion can up-regulate VEGF of myocardial cells or endothelial cells by interacting with the angiogenic adenosine A2 receptor (70). It has been found that when muscle contraction and blood flow restriction are implemented at the same time (a method for maximizing local muscle hypoxia), the expression of VEGF in serum can be increased by about 150% (71), and neurodegenerative diseases and cognitive decline in the elderly can be reduced. The reason may be that it plays a neuroprotective role by reducing the damage caused by the pathological cascade in patients with cognitive dysfunction, which is beneficial to the integrity of the vascular structure.

Effect of a resistance exercise intervention on the cognitive function of healthy elderly people

Resistance exercise can not only delay the muscle reduction and degeneration of the elderly, reduce the risk of falls and fractures, but also improve the cognitive function of the brain (72), such as the attention and working memory of the elderly (temporarily storing the current information, and linking and comparing it with subsequent information or events), and impulse control of the young (consciously suppressing the initiation of dominant reactions and behaviors, or suppressing reactions and behaviors that do not meet the current goals) (73). At present, some studies have pointed out that acute aerobic exercise can significantly improve the cognitive function of MCI elderly people, but the effects of an acute and chronic resistance exercise intervention on cognitively healthy elderly people are still different, which will be discussed in the following categories (Tables 1, 2).

Effects of acute resistance exercise on cognitive function of healthy elderly people

With the increase of age, the cognitive flexibility required in the complex decision-making process is greatly reduced. However, resistance exercise can satisfy the functions of neurogenesis and neural circuits by supplying nutrition and energy (74), and provide multi-faceted health benefits for the body. In recent years, it has been confirmed that acute RE can improve cognitive executive function, including attention, working memory, problem-solving ability, cognitive flexibility, and verbal fluency. Chang et al. (76) conducted acute resistance exercise on 30 middle-aged and elderly people (7 actions,

TABLE 2 Effect of chronic resistance exercise on the cognitive function of the elderly.

Researcher	Research objects	Resistance exercise program		Research results	
		Training content	Training design	Physiology	Cognition
Keigo et al. (79)	$N = 50$ Age:50–77 y Sex: NS Condition: Health	Legs, stretching sitting posture, leg bending, squat, bench pushing. 3:RT (L), RT (M), CON	Number of groups: 3 Frequency: 3 times/week Strength: 40%1RM, 60%1RM Repetitions: 14 Rest: 2min Duration: 24 weeks	NS	Working memory ↑[a] Short memory↑[a] Control ↑[a]
Coelho et al. (80)	$N = 48$ Age:70.5 ± 4.6 year Sex:48F Condition: Healthy, pre-weak.	Knee flexion and extension (progressive dynamic resistance training) 2: RT (healthy), RT (pre-weak)	Number of groups: 3 Frequency: 3 times/week Strength First2weeks:50%1RM 2–10 weeks: 75%1RM Repetitions: 8 Rest: NS Duration: 10 weeks	BDNF↑[b] GNDF? NGF?	NS
FurlaNo et al. (81)	$N = 24$ Age:60–80 year Sex: NS Condition: Health	Progressive resistance (weight) training, balance, and coordination (stretching) 2:RT, BAT	Group number: NS Frequency: 3 times/week Intensity: increasing gradually. Repetitions: NS Rest: NS Duration: 6 months	Hippocampus activation ↑[a]	Memory ↑[a] Cognitive expressiveness ↑[a]
Fort et al. (82)	$N = 49$	Leg flexion and extension, sitting rowing	Number of groups: 1–2	BDNF↑[a]	NS

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TABLE 2 (Continued)

Researcher	Research objects	Resistance exercise program		Research results	
		Training content	Training design	Physiology	Cognition
	Age:68.0 ± 5.0 year Sex:24M, 25FM Condition: Health	3:RT (H), RT (H + L), RT (L)	Frequency: 3 times/week Strength:20%1RM(L),20–40%; 1RM(H + L),80%1RM(H) Repetitions:10–15(H),8–10(L),6–20(H + L) Rest: 60s Duration: 12 weeks		
Tsai et al. (83)	$N = 48$ Age:71.4 ± 3.8 year Sex:48M Condition: Health	Biceps bend, leg push, triceps extension, high pull-down, lift heel, sitting rowing. 2:RT, CON	Number of groups: 3 Frequency: 3 times/week Strength: 75–80%1RM Repetitions: 10 Rest: 90s Duration: 12 months	homocyst -eine↓[a] IGF-1↑[a] GH?	Executive function ↑[a] accuracy↑[a] Reaction time ↑[a]
Liu-Ambrose et al. (84)	$N = 52$ Age:69.2 ± 3.0 year Sex:52F Condition: Health	Biceps bending, triceps stretching, sitting boating, high drop-down, leg pushing, squat, lunge walking. 3:BAT, RT (1)RT (2)	Number of groups: 2 Frequency: 1/week, 2/week Strength:7RM(gradually increasing) Repetitions: 6–8 Rest: NS Duration: 52 weeks	White matter atrophy ↓	Cognitive expressive ↑
Coetsee et al. (85)	$N = 67$ Age:62.7 ± 5.7 year Sex:21M, 46F Condition: Health	Upper and Lower body muscles (equipment and free weight) 4:RT, MCT, HIIT, CON	Number of groups: 3 Frequency: 3 times/week Intensity:50, 75, 100%10RM (first 8 weeks) 75, 85, 100%10RM (last 8 weeks) Repetitions: 10	Hemoglobin ↓	Reaction time ↑

(Continued)

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TABLE 2 (Continued)

Researcher	Research objects	Resistance exercise program		Research results	
		Training content	Training design	Physiology	Cognition
			Rest: NS Duration: 16 weeks		
Liu-Ambrose et al. (86)	$N = 155$ Age:65–75 year Sex: Female Condition: Health	Biceps, triceps extension, sitting rowing latissimus dorsi pull-down, kick trainer, leg curl, lift the heel. 2:RT (1), RT (2)	Number of groups: 2 Frequency:1/week, 2/week Strength: 70–80%1RM Repetitions: 6–8 Rest: NS Duration: 12 months	NS	Execute control ↑[a] Attention↑[a] Conflict resolution ↑[a]

N, the number of subjects; H, high load; L, low load; RT, resistance exercise group; HIIT, High-intensity aerobic interval training group; MCT, moderate-intensity continuous aerobic training group; CON, control group; RM, the maximum number of repetitions; BDNF. Brain-derived neurotrophic factor; IGF-1, insulin growth factor-1; FGF-1, fibroblast growth factor-1; MCI, mild cognitive impairment; RM, the maximum number of repetitions; VEGF, vascular endothelial growth factor; a, between-group differences; b, within-group differences; *: significant; NS, not specified.

2 groups, 70%1RM, 10 repetitions), and found that the performance of the exercise group under all Stroop tests was significantly improved compared with the control group. The study pointed out that acute resistance exercise can improve general cognition, but it is more beneficial to cognitive executive control ability. Hsieh et al. (77) observed from different age groups that acute moderate resistance exercise (70%1RM) is beneficial to the working memory of male adults (21–30 years old) and the elderly (65–72 years old), but it has a greater impact on the elderly when it comes to work tasks with higher memory requirements. Hsieh et al. (78) studied the difference in attention between male adults (21–30 years old) and the elderly (65–69 years old) in the same way of exercise and found that attention was improved after exercise, and pointed out that impact of acute resistance exercise on cognition would not be weakened with age.

However, acute resistance exercise may only have short-term benefits. Nicklas et al. (87) measured that the concentration of growth hormone GH in the elderly after acute resistance training increased by as much as 18 times compared with that before training, but after 10–15 min of training, these increased concentrations would return to the initial concentration value. Basso et al. (5) also found that acute isokinetic RE of lower limbs only temporarily increased the concentration of IGF-1 in peripheral blood, and the cognitive benefits could only be maintained for 2 h after exercise. Chang et al. (88) discussed the application time after the meta-analysis. If the cognitive task is applied within 5 min after exercise, the effect of exercise is negative (Cohen's $d = -0.06$), which may be due to the influence of exercise-induced tachycardia and hyperthermia on cognitive function. If the test time is 11–20 min or more after exercise, the effect of exercise is positive (Cohen's $d = 0.26$ or 0.17), which indicates that the benefit of acute resistance exercise on cognitive function comes into being about 10 min after the end of the exercise, and then this benefit gradually disappears (89). It is suggested that exercise intensity, amount of exercise, duration, evaluation of test time, and participants' health status are important factors that affect cognitive performance.

Effects of chronic resistance exercise on cognitive function of healthy elderly people

Although the circulatory process (blood flow, hormones) seems to moderate the changes in cognitive ability caused by acute exercise, the long-term response may be explained by structural adaptation. It was found that after 52 weeks of resistance exercise, the concentration of IGF-1 in the peripheral serum of the elderly increased, and at the same time, the cognitive behavior (such as the accuracy and reaction time in the executive function test) and cognitive function (such as

P3 amplitude) were improved (90). Coesee (85) found that during the Stroop test, the activation index of the prefrontal cortex decreased, the oxyhemoglobin and total hemoglobin of the left prefrontal cortex decreased (both of which were compared with the pre-test), and the cognitive task performance (i.e., reaction time) improved after 16 weeks of resistance exercise intervention for healthy elderly people. In another study of resistance exercise, it was found that after completing resistance exercise for up to 52 weeks, the performance of the Stroop test increased and the atrophy of cortical white matter decreased (compared with the elderly who performed balance and conditioning exercises). In addition, the study (84) also found that the decrease in brain activation was observed under relatively easy task conditions, while the increase in brain activation was found under more difficult task conditions.

Coelho et al. (80) proposed that chronic RE can trigger neurogenesis more. Experiments showed that the plasma BDNF of elderly women increased by 65.2% after three times a week of lower limb resistance exercise for 10 weeks. This is consistent with the results of other studies (82), which hypothesized that the increase of peripheral BDNF caused by resistance exercise would help to increase the resistance to age-induced brain damage and neurodegeneration. In addition, Chang et al. (91) pointed out that to significantly improve the cognitive function of the elderly (including information processing speed and attention) and maintain chronic benefits, it should be done at least twice a week for 2–12 months. Nagamatsu et al. (92) found that resistance exercise twice a week for 6 months (40% increased to 80%1RM) can enhance selective attention, conflict resolution, and associative memory of the elderly. Liu-Ambrose (86) also found that moderate and high-intensity resistance exercise (70–80%1RM, 6–8 repetitions) once or twice a week for 12 months can improve the above cognitive function. Then, Tsai et al. (83) randomly assigned 48 healthy old men to the resistance exercise group (75–80%1RM, 10 repetitions) or the control group, and carried out exercise training three times a week for 12 months. The results showed that the accuracy and reaction time of the exercise group were improved in the Oddball cognitive test, pointing out that moderate and high-intensity resistance exercise can help reduce the cognitive deterioration rate of the elderly.

Discussion

This review is the first to summarize the available evidence for the acute effects of RE on cognitive function. Our findings demonstrate that both acute and chronic can increase GH and IGF-1 secretion and improve cognitive ability in the elderly. Because in the state of anaerobic exercise, it can stimulate vascular endothelial growth factor (VEGF) and pituitary gland to secrete GH, reduce the concentration of homocysteine and promote the liver to secrete IGF-1, increase c-Fos cells in the nerves, and trigger the activation and regeneration of neurons in the hippocampus, to improve the plasticity and memory function of synapses (55), which has positive effects on slowing down aging and improving memory function. Moreover, with aging, the oxidation-reduction state is out of balance due to immune system disorder. The reduction of antioxidant uptake results in the accumulation of active free radicals and a significant increase of pro-inflammatory factors in the body, such as interleukin-6(IL-6), IL-1β, and tumor necrosis factor (TNF-α). The anti-inflammatory factor IL-10 is significantly decreased compared with that in normal adults (93). The increase in inflammatory reaction and the production of reactive oxygen species may play an important role in the pathophysiological mechanism of MCI and AD. However, after the intervention of resistance exercise, peripheral or encephalitis cytokines can be down-regulated, delay telomere DNA damage and protein aggregation, inhibit mitochondrial dysfunction and the expression of pro-inflammatory factors in aging cells, reduce lipid peroxidation level, and regulate microglial activation (38), thereby preventing oxidation and inflammatory mechanisms from playing a role in aging and delaying or preventing the occurrence of MCI or AD.

For those who exercise regularly, their BDNF level is higher than those who exercise less in their lifestyle. The reason is that lactic acid released from the periphery (such as muscle tissue) after exercise can be used as a "fuel" for the cognitive process. With the help of monocarboxylic acid transporters, it passes through BBB (94, 95), triggering the activation of BDNF in the hippocampus and the release of BDNF in serum (96, 97), which is responsible for memory and learning, stimulating the function of the neural circuit and improving it. Importantly, BDNF produced after resistance exercise has direct or indirect interaction with IGF-1, that is, it can help the brain increase IGF-1, promote nerve growth and produce serum angiotensin and amino acid, and then stimulate more BDNF receptors to increase the connection between neurons. This neurobiochemical mechanism can act on such central nervous system regions as the forebrain, striatum, hippocampus, cerebral cortex, spetum neurons, cerebellum, and motor neurons (98). These brain structures are all related to cognitive processing.

We also found that the improvement effect of brain neurophysiology and cognitive function after a single acute resistance intervention was short-lived, and the accompanying time gradually disappeared. However, chronic resistance intervention can increase the concentration of IGF-1 in peripheral serum, increase the expression during the Stroop test, reduce the atrophy of white matter in the cerebral cortex, and improve the performance of cognitive tasks. Aleman et al. (99) recruited 25 elderly people with an average age of 69.1 years, who were in good health and had no mental or cognitive diseases, and tested them on eight cognitive tests (such as knowledge, language, visual-spatial perception, reading speed, structural organization, perceptual motor processing speed,

cognitive processing speed, and long-term memory). The results showed that there was a high correlation between IGF-1 concentration and cognitive performance. The elderly with higher IGF-1 concentration had better cognitive performance. In addition, if the progressive moderate and high-intensity resistance exercise is used for more than 6 months, it can improve the selective attention, conflict resolution ability, and associative memory of healthy elderly people, while 12 months of moderate and high-intensity resistance exercise (70–80%1RM) can improve attention, accuracy, and reaction time. Therefore, acute resistance exercise may need to improve the cognitive flexibility and enhance the cognitive ability (such as working memory, attention reaction time, executive control ability, or information processing speed) of adults and the elderly in the long-term or in the case of moderate and high-intensity exercise, especially for the elderly. Compared with chronic resistance exercise, acute resistance seems to be inferior. However, the acute enhancement of cognitive function may have value in different situations. For example, the use of acute resistance exercise during athlete warm-up can play a role in sports injuries. Because in most cases of possible trauma, athletes need to quickly integrate and process large amounts of sensory information at the upper spine level, to develop and adjust exercise programs in time-tight situations. At the same time, help them make relevant decisions during the competition, and then improve their sports performance.

Finally, based on the above literature, the factors that affect the cognitive effect may be related to the intensity, amount, and duration of resistance exercise, and the difference between the evaluation time and the subjects. Importantly, these regulators do not influence the relationship between resistance exercise and cognitive function alone but interact with other regulatory factors to influence the cognitive benefits of resistance exercise. In a word, these results support the view that acute resistance usually has little effect on cognitive performance, and it may have great benefits when specific intervention measures and exercise parameters are needed. However, no matter what type of exercise (acute or chronic) is selected, it can cause changes in brain neuroplasticity, improve the cognitive function of healthy elderly people, and ensure that physical function and cognitive function can be maintained with age.

Conclusion and further directions

Conclusion

(1) Resistance training can have a beneficial effect on the brain function of the elderly population by changing blood flow, stimulating the metabolism of nerve conduction substances, neurotrophic substances, and endocrine hormones, promoting the neogenesis of cerebral vessels, and increasing the volume of gray matter in the brain, thereby improving the communication between muscle fibers stimulated by motor nerves and the brain, and preventing or delaying the cognitive deterioration of the brain during aging.

(2) Both acute resistance exercise and chronic resistance exercise can improve the cognitive function of the elderly, but acute resistance can only stimulate hormone secretion temporarily and improve the short-term recall effect, which has little effect on the cognitive performance of the elderly; Chronic resistance can significantly increase the secretion of nerve substances related to cognitive function in the brain of the elderly, such as hormones, neurons, growth factors, etc.

(3) It is suggested that gradual moderate and high-intensity resistance exercise (50–80%1RM, 1–3 times/week, 2–3 groups/time) be intervened for at least 6 months, which can significantly improve the working memory and cognitive processing speed the elderly, enhance cognitive behavior performance and achieve continuity effect.

Further directions

(1) The decrease of brain activation caused by acute resistance or chronic resistance may be different from the neurobiological mechanism induced by acute aerobic or chronic aerobic. In the future, it is urgent to study the potential biological mechanism of cognitive function changes caused by different types of acute exercise and chronic exercise intervention to better understand the changes in brain function.

(2) The substantial correlation between hormone secretion and cognitive function induced by different intervention modes is also worthy of further study. Moreover, the research on different combination effects among variables such as training intensity, frequency, duration, and resistance is still scarce, which needs to be further clarified in the future.

(3) Moderate and high-intensity resistance exercise has certain risks to the elderly. Future research should pay more attention to individual differences, and the safety of resistance exercise prescription in different physical states should be given priority.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

AC was in charge of proposing topics and writing articles. JL was in charge of directing and revising articles, and the rest

of the participants were in charge of collecting data, evaluating the quality of the literature, and drawing tables. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Internet use and health status among older adults: The mediating role of social participation

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Background: The acceleration of population aging and the arrival of the informatization make more and more older adults use the Internet, and its use is having an impact on their health. However, the relationship between internet use and the health of older adults and the mechanism of the effect of internet use on the health are not very clear.

Methods: Multiple linear regression models to explore the correlation between internet use and health status in the 3,141 individuals aged ≥60 years were used. Propensity score matching (PSM) method was used to test the robustness of the regression results. In addition, sequential recursive models was used to examine the mediating effect of social participation on the relationship between internet use and health status.

Results and discussion: We found a significant positive relationship between internet use and health status, and social participation mediated the relationship between internet use and health status. In addition, the effect of internet use on health status was different among older adults in rural and urban areas.

Conclusions: The development and application of internet products adapted to the development of an aging society should be accelerated to meet their needs for continued socialization. The forms and activities of social participation for the elderly groups should be enriched and public service internet usage training seminars should be conducted to improve internet skills.

KEYWORDS

internet use, health status, social participation, older adults, aging

Introduction

Relevant statistics show that in 2018, for the first time, the number of older people (over 60 years old) in China exceeded the number of people under the age of 15. In 2019, the number of people aged 60 and older in China was 253 million, accounting for 18.1% of the total population and 12.6% of the population aged 65 and over. With the

rising trend of population aging, the health problems of the elderly population cannot be ignored (1, 2). Good health not only enables the elderly to enjoy a good life in their old age but also helps to reduce the burden of China's social retirement, alleviate the pressure of insufficient medical resources, and provide a guarantee of economic development. Therefore, it is an important task for China to improve the health of elderly individuals, ensure their wellbeing and enable them to achieve "healthy aging".

Along with aging comes high-speed informatization. The popularity of the internet has changed people's lifestyles, and an increasing number of people enjoy convenient information delivery and rich life services through the internet (3, 4). In June 2020, the proportion of Chinese internet users reached 940 million, and the internet penetration rate reached 67.0%. Meanwhile, the proportion of older internet users is also increasing. The proportion of internet users aged 60 and above rose from 6.7% in March to 10.3% in June. The use of the internet has also continued to change the daily lifestyle, behavior and attitude of the elderly population (5, 6). Scholars have proposed socialization theory, which suggests that socialization can be divided into four parts: basic socialization, anticipatory socialization, developmental socialization and resocialization. Resocialization is the idea that individuals still need to adapt to society and engage in self-improvement through continuous learning in old age. For older adults, resocialization is also key to maintaining health and achieving longevity (7). In the context of information technology, older adults need to continuously learn new skills and actively adapt to new lifestyles through the application of the internet to facilitate their successful resocialization. The use of the internet as a new skill and lifestyle can play an important role in the resocialization process of older adults, which in turn can contribute to the improvement of their health status. Therefore, in the context of aging, this paper examines the impact of internet use on the health status of older adults using data from the CGSS 2018 to analyze the mediating effect mechanism of social participation and to examine the heterogeneity of the effect of the internet on the rural and urban elderly populations.

Literature review and hypotheses

With increasing age, individuals suffer from significant changes in their physical, psychological and social roles. When entering old age, people experience a significant increase in physical and psychological morbidity, making older adults the most vulnerable group in terms of health (8). Previous studies on factors influencing the health of older adults have addressed factors such as gender, age, educational attainment, marital status, physical activity, socioeconomic status, and participation in social insurance. Older male adults have better health status than older female adults (9). Age is inversely related to the health status of older adults to some extent (10). Improvement in education leads to improvement in the health status of older adults (11). Older married adults are healthier than old unmarried and widowed adults (12). Older adults who participate in regular physical activity have higher health indices (13). Higher socioeconomic status significantly affects the health of older adults (14). Older adults who participate in health insurance have higher self-rated health scores (15). Pensions also significantly improve the mental health of older adults (16). Therefore, we added these factors as control variables in the regression models that followed.

Previous studies have shown that internet use significantly affects the health status of individuals. However, scholarly research on this issue presents two contrasting views. Some studies argue that internet use is beneficial to the health status of individuals (17–20). Specifically, this health-promoting effect is reflected in three aspects. First, internet use helps individuals have sufficient health information for better self-management. Scholars have found that older adults can significantly improve their health by acquiring health-related knowledge through the internet (21). Internet use breaks the monopoly of doctors on professional information, alleviates information asymmetry between doctors and patients, and facilitates residents to better manage their health (22). In addition, the researchers assessed the relationship between internet use, socioeconomic status and social support and self-rated health, and the results showed that internet health information users had better health status than users who did not use online health information as a reference (23). Second, as a tool for communication, the internet can alleviate users' loneliness, depression, and anxiety and enhance users' health. Researchers used the U.S. Health and Retirement Survey (HRS) data from 2002 to 2008 in the United States to examine the effect of internet use on depression among older adults and found that compared to not using the internet, when using the internet, older adults were 33% less likely to be depressed (24). Using a sample of 245 U.S. adults, researchers examined the psychological determinants of internet health information use with structural equation modeling and showed that the internet can reduce stress and lower levels of depression and loneliness (25). Third, internet use can alleviate and prevent a variety of health disorders. Residents who use the internet regularly are less likely to suffer from depression (26), and internet use also reduces anxiety levels in patients with cardiomyopathy (27). Other studies have suggested that the internet can lead to health deterioration due to addiction. Researchers have found that increased internet use may predispose people to internet addiction and online gaming, which in turn increases psychological anxiety, depression and social fear (28–31).

Based on the above discussion, we propose the following hypotheses.

Hypothesis 1: Internet use significantly affects the health status of older adults.

Social participation is an important way for older individuals to reach out to society, engage in interpersonal interactions, and maintain social connections, and it is an important intervention to promote active and healthy aging, which can effectively prevent individuals from being closed off to others (32). It enables older adults to participate in the political life of the community (33), work for pay (34), and socialize with others (35). Social participation has an impact on older adults' cognitive ability as they age, and the higher the ability to participate socially is, the stronger the cognitive ability (36). Social-emotional choice theory points out that social participation requires a certain cost investment, and members who engage in social participation are bound to consider cost-benefit issues (37). Offline social participation decreases as the physical and mental ability of elderly individuals decreases. The attributes of the internet can break through the limitations of time and space and reduce the physical ability requirements, which can compensate for the reduced offline social participation due to declining physical ability. Previous research suggests that internet use affects individuals' social participation in different ways. The internet may be an important means for older adults to maintain existing interpersonal relationships and expand their social networks (38). A statistical analysis of data from a large U.S. survey found that internet use increased residents' motivation to participate in community activities (39). Researchers studying internet use among older adults in the Netherlands noted that internet use plays a positive role in increasing older adults' social capital, allowing them to expand or maintain social connections and expand their access to information (40). In addition, social engagement can have a significant impact on an individual's health status. Researchers analyzed a sample of 43 neighborhoods in Shanghai across age groups and found that neighborhood environment and social engagement in all samples had a significant positive impact on older adults' health. At the same time, social participation became a mediator of the relationship between the interpersonal environment and older adults. The study also found that social participation mediated the relationship between the interpersonal environment and the health of older adults (41). A survey of 28,895 individuals aged 45–84 years in China found that social participation positively affects health by improving individual mental health effects and increasing individual income effects (42).

On the basis of the above discussion, we propose the following hypothesis:

Hypothesis 2: Social participation mediates the relationship between internet use and older adults' health.

Therefore, this study aimed to explore the relationship between internet use and older adults' health to provide guidance and help improve older adults' health. Meanwhile, to further understand the impact of internet use on the health of elderly individuals and to find ways to improve their health, this study chose social participation as a mediating variable. The findings of this paper facilitate a deeper understanding of the relationship between internet use and residents' health while examining the possible channels through which internet use affects older adults' health from the comprehensive dimension of social participation. This study fills the gaps in existing studies and provides a realistic basis for better guidance on internet use to improve older adults' health.

Methods

Data and study sample

This study used data from the CGSS collected by the China Survey and Data Center of Renmin University of China. The data was collected using a stratified sampling method, and the database covers 28 provinces (municipalities and autonomous regions) in China with details about the health status, individual characteristics, and household characteristics of the population. The CGSS 2018 data were used in this study. The population of this study is the elderly population, and the method of screening the study population is to first find the variable of the year of birth of the sample in the questionnaire, then subtract the year of birth from 2018 to obtain the age of the sample, and finally screen out individuals 60 or older. In this study, a total of 3,141 valid sample sizes were obtained after removing the missing values of the independent, dependent and control variables.

Measures

Dependent variable

The dependent variable in this study is the health status of elderly individuals. Self-rated health (SRH) was used to measure health status. The question was "What do you think of your current health status?". Possible responses were "1 = very unhealthy", "2 = less healthy", "3 = fair", "4 = healthy", and "5 = very healthy"; the higher the value was, the better the health condition. Self-rated health status is considered to be a simple indicator to measure the health status of the old population and was found to predict future health outcomes (43, 44).

Independent variable

The independent variable in this study is internet use. The question used to measure the dependent variable was "In the past year, how much did you use the internet?" Responses were "1 = never", "2 = rarely", "3 = sometimes", "4 = often", and "5 = very often"; options 2 to 5 were combined and coded as "1 = use the internet"; and option 1 was coded as "0 = never use the internet", making it a binary categorical variable.

Mediating variable

The mediating variable in this study is social participation, and according to the definition of social participation in previous studies, economic participation (45), political participation (46), and social participation (36, 47) are included in the measurement of social participation variables in this study. In particular, economic participation is measured by the question "What is your work experience and status?" The responses "currently working in non-farm work", "currently working in farming", "have worked in non-farm work", "currently working in farming," and "have not worked in non-farm work" were combined to form "1 = participation". The responses "not currently working", "have only worked in agriculture", and "have worked in non-farm work" were combined to form "0 = not participation". The question to measure political participation was "Did you vote in the last neighborhood council/village council election?" Responses were "1 = participated" and "0 = not participated". The questions measuring social participation were "In the past year, did you often get together with relatives who do not live together during your free time?" and "In the past year, did you often get together with your friends in your free time?" For these two questions, those who attended parties were coded as "1 = participated", and those who did not were coded as "0 = did not participated". These three types of questions were summed to obtain a total score measuring social participation, ranging from 0 to 4. The higher the value was, the higher the social participation.

Control variables

We controlled for confounding variables affecting internet use, social participation, and the health status of older adults. These variables included individual characteristics, household characteristics, and social characteristics. Among them, individual characteristics included age, gender (0 = female, 1 = male), education level (0 = illiteracy, 1 = primary school, 2 = junior middle school and high school, 3 = university or more), and marital status (0 = unmarried, divorced or widowed, 1 = married); household characteristics included number of children, cohabitation (0 = not living together, 1 = living together), and housing area. Social characteristics variables included physical exercise (0 = not participating, 1 = participating), residence (0 = rural, 1 = urban), personal socioeconomic status (1 = lower class, 2 = middle class, 3 = upper class), participation in pension insurance status (0 = not participating, 1 = participating), and participation in medical insurance status (0 = not participating, 1 = participating).

Statistical analysis

Stata 16.0 was used to analyze the effect of internet use on the health status of older adults. First, descriptive statistical analysis was used to describe the data distribution of the independent, dependent, and mediating variables as well as other control variables. Second, a multiple linear regression model was used to analyze the relationship between physical activity and older adults' health status, and then an ordered probit model and propensity score matching method were used to address the endogeneity of the relationship between physical activity and older adults' health status. Finally, we used stepwise regression mediation measures to measure the mediating effect of social participation.

Results

Descriptive analysis

Table 1 shows that the mean score for the health status of the sample was 3.164, indicating that the majority of older adults are in a moderate state of health. The mean value of internet use in the sample was 0.334, indicating that less than half of the older adult group used the internet. In addition, 53.33% of the sample was male, 99.33% was married, more subjects had a primary school education level, the average number of children in the sample was 2, 91.72% of the sample lived with their spouses, the housing area was approximately 100.737 square meters, 52.94% participated in physical exercise, and the sample was basically divided equally between rural and urban residences. The socioeconomic status of the sample was at the lower-middle level; 85.23% of the sample participated in pension insurance, and 94.01% participated in medical insurance.

Impact of physical exercise on health status

This study used multiple linear regression to analyze the effects of internet use on the health status of older adults, and Table 2 demonstrates the specific regression results by gradually putting in individual characteristic variables, family characteristic variables, and social characteristic variables.

The regression results from Model 1 reveal that internet use significantly and positively affects the health status of older adults at the 1% significance level. After adding individual characteristic variables, family characteristic variables and social characteristic variables in turn, the regression coefficients of internet use are 0.323, 0.331, and 0.257 shown in Model 2, Model 3, and Model 4, respectively, and they are significant and positive at the 1% significance level, which indicates that internet use has a significant effect on the health status of elderly individuals. The above results support the conclusion that internet use can enhance the health of individuals.

In addition, Model 4 shows the results of the effects of other control variables on the health status of elderly individuals.

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TABLE 1 Sample characteristics.

Variables		Variable definitions	Mean	SD
Dependent variable	Health status	Continuous variable, ranging from 1 to 5	3.164	1.046
Independent variable	Internet use	Categorical variable, 0 = never use the internet, 1 = use the internet	0.334	0.472
Mediating variable	Social participation	Continuous variable, ranging from 0 to 4	2.417	0.978
Individual characteristics	Age	Continuous variable	68.146	6.598
	Gender	categorical variable, 0 = female, 1 = male	0.533	0.499
	Marital status	Categorical variable, 0 = unmarried, divorced or widowed, 1 = married	0.993	0.082
	Education level	Categorical variable, 0 = illiteracy, 1 = primary school, 2 = junior middle school and high school, 3 = university or more	1.327	0.909
Household characteristics	Number of children	Continuous variable	2.229	1.267
	Cohabitation	Categorical variable, 0 = not living together, 1 = living together	0.917	0.276
	Housing area	Continuous variable	100.737	56.493
Socialcharacteristics	Physical exercise	Categorical variable, 0 = not participating, 1 = participating	0.529	0.499
	Residence	Categorical variable, 0 = rural, 1 = urban	0.493	0.500
	Personal socioeconomic status	Categorical variable, 1 = lower class, 2 = middle class, 3 = upper class	1.516	0.618
	Participation in pension insurance status	Categorical variable, 0 = not participating, 1 = participating	0.852	0.355
	Participation in medical insurance status	Categorical variable, 0 = not participating, 1 = participating	0.940	0.237

Gender positively influenced the health level of older adults at the 5% significance level, with older male adults having a higher health status than older female adults. The group with an education level of university or more positively influenced the health of elderly individuals at the 10% significance level, indicating that the higher the education level was, the better the health status. Housing area positively influenced the health of the elderly populations at the 1% significance level. Physical exercise significantly and positively affected the health of elderly individuals at the 1% significance level, and participation in physical exercise can make the elderly healthier. Socioeconomic status positively affects the health of elderly individuals at the 1% significance level, indicating that the higher the socioeconomic status is, the better the health status.

Robustness test

Ordered probit model

The dependent variable of this study, the health status of elderly individuals, takes values from 1 to 5, which can be considered discrete and ordered variables, so we can construct an ordered probit model to test the robustness of the model results in Table 2 to prove the credibility of the regression results in Table 2. Table 3 shows the results of the robustness test, from which we find that the effects of internet use on the health status of elderly individuals are positively correlated at the 1% significance level, which indicates the robustness of the results of this study.

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TABLE 2 Regression analysis of Internet use on health status of older adults.

	Model 1 Health status	Model 2 Health status	Model 3 Health status	Model 4 Health status
Internet use	0.418***	0.323***	0.331***	0.257***
	(0.039)	(0.045)	(0.045)	(0.046)
Age		−0.000**	−0.000	−0.000
		(0.000)	(0.000)	(0.000)
Gender (female)				
Male		0.082**	0.074*	0.092**
		(0.038)	(0.038)	(0.037)
Marital status (unmarried, divorced, or widowed)				
Married		0.230	0.310	0.214
		(0.224)	(0.232)	(0.229)
Education level (illiteracy)				
Primary school		0.106**	0.101*	0.066
		(0.052)	(0.052)	(0.051)
Junior middle school and high school		0.144***	0.149***	0.048
		(0.053)	(0.053)	(0.055)
University or more		0.348***	0.339***	0.153*
		(0.086)	(0.086)	(0.090)
Number of children			−0.033**	−0.019
			(0.017)	(0.017)
Cohabitation (not living together)				
Living together			−0.078	−0.068
			(0.069)	(0.068)
Housing area			0.002***	0.002***
			(0.000)	(0.000)
Physical exercise (not participating)				
Participating				0.233***
				(0.040)
Residence (rural)				
Urban				0.050
				(0.047)
Personal socioeconomic status (lower class)				
Middle class				0.269***
				(0.038)
Upper class				0.373***
				(0.076)
Participation in pension insurance status (not participating)				
Participating				−0.074
				(0.054)
Participation in medical insurance status (not participating)				
Participating				−0.025
				(0.080)
Constant term	3.024***	2.869***	2.670***	2.690***
	(0.022)	(0.243)	(0.247)	(0.254)
N	3,141	3,141	3,141	3,141
R^2	0.036	0.045	0.053	0.086

*$P < 0.10$, **$P < 0.05$, ***$P < 0.01$. Values in brackets are standard errors.

TABLE 3 Robustness test results.

Variables	Model 1	Model 2	Model 3	Model 4
Internet use	0.416***	0.322***	0.332***	0.263***
	(0.040)	(0.046)	(0.047)	(0.049)
Control variables	No control	Individual variables	Individual and household variables	All control variables
N	3,141	3,141	3,141	3,141
LR statistic	107.86***	139.21***	163.25***	275.41***
Pseudo R^2	0.012	0.016	0.018	0.031

*$P < 0.10$, **$P < 0.05$, ***$P < 0.01$. Values in brackets are standard errors.

TABLE 4 Propensity score matching results (ATT).

		ATT	SE	t
Dependent variable: Mental health				
Nearest neighbor matching	1 to 1 matching	3.43***	0.23	4.36
	1 to 4 matching	3.31***	0.25	4.23
	Radius matching	3.67***	0.33	4.19
The whole matching	Kernel matching	3.19***	0.37	4.26
	Local linear regression matching	3.26***	0.27	4.51

***$P < 0.01$ (t > 2.76), **$P < 0.05$ (t > 1.96), *$P < 0.1$ (t > 1.65).

Propensity score matching

Because of confounding factors that affect both internet use and health status of older adults, sample selection bias was introduced into our results. Therefore, we used propensity score matching to correct the regression results. First, considering that the independent variable used for propensity score matching was a dummy variable, the samples were divided into two groups: the group of participants that participated in internet use and the group that did not. Second, we matched the samples according to the following procedure: (1) We condensed the control variables into an index to calculate the likelihood of each sample belonging to the experimental group. (2) We used five matching methods (1-to-1 nearest neighbor, 1-to-4 nearest neighbor, radius, kernel, and local linear regression matching) to match the experimental group and the control group and to classify individuals with similar values into the same groups to ensure that members of groups had similar characteristics. (3) We calculated the average treatment effect (ATT) on the participants, representing the difference in health status between the experimental and control groups.

Table 4 presents the ATT calculated using different matching methods. The ATT values were >0 in all the models and were statistically significant, indicating that results that internet use has a significant positive impact on the health status of older adults are robust.

Testing the mediating effects of social participation

Currently, the mechanism by which internet use affects the health of the population is unclear (20, 24). To effectively reveal this transmission mechanism, the following sequential recursive model was set to test the mediating effect of social participation according to the mediating effect test proposed by Baron and Kenny (48). The first step is to test the effect of internet use on the health status of elderly individuals. If the coefficient of internet use is significant, it indicates that internet use has a significant effect on the health status of elderly individuals. The second step is to test the effect of internet use on social participation as a mediating variable. If the coefficient of internet use is significant, it indicates that internet use can influence the social participation of elderly individuals. The third step is to add the social participation variable to the first step. If the effect of the mediating variable is significant, while the coefficient of internet use decreases or is insignificant relative to the coefficient in the first step, then it indicates that social participation has a partial or even full mediating effect.

Table 5 shows the results of the mediating effects of social participation. In Model 1, internet use positively affects the health status of older adults at the 1% significance level, indicating that internet use enhances the health status of older adults. In Model 2, internet use positively affects older adults' social participation at the 1% significance level, indicating

TABLE 5 Internet use and health status of older adults: Mediating role of social participation.

Variables	Model 1 Health status	Model 2 Social participation	Model 3 Health status
Internet use	0.257***	0.137***	0.248***
	(0.046)	(0.043)	(0.046)
Social participation			0.065***
			(0.019)
Constant term	2.690***	2.452***	2.531***
	(0.254)	(0.238)	(0.258)
Control variables	All control variables	All control variables	All control variables
N	3,141	3,141	3,141
R^2	0.086	0.083	0.089

*$P < 0.10$, **$P < 0.05$, ***$P < 0.01$. Values in brackets are standard errors.

TABLE 6 Mediation test results.

Mediating variable	Effect of type	Coefficient	Standard error	Z	P
Internet use	Total effect	0.418***	0.039	10.81	0.000
	Direct effect	0.394***	0.039	10.11	0.000
	Indirect effect	0.024***	0.006	4.16	0.000

*$P < 0.10$, **$P < 0.05$, ***$P < 0.01$.

that internet use enhances older adults' social participation. In Model 3, internet use and social participation significantly and positively affect the health status of older adults at the 1% level of significance, and the coefficient of internet use decreases compared to the coefficient of Model 1, which indicates that social participation is one of the mechanisms of action of internet use affecting the health status of older adults, i.e., social participation plays a mediating role in the effect of internet use on the health status of older adults. Internet use can encourage the social participation of older adults, thus enhancing their health. It also confirms the conclusions of existing studies. For example, using survey data from the 2018 China Longitudinal Study of Health and Retirement, the researchers analyzed how Internet use reduced the risk of depressive symptoms through social participation among a sample of 4,645 older adults. The results showed that Internet use improved their health status by increasing social participation (49).

In this study, the mediating effect of social engagement ability was tested again using the KHB method. Table 6 shows the results of the tests of mediating effects. Among them, the total effect of internet use on the health status of the elderly was 0.418, which passed the 1% significance test. The direct effect was 0.394, which passed the 1% significance test, and the indirect effect of internet use on the health status of elderly individuals through social participation ability was 0.024, which passed the 1% significance test, indicating that the mediating effect of social participation ability existed. Therefore, both the stepwise regression mediating effect test and the KBH test in this study found that social participation plays a mediating role between internet use and the health status of elderly individuals. Social participation is the mechanism of action that occurs between internet use and the health status of elderly individuals.

TABLE 7 Heterogeneity analysis.

	Rural elderly OLS	Urban elderly OLS
Internet use	0.307***	0.220***
	(0.084)	(0.054)
Control variables	All control variables	All control variables
N	1,593	1,548
R^2	0.060	0.091

*$P < 0.10$, **$P < 0.05$, ***$P < 0.01$. Value in brackets are standard errors.

Heterogeneity analysis

The frequency of individual internet use can be influenced by residence (50, 51), and there are differences in the health status of individuals located in different regions (52, 53). Therefore, we asked whether the relationship between internet use and health status differs among older adults located in different regions. We compared the effects of internet use on

the mental health of urban and rural older adults (Table 7). The results show that internet use significantly and positively affects the health status of the rural elderly population and the urban elderly population. The marginal effect of internet use on the health status of the rural elderly population was greater than that of the urban elderly population.

Discussion

Internet use can significantly improve the health status of older adults

In this study, we analyzed the relationship between internet use and health status among older adults in China by using the 2018 CGSS data. We identified a significant positive correlation between internet use and health status among older adults in China, which supports H1: Internet use significantly affects the health status of older adults. This conclusion is consistent with previous research findings on the relationship between internet use and health status. For example, in 2008, using data from a survey on the digital divide and quality of life of older adults in Spain, researchers analyzed internet use among the Spanish adult population in two age groups (55–64 and 65–74 years). They found a significant relationship between internet use and poor self-rated health, with internet users having self-rated health status better than that of non-users (54). In addition, researchers selected 3,042 cases of older adults aged 55 years or older in Jiangxi Province, China, in 2018 to analyze the effect of internet use and smartphones on the net effect of internet use and smartphone use on the health of older adults and found that both internet use and smartphone use improved older adults' self-rated health status (55).

Social participation plays a mediating role in the relationship between internet use and health status

In the present study, we discovered that social participation plays a significant mediating role in the relationship between internet use and health status; that is, social participation is a key mechanism through which internet use affects the health status of older adults, and internet use can improve the health status of older adults by enhancing their social participation. Therefore, H2 is supported. This finding is consistent with previous research findings. For example, researchers analyzed a cross-sectional sample of 11,000 subjects in European countries and found that internet use increased individuals' life satisfaction and decreased their social isolation by increasing their social participation (56). In addition, the researchers analyzed a sample of 240 older adults based on actor network theory and activity theory and found a significant positive relationship between internet use and social participation, with the size of social networks constituting a significant factor in the association between internet use and social participation (57).

Effect of internet use on health status varies among older adults living in different regions

In the present study, we determined that internet use significantly and positively affects the health status of the rural elderly population and the urban elderly population. The marginal effect of internet use on the health status of the rural elderly population was greater than that of the urban elderly population. A possible explanation for this is that internet penetration is higher in urban areas than in rural areas, so the health promotion effect of internet use on older adults in urban areas becomes equalized. In contrast, in rural areas, internet penetration and use differed between individuals and households, and thus internet use showed differences in health promotion for individuals.

Limitations

There are some limitations in this study. First, the issues discussed in this paper focus on the difference between use and non-use. In fact, the ability to use internet devices to access information is only a basic skill; the ability to recognize the value of information and quickly access the information needed is more important. However, due to the availability of data, this paper has not been able to examine the impact of internet usage quality on the health of the population, and this issue will be further examined in the future. Second, due to the limitations of public survey data, although this paper reveals the relationship between internet use and the health status of older adults at the individual level, it is unable to explore the psychological mechanisms underlying the interaction between the two at the more microscopic cognitive level. In future research, secondary data studies can be supplemented with quantitative methods such as primary data surveys and experiments to further investigate the impact of internet use on the health status of older adults in different dimensions.

Conclusions

The results of this study indicate that internet use is significantly and positively correlated with the health status of older adults and that social participation plays a mediating role in the relationship between internet use and health status among older adults. Accordingly, we propose the following

suggestions. First, the development and application of internet products adapted to the development of an aging society should be accelerated to enhance the benefits of health improvement for elderly individuals. Internet applications suitable for the elderly individuals should be launched as soon as possible to provide a better experience for them the elderly; further, the functions of terminal devices should be optimized to assist elderly internet users to meet their needs for continued socialization. Second, we enrich the forms and activities of social participation for the elderly groups. The community should provide more internet-related social activities to improve their social participation and encourage users to expand their social participation scope and increase social connection channels, thus improving their health status. Third, public service internet usage training seminars should be conducted to improve internet skills. The findings of this paper indicate that there are urban-rural differences in the effects of internet use on residents' health. Compared with urban areas, the health promotion effect on rural residents is greater. However, non-internet users are mainly concentrated in rural areas, and lack of skills and limited education are important reasons for their lack of access. Therefore, increasing internet skills training is conducive to expanding the population of internet users and enhancing the value of the internet.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Author contributions

BH were responsible for writing and contributed to the conception of the work, data analysis and interpretation, and drafting the article. HW contributed to the data collection, data analysis, and interpretation. YL contributed to give important revising suggestions. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Global trends and hotspots in research on osteoporosis rehabilitation: A bibliometric study and visualization analysis

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Background: The field of rehabilitation medicine plays an essential role in the comprehensive management of osteoporosis and its consequences. The benefits of therapeutic exercise are increasingly being recognized in this area, which receives an increasing number of publications. this study was designed to comprehensively identify collaborative networks, parse and track research trends, spotlight present hotspots, and accurately predict frontiers and focus on the health topics related to osteoporosis rehabilitation.

Methods: This research adopted computer retrieval of osteoporosis rehabilitation-related research published in the Web of Science Core Collection (WoSCC) from inception to June 14, 2022. The bibliometric visualization and comparative analysis involving countries, institutions, journals, authors, references, and keywords were performed using the CiteSpace and VOSviewer software.

Results: A total of 3,268 articles were included, and the number of articles published each year has demonstrated a steady increase. The United States and the University of Melbourne were the highest productive country and institution, with 1,325 and 87 articles, respectively. The journal of osteoporosis international has published the greatest number of articles, with 221 publications, and the journal of bone and mineral research ranked first in the co-citation counts (cited by 11,792 times). The most productive and highly-cited authors were Heinonen A and Cummings S, with 35 publications and 680 citations.

Conclusions: At present, "physical activity," "weight bearing exercise," "muscle strength," "whole body vibration," "postmenopausal women," "older women," children, men are the noteworthy research hot topics. Future research that focus on the major modes and parameters of physical activity/exercise for osteoporosis (including whole body vibration, weight bearing exercises, resistance training), targeted multicomponent training regimens, rehabilitation therapy for postmenopausal women, older women, children and men, osteoporosis related-sarcopenia and fractures, and mesenchymal stem cells

are becoming frontiers and focus on the health topics related to osteoporosis rehabilitation in the upcoming years, which are worthy of further exploration.

KEYWORDS

osteoporosis, rehabilitation, physical activity, bibliometric analysis, CiteSpace, VOSviewer

Introduction

Osteoporosis is a multifactorial disorder of bone metabolism associated with low bone mineral density and impaired microarchitecture that results in increased skeletal fragility and susceptibility to bone fracture (1). Consequently, patients who suffer from osteoporosis and fragility fractures frequently experience disability and therefore have decreased independence in daily life, and a low health-related quality of life (2–4). According to the National Osteoporosis Foundation, 10.2 million Americans suffer from osteoporosis, and an additional 43.4 million have decreased bone mass. It is predicted that by 2030, there will be will increase to 71 million low bone density and osteoporosis among adults (5), And more than nine million fractures are caused by osteoporosis worldwide every year one in five men and one in two women who are 50 years old will experience an osteoporotic fracture in their lifetime. Among women, the 10-year risk of developing fracture rises from 9.8 at 50 years to 21.7% at the age of 80 (6). Osteoporotic fractures often required hospitalization, especially hip fractures, which commonly account for 50% of osteoporotic fracture-related hospitalizations (7). Once in hospital, these patients have a high risk of complications including thrombosis (27%), urinary tract infections (12–61%), and pneumonia (7 %) (7), which increase the mortality and morbidity of patients with osteoporotic fractures. Therefore, osteoporosis and osteoporotic fractures pose a heavy public health burden on society. The research (7) showed that the average cost of a patient with a fracture in a hospital is close to $13,000 for all sorts of fractures.

The prevention and treatment of osteoporosis should incorporate both non-pharmacological and pharmacological approaches in order to minimize fracture risk (8). It is noteworthy that rehabilitation medicine takes a primary role in the comprehensive management of osteoporosis and its consequences, taking into account the benefits of therapeutic exercise for fall prevention as well as the functional recovery after fragility fractures, and it also can affect bone metabolism and thus enhance bone strength. Consequently, these fields receive an increasing number of publications. Exercise training interventions are recommended for osteoporosis management in many guidelines. Many clinical guidelines strongly recommend weight-bearing, muscle-strengthening exercises for maintaining bone health, preventing bone loss and falls, reducing discomfort (9–13), improving quality of life and according to Exercise and Sports Science Australia (ESSA) (14) evidence, muscle strength, balance, and mobility training also helps to minimize the risk of falling. Additionally, studies have evaluated the guidelines for osteoporosis using the AGREE II tool. The results showed that patients with osteoporosis and fragility fractures may benefit from moderate intensity therapeutic exercise, according to some guidelines, and a majority of the guidelines were high quality (15). In addition, there have been a large number of randomized controlled clinical trials and review that have demonstrated resistance training (RT) and impact training, whole-body vibration training, balance exercise programme can improve bone mineral density (BMD), physical function, muscle strength, balance and reduce fear of falling and pain (8, 16–23). However the majority of the studies discussed above have focused on specific and limited aspects. Research on osteoporosis rehabilitation and prevention, and the general overview of this field is lacking.

Bibliometric visualization analysis is a quantitative analysis integrating mathematics and statistical methodologies, which can assist researchers in understanding the characteristics of the field's development over time (24). It is possible to perform an in-depth assessment of research trends and the focus of a specific topic employing comprehensive indexes such as journals, authors, countries, and institutions (24, 25). Authors with a high number of total citations are recognized for their scientific achievements by their peers (26). In addition, bibliometric evaluation results can also provide suggestions for further research and decision-making. CiteSpace visual analysis software produces co-citation networks based on reference citations to expose the structure of a research field, enabling visual knowledge discovery in bibliographic databases. VOS viewer is another scientometric application for producing and viewing network maps. Those knowledge maps can illustrate the output of authors and institutions, cooperation linkages, geographic dispersion, the most cited and critical documents, the emergence of research topics, highlighting disciplinary development and research tendencies within a particular area. In recent years, CiteSpace and VOS viewer have been used in a variety of fields, including medical treatment,machine learning, cities or communities research, agriculture and environment management (27–31). There are also currently studies evaluating bisphosphates for osteoporosis, research trends on male osteoporosis, miRNAs in osteoporosis-related research (32–34). However, there is no targeted bibliometric analysis of

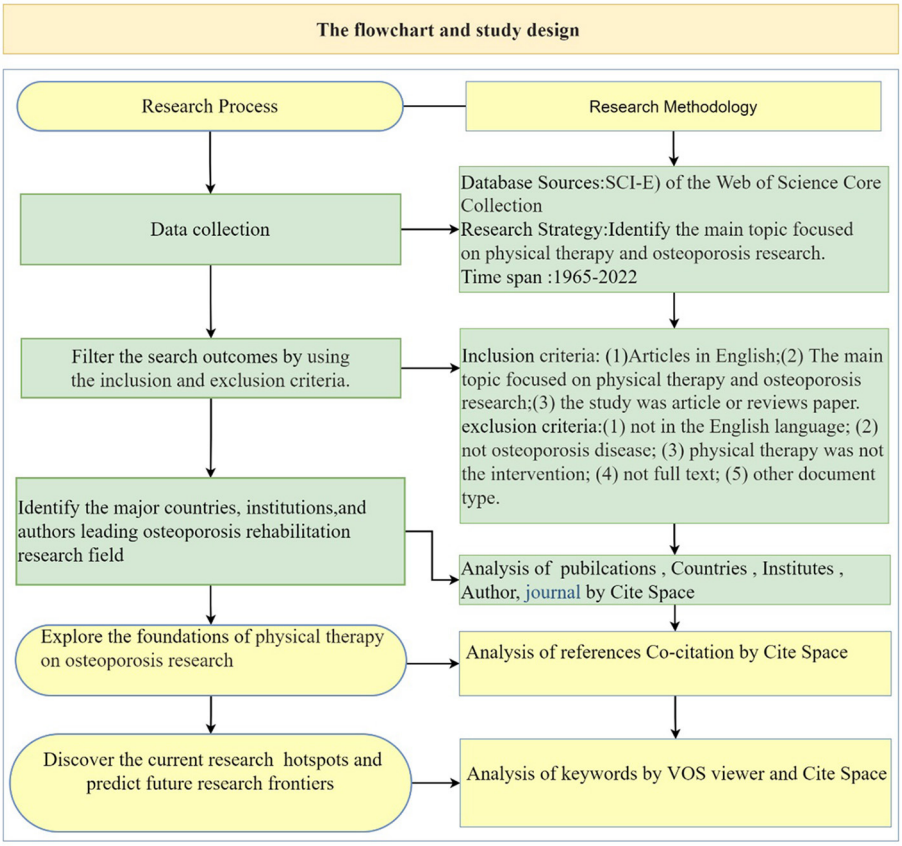


FIGURE 1
The summary of the flowchart and study design.

worldwide scientific studies on rehabilitation therapies for osteoporosis. Therefore, the aim of this study is to provide a summary of the global research base, as well as hotspots and frontiers of rehabilitation treatment for osteoporosis through bibliometric analysis.

Materials and methods

Data source and search strategy

All published literature was obtained online from the Science Citation Index-Expanded (SCI-E) of the Web of Science Core Collection (WoSCC) on June 14, 2022.The following retrieval strategy were conducted for search publications (Supplementary Table S1), which the main topic focused on physical therapy and osteoporosis research. The range of publication dates was selected from inception to June 14, 2022. According to the previous bibliometric research (35, 36). The "articles or reviews" were chosen for analysis, and the language was limited to "English," non-English articles and other document type, such as conference abstracts, letters, reviews, news, were excluded. An overview of the comprehensive search approach and inclusion criteria used in this research was showed in Figure 1.

Literature screening and data extraction

Screening was conducted in two stages, namely, preliminary screening was conducted according to the title and abstract, and then full-text screening was carried out using the inclusion and exclusion criteria. Studies were included should meet all of the following criteria: (1) Articles in English; (2) The main topic focused on physical therapy and osteoporosis research; (3) the study was article or reviews paper. Accordance with the following exclusion criteria, records were excluded: (1) not in the English language; (2) not osteoporosis disease; (3) physical therapy was not used for the intervention programs; (4) not full text; (5) other document type: conference abstracts, letters, news, editorial materials, proceeding papers, short reports, case studies.

TABLE 1 Ranking of top 10 countries and institutions involved in the osteoporosis rehabilitation field.

Rank	Country	Publications	Centrality	Institution	Publications	Centrality
1	United States	1,325	0.52	University of Melbourne	87	0.05
2	China	390	0.01	University of British Columbia	86	0.11
3	Australia	303	0.21	McMaster University	70	0.08
4	United Kingdom	293	0.25	University of São Paulo	51	0.04
5	Canada	286	0.04	Harvard University	49	0.09
6	Germany	179	0.19	University of Toronto	48	0.04
7	Brazil	152	0	University of Waterloo	40	0.01
8	Japan	145	0.04	University of Colorado	38	0.01
9	Austria	141	0.07	Griffith University	37	0.01
10	Spain	131	0.15	Columbia University	36	0.03

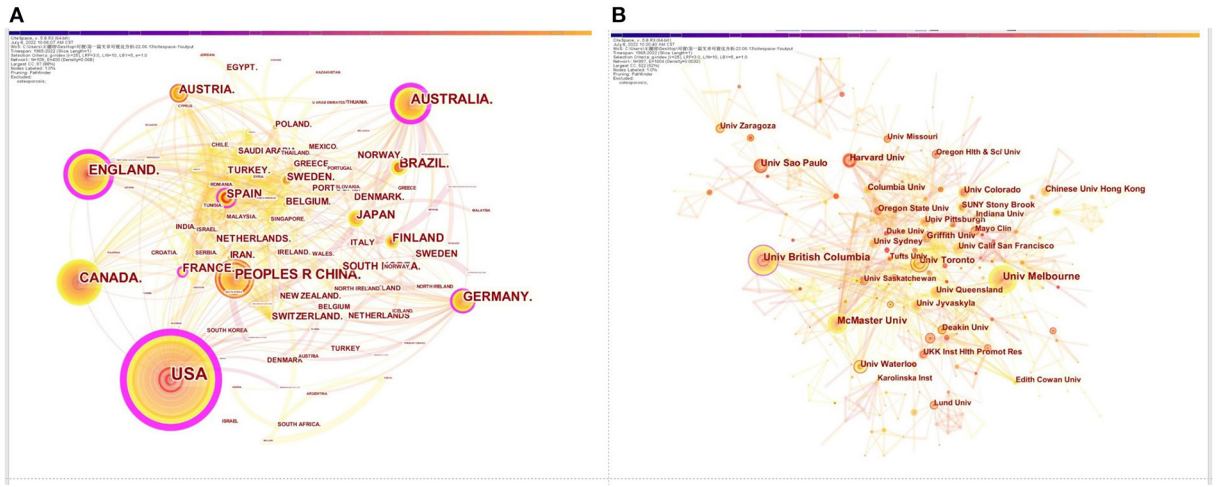


FIGURE 2
Cooperation network diagram of countries **(A)**; Cooperation network diagram of institutions **(B)**.

Data analysis tool and statistical methods

VOS viewer 1.6.18 (Leiden University, Van Eck NJ) and CiteSpace 6.1.R2 (Drexel University, Philadelphia, PA, United States) were used for the statistical analyses of extracted literature. Visualized networks by VOS viewer based on bibliographic data were presented, including the full counting bibliographic coupling analysis of journals, co-occurrence of all keywords, co-citation analysis of cited journals in the references. The following parameters are chosen: counting method (full counting), Type of Analysis (co-occurrence), Unit of Analysis (All Keywords), Minimum number of occurrences of a keyword (5), Number of keywords to be selected (1000).

CiteSpace is an important bibliometric analysis software, we investigated the primary areas of osteoporosis rehabilitation therapy, as well as research hotspots and frontiers by it. The parameters are set as follows; time slicing (1965–2022), years per slice (1), term source (all chosen), node type (one at a time), the threshold (top $N = 50$), pruning (Pathfinder, pruning sliced networks), and visualization (cluster view-static, show merged network). In order to create the co-citation knowledge graph, authors, institutions, countries, cited authors were chosen for node type co-occurrence analysis. the size of the node denotes the number or frequency of documents. The relationships between nodes are represented by their connections, such as coexistence, co-occurrence, or co-citation (37, 38). The purple outer ring of the circle represents centrality, the wider the circle, the higher is the centrality. In addition, reference citation clusters analysis and citation bursts were performed, and the top 10 paper with the highest cited frequency and strongest citation bursts were also summarized. Reference co-citation clusters were generated using the log-likelihood ratio (LLR) strategy, with the selection type adopted "keyword option." The modularity value

(Q-value) and the weighted mean silhouette value (S-value) were used as clustering criteria. As for keyword analysis, the top 30 keywords are summarized, and the top 30 keywords with the strongest citation bursts also were diagrammed.

Results

The number and growth trend of annual publications

A total of 3,268 articles were included from 1965 to 2022, the number of publications was summarized in Supplementary Table S2. The numbers of papers published each year and the development tendency on physical therapy of osteoporosis health promotion field is shown in Supplementary Figure S1. Overall, the number of published papers increased steadily during three stages. In the first stage (1965–1990), publications remained at a low level of no more than 10 per year before 1990. After that, the number of published papers climbed from 35 in 1991 to 102 in 2006, and broke through 100 for the first time in 2006 in the second stage (1991–2006). The period from 2007 to 2022 was the third stage, the annual publication rapidly increased and the average number of published articles was (136.62 ± 32.25), accounting for 66.89% of the total publications. Since only 7 months were included for 2022, the numbers dropped slightly.

TABLE 2 Ranking of top 10 authors, co-cited authors in the physical therapy for osteoporosis research domain.

No.	Author	N	Cited author	Frequency
1	Heinonen A	35	Cummings S	680
2	Sievanen H	31	Sinaki M	495
3	Sinaki M	25	Rubin C	472
4	Vuori I	21	[Anonymous]	452
5	Khan KM	20	KANIS JA	429
6	Giangregorio L	19	Frost HM	391
7	Snow CM	18	Heinonen A	367
8	Oja P	17	Cooper C	357
9	Mckay HA	16	Kanis J	342
10	Kannus P	16	RUBIN CT	338

Distribution of countries and institutes

The details of the top 10 countries and institutions in terms of the numbers of publications are showed in Table 1. The US had the most publications (1,325), followed by China (390), Australia (303), the UK (293), Canada (286), and Germany (179 publications). Articles published in the above six countries accounted for 84.94% of the total articles. The collaborations among various countries were showed in Figure 2A. United States had the highest centrality (0.52), which was followed by United Kingdom (0.25) and Australia (0.21). According to the relevant definition of centrality, these countries had close cooperation with other countries and represented tremendous academic influence. When publications and centrality analysis were combined, United States, United Kingdom and Australia were in the dominant positions. The top 10 institutions by the amounts of published papers were listed in Table 1. University of Melbourne (87 publications) was the leading institution, followed by University of British Columbia (86 publications), McMaster University (70 publications), University of São Paulo (51 publications), Harvard University (49 publications). The

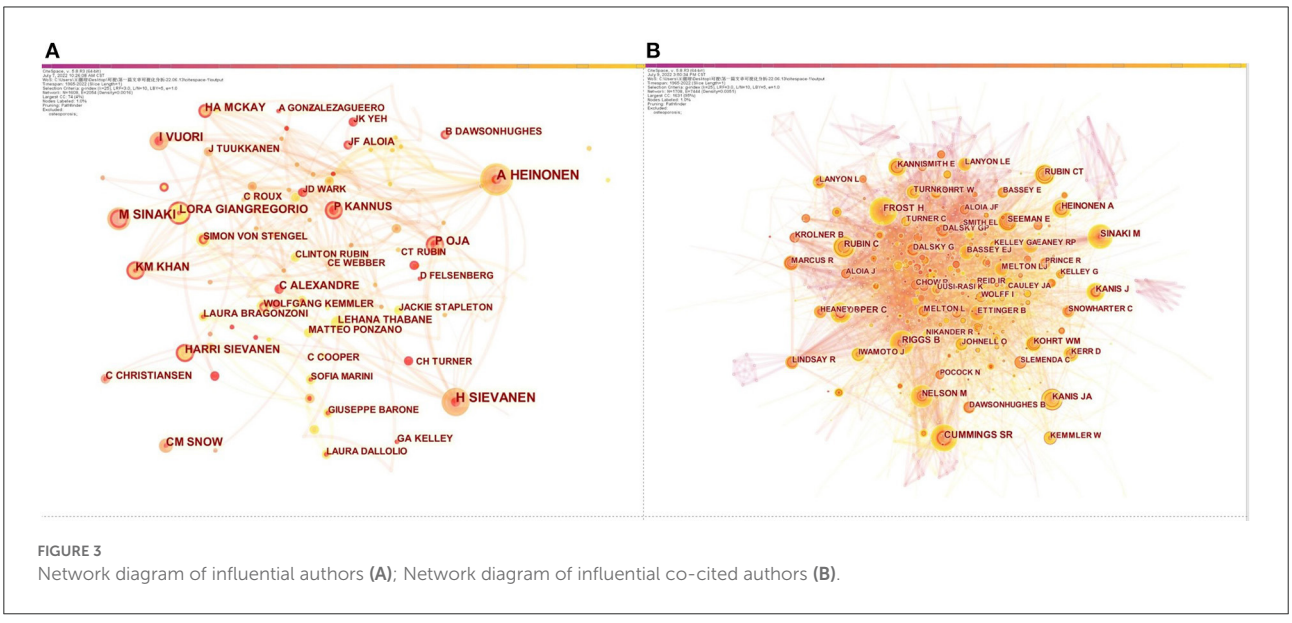


FIGURE 3
Network diagram of influential authors **(A)**; Network diagram of influential co-cited authors **(B)**.

TABLE 3 List of the top 15 journals and cited journals in the references.

NO.	Journal	Documents	Citations	Cited journal	Citations
1	Journal of Bone and Mineral Research	123	11,222	Journal of Bone and Mineral Research	11,792
2	Osteoporosis International	221	10,671	Osteoporosis International	8,146
3	Bone	133	6,621	Bone	6,396
4	Medicine and Science in Sports and Exercise	63	5,543	Calcifiedtissue International	4,146
5	Calcified Tissue International	84	3,751	Medicine and Science in Sports and Exercise	3,682
6	Sports Medicine	31	3,209	Journal of Clinical Endocrinology & Metabolism	3,214
7	Scandinavian Journal of Medicine & Science in Sports	26	2,741	New England Journal of Medicine	3,177
8	New England Journal of Medicine	5	2,231	Jama-Journal of the American Medical Association	2,703
9	Journal of Clinical Endocrinology & Metabolism	22	2,063	Applied Physiology	2,614
10	Journal of Applied Physiology	35	1,973	American Journal of Clinical Nutrition	2,132
11	Archives of Physical Medicine and Rehabilitation	31	1,776	Journal of the American Geriatrics Society	1,920
12	American Journal of Clinical Nutrition	19	1,762	Lancet	1,809
13	Annals of Internal Medicine	6	1,572	Archives of Internal Medicine	1,679
14	Bone and Mineral	6	1,451	Archives of Physical Medicine and Rehabilitation	1,576
15	Applied Physiology Nutrition and Metabolism	13	1,420	Journals of Gerontology. Series A,Biological Sciences & Medical Sciences	1,307

network cooperation map among various institutions were depicted in Figure 2B. In terms of centrality, University of British Columbia showed maximum centrality (0.11), followed by Harvard University (0.09), McMaster University (0.08). Based on the analysis of the number and centrality of publications, University of British Columbia, Harvard University and McMaster University showed close cooperative relationship and exhibited strong academic influence.

Distribution of authors and co-cited authors

The top 10 authors, co-cited authors on physical therapy of osteoporosis research were listed in Table 2. Among the top 10 authors, Heinonen A had the most publications (35 publications), followed by Sievanen H (31 publications), and Sinaki M (25 publications). In terms of co-cited authors, Cummings S had the most cited times (680 cited times), followed by Sinaki M (495 cited times) and Rubin C (472 cited times). These authors were actively involved in the physical therapy for osteoporosis research field. Cooperation between authors and co-cited authors is analyzed in Figures 3A,B. Connections showed cooperation relationships among nodes, the bigger the circle, the more it appears, and lines represents the connections between authors, the thicker the lines, the closer the connections. The network diagram of authors in Figure 3A is composed of 1,608 nodes and 2,054 links the connections between co-cited authors (nodes = 558, links = 3,288) was illustrated in Figure 3B. The maps of the authors and co-cited provided significant information on influential research collaborators, enabling close collaboration among researchers.

Distribution of journals and co-cited journals

The publications were concentrated published in 132 scholarly journals, according to the full counting bibliographic coupling analysis of journals (Figure 4). The top 10 journals that were most cited were listed in Table 3. Bone and Mineral Research had 11,222 citations and 123 publications, making it the most cited journal, followed by Osteoporosis International with 10,671 citations and 221 publications, the third is Bone with 6,621 citations and 133 articles. The most frequently cited in the references, according to the full counting co-citation analysis of cited journals, were Journal of Bone and Mineral Research (cited by 11,792 times). The second was Osteoporosis International (cited by 8,146 times). followed by Bone (cited by 6,396 times) (Figure 5). The top 10 cited journals in the references were showed in Table 3.

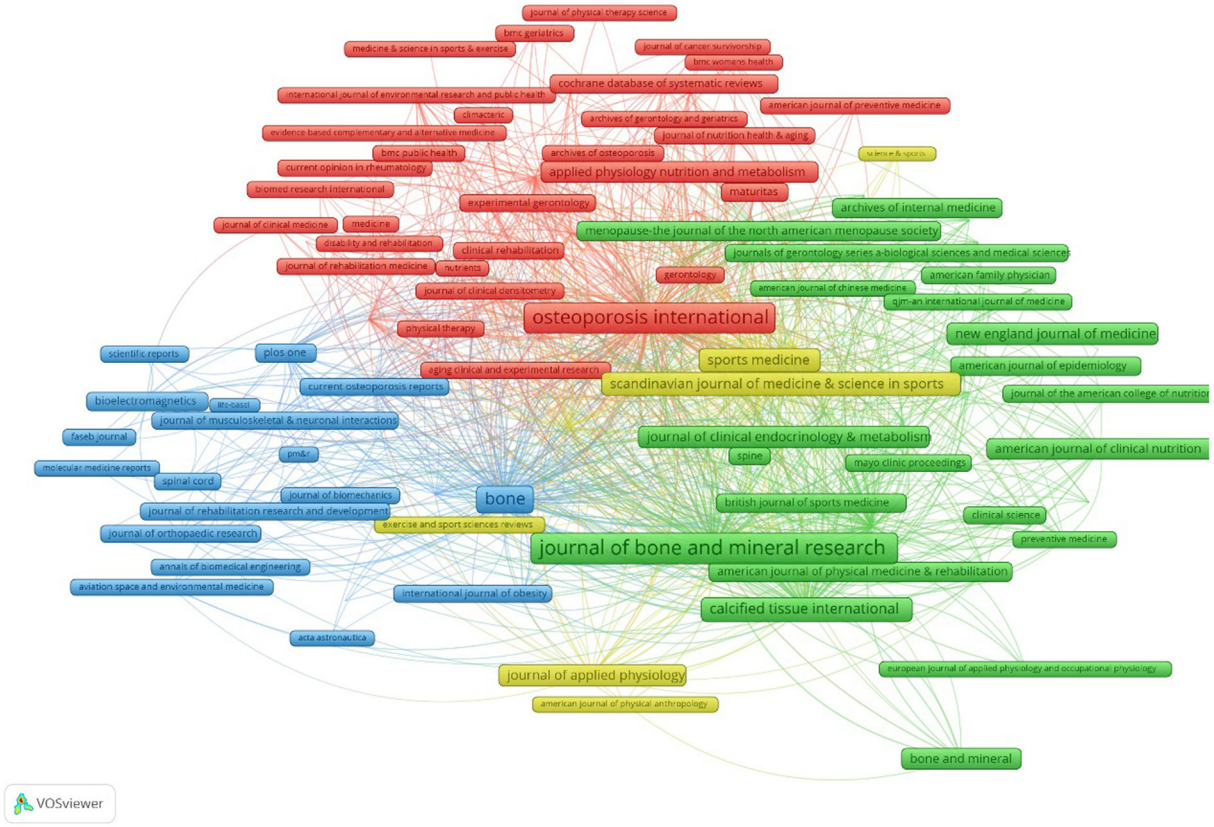


FIGURE 4
Bibliographic coupling analysis highly cited journals, weighted by citations, visualized map.

Analysis of reference co-citation

Reference co-citation analysis was utilized to explore research priorities in academic fields. The co-citation analysis gained 4,106 recorded and the co-citation network is shown in Figure 6A, Table 4. Reference co-citation clusters were generated using the log-likelihood ratio (LLR) strategy, with the selection type adopted "keyword option." The Q-value and S-value were used as clustering criteria. Estimation strategies with means Q > 0.5 and S > 0.7 suggest that the clustering is convincing. In Figure 6A, the modularity Q is 0.863 (>0.5), indicating that the clustering of the network is reasonable, and the S-value is 0.9387 (>0.5), indicating that the homogeneity of the clustering is acceptable. References with the highest cited frequency and strongest citation bursts are regarded as the research basics of frontiers in the future. The top 20 papers with the strongest citation bursts on osteoporosis rehabilitation research were showed in Figure 6B. The important 10 articles integrating the cited frequency and burst strength were discovered (Table 5).

Analysis of keywords

When the keywords with the equal meaning were combined, the frequency of the published keywords was statistically determined and the top 30 keywords are summarized in Table 6. A map of keywords can present major objects and hot topics of research. The co-occurrence network of keywords was performed by applying VOS viewer software. We created the map based on bibliographic data with a full counting strategy, which set the minimum number of occurrences of a keyword as five. 1,062 of 7,677 keywords met the criterion after being thesaurus-cleaned. Based on keyword research categories, we incorporated VOS viewer's classification and separated keywords into three color-coded groups (Supplementary Figure S2). In this figure, purple, red, and grass green are represented for the applications of Physical Activity/ Exercise in menopausal osteoporosis, age-related osteoporosis, juvenile osteoporosis, preclinical study, osteoporosis-related fractures, respectively. These application domains would be further discussed in the next part. In addition, we also performed co-occurrence analysis of

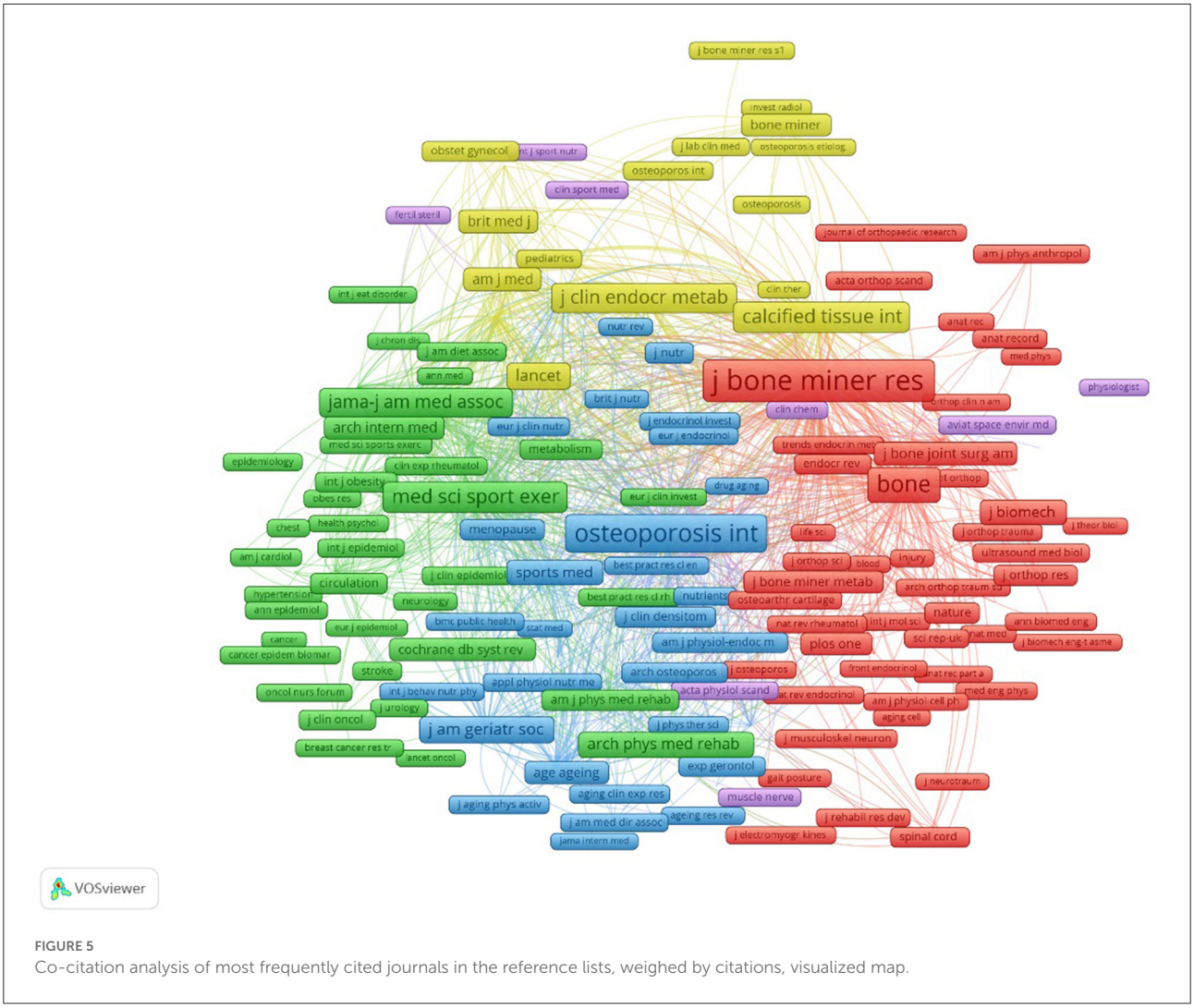


FIGURE 5
Co-citation analysis of most frequently cited journals in the reference lists, weighed by citations, visualized map.

keywords by density visualization and overlay visualization in Figures 7, 8.

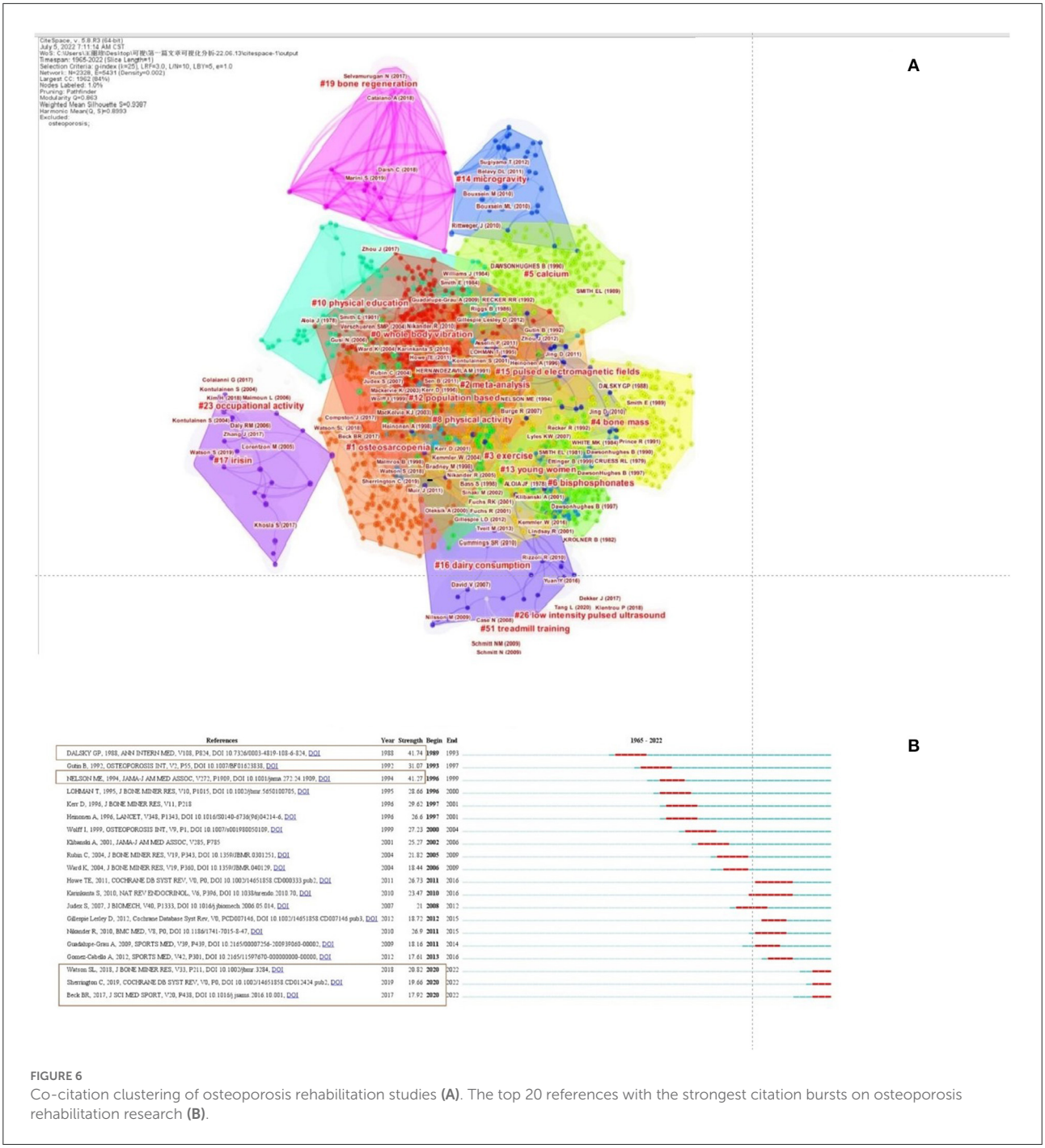
Analysis of the burst of keywords

The "burst words" serve as words that are cited frequently over a period of time, which can display the frontier topics and key areas of research. The top 30 keywords with the strongest citation bursts from 1965 to 2022 was shown in Figure 9. The top five keywords with the highest strength burst were calcium supplement calcium supplement (34.24), young woman (29.28), X-ray absorptiometry (29.17), hormone replacement therapy (25.23), age (22.64), Quality of Life (21.67), low magnitude (20.97), older woman (20.47), weight bearing exercise (20.06). The values in brackets follow the strength of burst, occurrence burst, The top five keywords with the most duration of burst included weight bearing exercise (1992–2005), X-ray absorptiometry (1994–2006), resistance exercise (2008–2020), fracture risk (2010–2020). During the decade of 1990–2000, Trabecular bone, lumbar spine, calcium supplement grew to be the focal point of research in this time period. From 2015 to 2022, keywords with the strongest citation bursts including fracture risk, mesenchymal stem cell, Quality of Life, sarcopenia were widely mentioned and studied.

Discussion

International research status of osteoporosis rehabilitation

The research presented the first bibliometric analysis of the global research trends in rehabilitation therapy for osteoporosis. Until 1991, there was a very low number of published documents per year, a sharp rise was observed in the following year. Throughout the investigated period of 31



References	Year	Strength	Begin	End
DALSKY GP, 1988, ANN INTERN MED, V108, P824, DOI 10.7326/0003-4819-108-6-824, DOI	1988	41.74	1989	1993
Gutin B, 1992, OSTEOPOROSIS INT, V3, P55, DOI 10.1007/BF01623838, DOI	1992	31.07	1993	1997
NELSON ME, 1994, JAMA-J AM MED ASSOC, V272, P1909, DOI 10.1001/jama.272.24.1909, DOI	1994	41.27	1996	1999
LOHMAN T, 1995, J BONE MINER RES, V10, P1015, DOI 10.1002/jbmr.5650100705, DOI	1995	28.66	1996	2000
Kerr D, 1996, J BONE MINER RES, V11, P218	1996	29.62	1997	2001
Heinonen A, 1996, LANCET, V348, P1343, DOI 10.1016/S0140-6736(96)04214-6, DOI	1996	26.6	1997	2001
Wolff I, 1999, OSTEOPOROSIS INT, V9, P1, DOI 10.1007/s001980050109, DOI	1999	27.23	2000	2004
Kiibomäki A, 2001, JAMA-J AM MED ASSOC, V285, P785	2001	25.27	2002	2006
Robin C, 2004, J BONE MINER RES, V19, P343, DOI 10.1359/JBMR.0301251, DOI	2004	21.82	2005	2009
Ward K, 2004, J BONE MINER RES, V19, P360, DOI 10.1359/JBMR.040129, DOI	2004	18.44	2006	2009
Howe TE, 2011, COCHRANE DB SYST REV, V0, P0, DOI 10.1002/14651858.CD000333.pub2, DOI	2011	26.73	2011	2016
Kanis JA, 2010, NAT REV ENDOCRINOL, V6, P396, DOI 10.1038/nrendo.2010.70, DOI	2010	23.47	2010	2016
Judex S, 2007, J BIOMECH, V40, P1333, DOI 10.1016/j.jbiomech.2006.05.014, DOI	2007	21	2008	2012
Gillespie LeSley D, 2012, Cochrane Database Syst Rev, V0, PCD007146, DOI 10.1002/14651858.CD007146.pub3, DOI	2012	18.72	2012	2015
Nikander R, 2010, BMC MED, V8, P0, DOI 10.1186/1741-7015-8-47, DOI	2010	26.9	2011	2015
Guadalupe-Grau A, 2009, SPORTS MED, V39, P439, DOI 10.2165/00007256-200939060-00002, DOI	2009	18.16	2011	2014
Gomez-Cabello A, 2012, SPORTS MED, V42, P301, DOI 10.2165/11597670-000000000-00000, DOI	2012	17.61	2013	2016
Watson SL, 2018, J BONE MINER RES, V33, P211, DOI 10.1002/jbmr.3284, DOI	2018	20.82	2020	2022
Sherrington C, 2019, COCHRANE DB SYST REV, V0, P0, DOI 10.1002/14651858.CD012424.pub2, DOI	2019	19.66	2020	2022
Beck BR, 2017, J SCI MED SPORT, V20, P438, DOI 10.1016/j.jsams.2016.10.001, DOI	2017	17.92	2020	2022

FIGURE 6
Co-citation clustering of osteoporosis rehabilitation studies **(A)**. The top 20 references with the strongest citation bursts on osteoporosis rehabilitation research **(B)**.

years, the number of papers produced per year shown a gradual upward trend. Particularly, over the past decade, there has been a continual and significant growth in the number of publications published. There were 197 articles published in 2021, which is a historical peak, indicating an increase in interest in osteoporosis rehabilitation research. Several factors contribute to the rapid advancement of research on osteoporosis rehabilitation, according to available knowledge.

Research hotspots by country (region)

The USA accounted for approximately one-fourth of the top 10 countries' documents, reflecting its strong research capacity and commitment to the advancement of the field. A noteworthy fact is that China ranked second in terms of the number of articles published. This indicates that China is placing a greater emphasis on research advancements in this subject. In

TABLE 4 Co-citation clustering of osteoporosis rehabilitation studies that were published from 1965 to 2022.

Cluster ID	Size	Silhouette	Silhouette mean (Year)	Label (LLR)
0	271	0.872	2009	Whole body vibration
1	211	0.983	2017	Osteosarcopenia
2	178	0.929	1995	Meta-analysis
3	168	0.892	2003	Exercise
4	159	0.945	1989	Bone mass
5	153	0.907	1991	Calcium
6	125	0.923	1997	Bisphosphonates
8	81	0.957	1999	Physical activity
10	72	0.994	1981	Physical education
12	55	0.97	2002	Population based
13	51	0.991	1980	Young women
14	37	0.965	2011	Microgravity
15	35	0.996	2012	Pulsed electromagnetic fields
16	32	0.992	2011	Dairy consumption
17	24	0.99	2018	Irisin
19	19	0.998	2017	Bone regeneration
23	11	0.997	2005	Occupational activity
26	10	0.992	2017	Low intensity pulsed ultrasound
51	4	0.998	2008	Treadmill training

addition, the USA is also followed by high-developed countries such as the UK or Australia. This is due to the fact that they have been well represented and consolidated within the World Confederation for Physical Therapy, an organization that provides support and promotes research pertaining to physical therapy (PT). Furthermore, since the USA possessed the highest degree of centrality, it also serves as the central collaborator of other countries.

Research hotspots by institutions

Among the research institutions, University of Melbourne published the greatest number of articles, which could be attributable to universities' robust academic environments and scientific research foundations. Researchers can acquire timely information regarding osteoporosis rehabilitation research. Cooperation between institutions is mainly distributed in European and American countries based on the cooperation network of institutions. Unfortunately, despite China's large population, research on osteoporosis rehabilitation therapy is still in its infancy, and interinstitutional collaboration is lacking. Asian countries were not represented in the top 10 institutions for osteoporosis rehabilitation research, which could impediment the development of this field. Collaboration among osteoporosis rehabilitation researchers helps advance the field. Consequently, we advised strengthening collaboration networks between European, American, and Asian research institutes.

Research hotspots by journals

The top three published journals are Osteoporosis International, Bone, and Journal of Bone and Mineral Research. Osteoporosis International journal established by the International Osteoporosis Foundation and the National Osteoporosis Foundation of the USA. It facilitates the exchange of ideas about osteoporosis and other metabolic bone diseases Journal of Bone is an unsurpassed reputation for excellence international journal that dealing with both normal and pathological processes affecting bone metabolism. The Journal of Bone and Mineral Research provides a diverse, highly impactful research with the latest insights into musculoskeletal system and mineral metabolism. It is worth noting that New England Journal of Medicine, with its impact factor of 74.699, has also published many studies on osteoporosis rehabilitation. Furthermore, four out of the 11 leading prolific publications were dedicated to the scope of rehabilitation therapy: Medicine and Science in Sports and Exercise, Sports Medicine, Scandinavian Journal of Medicine & Science in Sports, Archives of Physical Medicine and Rehabilitation. In spite of the fact that other journals such as Calcified Tissue International, Journal of Clinical Endocrinology & Metabolism are not exclusively PT-oriented, these journals have a significant advantage in our results. This may be due to osteoporosis being a multidisciplinary field, which typically provides authors with a variety of publishing alternatives, the dynamics of these journals should therefore be considered in future research.

TABLE 5 The top 10 papers with the highest cited frequency and strongest citation bursts on osteoporosis rehabilitation research.

No.	Author/Year	Cited frequency	Burst	Centrality	Document title	Source
1	(39)	81	41.27	0.02	Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures: a randomized controlled trial	JAMA-J AM Med Assoc
2	(40)	73	26.73	0.04	Exercise for preventing and treating osteoporosis in postmenopausal women.	Cochrane DB Syst Rev
3	(41)	69	41.74	0.09	Weight-bearing exercise training and lumbar bone mineral content in postmenopausal women	Ann Intern Med
4	(42)	65	23.47	0.04	Physical therapy approaches to reduce fall and fracture risk among older adults	Nat Rev Endocrinol
5	(43)	60	31.07	0.18	Can vigorous exercise play a role in osteoporosis prevention? A review	Osteoporosis int
6	(44)	59	29.62	0.01	Exercise effects on bone mass in postmenopausal women are site-specific and load-dependent	J Bone Miner Res
7	(45)	57	28.66	0.03	Effects of resistance training on regional and total bone mineral density in premenopausal women: a randomized prospective study	J Bone Miner Res
8	(46)	53	26.6	0.02	Randomized controlled trial of effect of high-impact exercise on selected risk factors for osteoporotic fractures	Lancet
9	(47)	52	27.23	0	The Effect of Exercise Training Programs on Bone Mass: A Meta analysis of Published Controlled Trials in Pre- and Postmenopausal Women	Osteoporosis Int
10	(48)	50	18.72	0.2	Interventions for preventing falls in older people living in the community.	Cochrane Database Syst Rev

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TABLE 6 The top 30 keywords of osteoporosis rehabilitation-related studies that were published from 1965 to 2022.

Rank	Frequency	Centrality	Keyword
1	2,024	0	Bone mineral density
2	972	0	Postmenopausal women
3	928	0.02	Physical activity
4	893	0.01	Exercise
5	827	0.02	Muscle strength
6	827	0.01	Fracture
7	814	0.02	Risk factor
8	549	0.05	Women
9	464	0.05	Randomized controlled trial
10	340	0.03	Calcium supplementation
11	338	0.04	Prevention
12	328	0.08	Bone
13	273	0.06	Men
14	260	0.08	Body composition
15	238	0.02	Quality of life
16	200	0.06	Age
17	193	0.04	Health
18	167	0.01	Older adult
19	164	0.03	Hormone replacement therapy
20	162	0.05	Cigarette smoking
21	157	0.03	Young women
22	149	0.06	Skeletal muscle
23	145	0.04	Weight bearing exercise
24	144	0.05	Estrogen
25	142	0.05	Older women
26	131	0.02	Children
27	130	0.01	Whole body vibration
28	127	0.04	Metabolism
29	126	0.04	Parathyroid hormone
30	125	0.04	Therapy

Research hotspots by author

Based on author contribution and co-citations, influential authors include Heinonen A, Sievanen H, Sinaki M. Cummings S and Rubin C. The researchers Heinonen A and Sievanen H, both of whom are affiliated with the UKK Institute for Health Promotion Research, have contributed 66 publications Heinonen's key academic achievements were published in the Lancet joins an increasing number of controlled trials that provide concrete evidence of the positive effects of exercise on the skeletal system a (46). According to Sievanen H, Among vitamin D-supplemented older adults living in the community, strength and balance training may be the most effective and feasible way to prevent injurious falls (49). Sinaki M is a well-known rehabilitation specialist from Mayo Clinic, she has designed a variety of exercise programs for strengthening the back muscles to reduce back pain, kyphosis, vertebral fractures, and the risk of falls. She also advocated that the Rehabilitation of Osteoporosis Program-Exercise (ROPE) incorporates complete osteoporosis management. Her research reported that exercise for patients with osteoporosis, providing recommendations for management of vertebral compression fractures and trunk strengthening for fall prevention (50). Cummings S is a famous professor from University of California San Francisco, Cummings's the major research contribution was to explore the role of various drugs such as Raloxifene, zoledronic acid, alendronate, Estrogen replacement therapy for the treatment and prevention of osteoporosis and osteoporotic fractures. Several of his articles have been published in internationally renowned magazines, including JAMA, New England Journal of Medicine, Lancet (51–56). Rubin C is from Stony Brook University and his research was focused on the effects of mechanical stimulation on bone cell and osteoporosis (57–61). He proposed that mechanical targeting of the bone marrow stem-cell pool might serve as a potentially effective, drug-free strategy of reversing the age-related decline of the musculoskeletal system (62). The authors mentioned above have published a lot of far-reaching literature on the prevention and treatment of osteoporosis and osteoporotic fractures, particularly in the area of rehabilitation for osteoporosis. It is therefore recommended that those concerned with osteoporosis pay more attention to these experts.

Citation information

Top 10 co-cited references are listed in Table 5, The 10 important articles discovered by integrating the cited frequency and burst strength. the disciplinary framework and knowledge basis of rehabilitation studies on osteoporosis by analyzing these key papers can be gained. Dalsky et al. (41) assessed the effect of weight-bearing exercise training and subsequent detraining on lumbar bone mineral content in postmenopausal women and Nelson et al. (39) investigated the effectiveness of high-intensity strength training on multiple osteoporotic fracture risk factors. Which these two studies represented a strong research hotspot with burst strength as 41.74 and 41.27. One reviews by Howe et al. (40) focusing on the effectiveness of exercise programs in preventing bone loss and fractures in postmenopausal women published in Cochrane Database of Systematic Reviews, and exercise may be a safe and effective strategy to prevent bone loss in postmenopausal women. Karinkanta et al. (42) provided insights that they concentrate on evidence-based physical therapy approaches such as exercise, vibration training and enhancements of security at home and during periods of mobility for reducing fall and fracture risk among older adults. In recent years, Watson et al. (17) showed

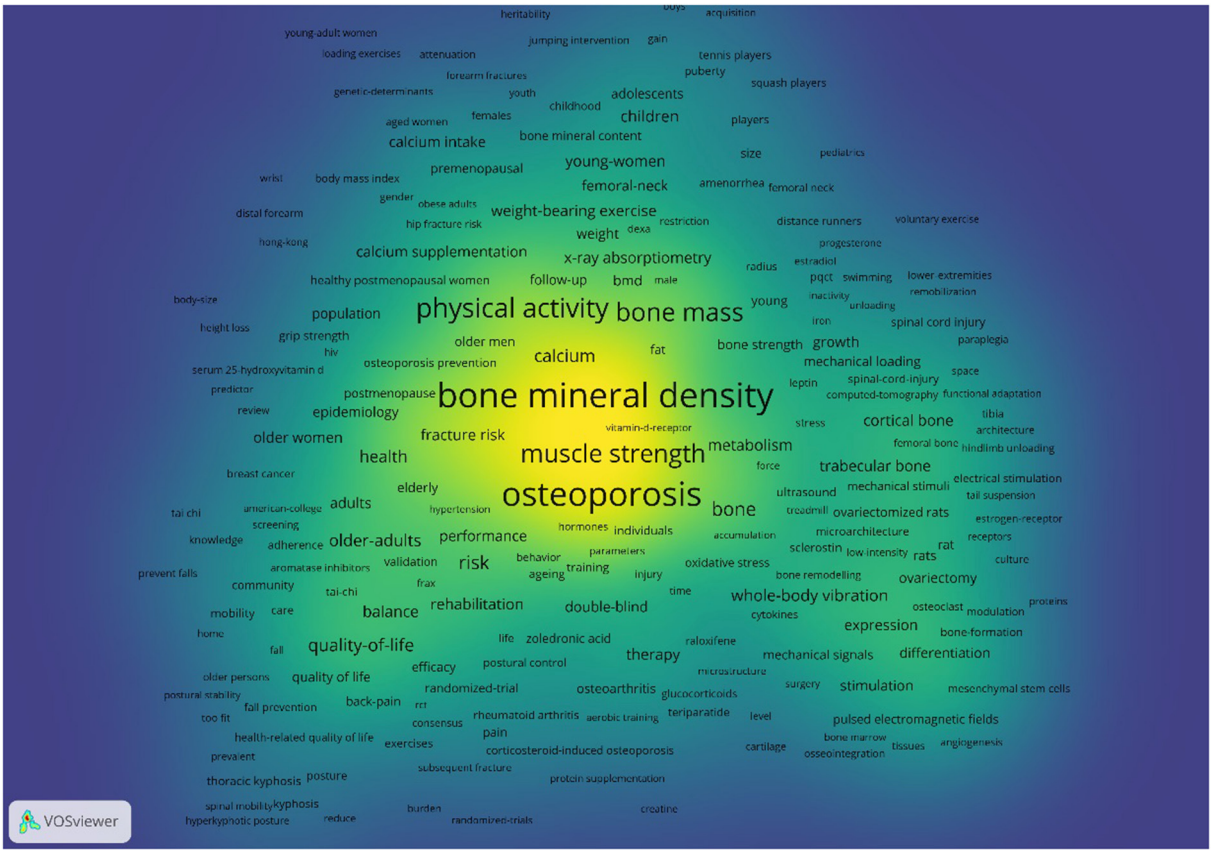

FIGURE 7
Co-occurrence analysis of keywords by density visualization.

that High-intensity resistance and impact training (HiRIT) program improved indices of bone strength and functional performance in postmenopausal women with low bone mass. HiRIT was effective and caused no unfavorable events under highly supervised prerequisites for the healthy postmenopausal women with low to very low bone mass. Sherrington et al. (63) provided insights that exercise programs help older adults in the community experience fewer falls and at a lower rate of occurrence, exercise program to reduce falls mainly involves balance and functional exercises. Beck et al. (14) provided detailed, evidence-based guidelines for safe and effective exercise prescription for osteoporosis prevention or management.

The hotspot and frontiers

Keyword co-occurrence and reference co-citation analysis may be performed to establish the current research focus and development trends of a specific area. Based on the overlay and density visualizations and the detection of burst keywords, we identified the research hotspots and development frontiers in osteoporosis rehabilitation-related research as discussed in the following paragraphs.

The significance of physical activity and exercise in the prevention and management of osteoporosis

The terms physical activity encompasses leisure time physical activities (exercise and sport), daily activities, household tasks and work (64), physical activity can vary significantly in terms of both intensity and duration. Exercise refers to a planned, systematic, and repetitive physical activity that involves bodily movements with or without a specific goal for improving fitness (65). Greater levels of physical activity have frequently been related with improved health and quality of life, whereas low levels of physical activity are linked to negative health outcomes.

A variety of physical activity interventions have been designed and evaluated, and its benefits for healthy aging are well established (66). The management of osteoporosis

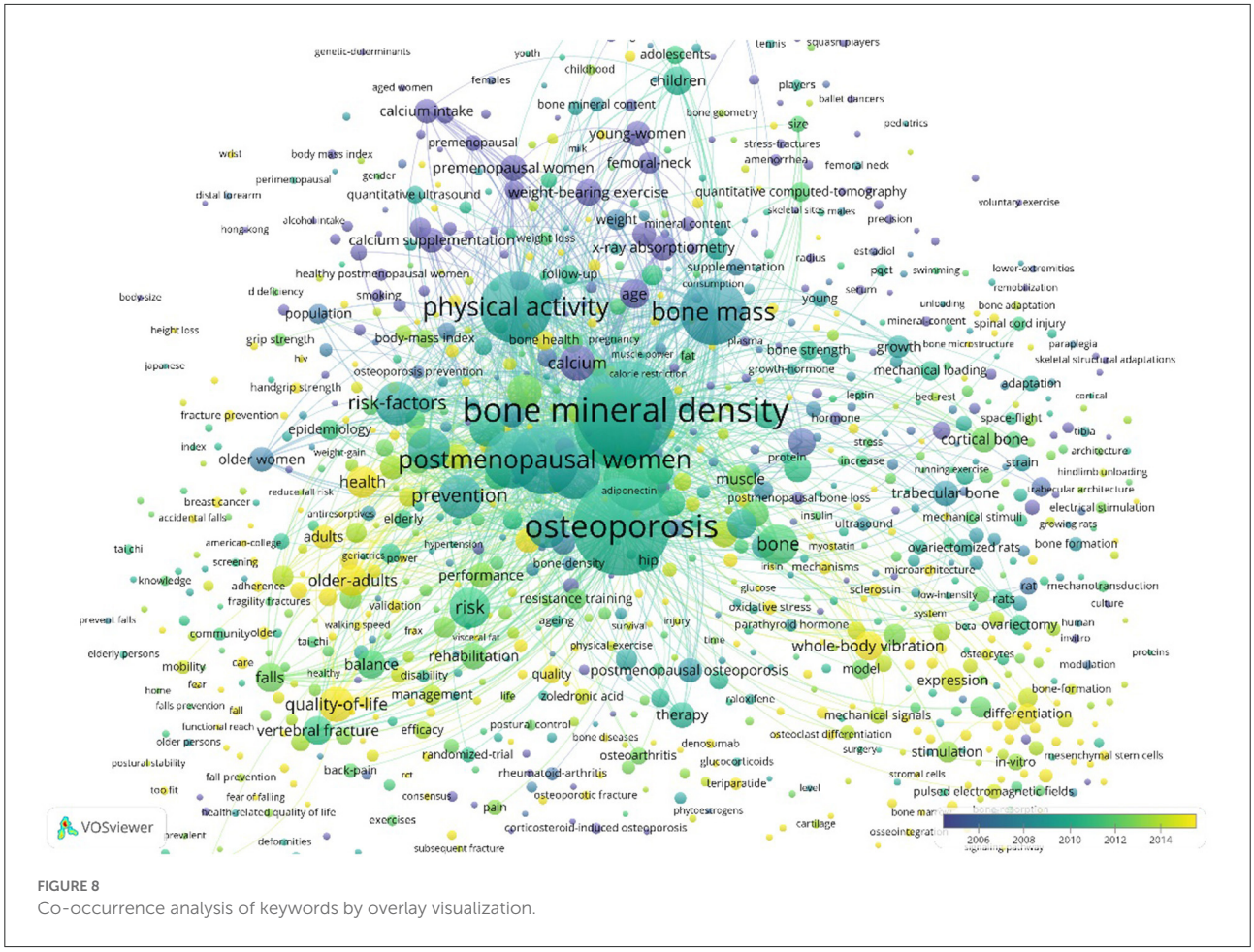

FIGURE 8
Co-occurrence analysis of keywords by overlay visualization.

can be improved by engaging in physical activity according to various guidelines. Some research indicated that physical activity programs probably increase bone mineral density in the lumbar spine and hip (femoral neck), and additionally improves muscle strength, balance, and joint proprioception reduce the risk of falls and fractures (67). Interestingly, physical activity and exercise seem to improve BMD both cross-sectionally and prospectively, at least appearing to exert a homeostatic effect on BMD during aging (68). Specifically, in older adults, research suggests that resistance training and weight-bearing exercise are most effective at maintaining and increasing BMD (68). Weight-bearing and resistance training can increase balance, posture, agility, and strength, which may lower the risk of falling. Moreover, some types of weight-bearing exercise may boost bone density are walking, jogging, Tai Chi, climbing stairs, and dancing. muscle-strengthening exercises usually involve weight training and other resistance exercises (9). For optimizing musculoskeletal health and function, targeted multimodal programs integrating conventional and high-velocity progressive resistance training (PRT), weight-bearing impact exercises, and challenging balance/mobility activities seemed to be the most effective (69). As reported in a meta-analysis by Martyn-St James and Carroll, that integrating jogging with low-impact exercise or trying to combine impact activities with high-intensity exercise (i.e., resistance training) is effective for maintaining BMD in postmenopausal women (70). A systematic review also revealed that multicomponent training (MT) comprising of strength, aerobic, high-impact, and weight-bearing exercises can improve or at the very least slow the age-related loss of bone mass (71). However, it is not clear which MT method will achieve better results. Therefore, further research is required to determine the appropriate multicomponent training regimens.

Furthermore, whole body vibration (WBV) training is regarded relatively safe, and does not require a high level of motivation for its practice therefore, it may be presumed as an adjunctive therapy to counteract BMD loss, particularly for those with barriers in the practice of high-impact physical exercise. Some meta-analysis and RCT demonstrated WBV significantly increased bone density (21, 72). WBV may be a practical and effective strategy to decrease well-recognized risk factors for fractures and falls, as well as to enhance balance

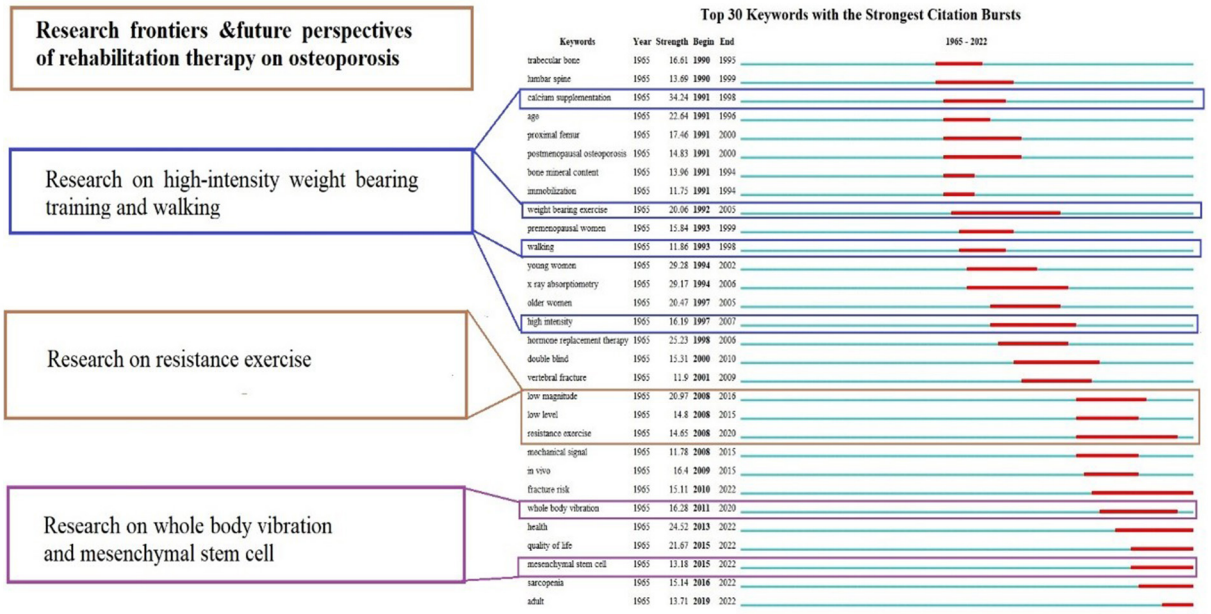

FIGURE 9
Top 30 keywords with the strongest citation burst in osteoporosis rehabilitation-related field.

and some aspects of neuromuscular function (73). However, parameters used in WBV (frequency, magnitude, cumulative dose, positioning on the oscillation board, and type of vibration) are extremely heterogeneous, which makes it difficult for studies to be compared. Furthermore, there has been a lack of high-quality trials showing positive associations so far. To address the knowledge gap regarding the osteogenic effects of WBV and the underlying processes in regulating osteoporosis treatment, future research should assess the effects of various WBV training protocols on bone health.

Enhancing the management of physical activity/ exercise on osteoporosis in adolescents and men

Postmenopausal and senile osteoporosis are the two most common types of osteoporosis, accordingly, more investigation has been conducted on these two forms of osteoporosis. It is worth noting that a growing body of research has been conducted on osteoporosis in adolescents and men in recent years as well. There are a variety of strategies for combating osteoporosis, with the optimization of peak bone mass (PBM) throughout childhood being one of the most frequently utilized preventive therapy (74). PBM is a critical determinant of osteoporotic fracture risk. It has been proven that when PBM increases by 10% in children and adolescents, the risk of osteoporotic fracture was reduced by 50%, and when BMD increases by 5%, the risk will decrease by 40% (75, 76). Multiple studies have demonstrated that premenarche, and even prepubertal vs. early pubertal, are stages of greater bone response to exercise relative to postmenarche (77–80). Therefore, childhood and adolescence are pivotal periods to adopt lifestyle interventions that may prevent osteopenia and osteoporosis-related fractures in later stages of life. Jumping exercises during childhood and adolescence enhance bone density, mineral content, and structural characteristics without causing any adverse outcomes. To enhance bone mass during early childhood these types of measures should thus be employed (81). Recent systematic reviews found weight-bearing activities in childhood and adolescence can dramatically increase bone mineral content (BMC) and bone mineral density (BMD) (82).

Research on osteoporosis and physical activity commonly focused on women, male osteoporosis is still underrecognized and underdiagnosed, which logically leads to a lack of therapy options for men. The quality of life (HRQoL) of these patients may be impaired by the inadequate management of osteoporosis in males. A recent systematic review and meta-analysis revealed that males with osteoporosis had a decreased HRQoL than men without the condition, with hip fracture, vertebral fractures, or wrist fractures dramatically reducing HRQoL of men. Importantly, BMD at the spine and femur was strongly associated with HRQoL (83). Research showed that higher BMD was maintained in older males who engaged in

high-impact, quick-impact physical activity, and a lower risk of falling was associated with higher energy expenditure (84). However, some study indicated that physical activity has almost no effect on BMD at the total hip and little or no effect on BMD at the femoral neck, lumbar spine, and whole body (85). The main reasons for inconsistent study results may be the diversity of the interventions, the small sample size, and the (relatively) short duration of the interventions. To improve the quality of the evidence, future research should enlarge sample size, identify interventions, engage in comprehensive reporting of HRQoL outcomes and prolong long-term interventions.

The key role of physical activity and exercise in the prevention and management of osteoporosis-related sarcopenia and fractures

Osteosarcopenia was first established by Duque and coworkers to represent a subpopulation of elderly individuals impacted by osteoporosis and sarcopenia (86) osteosarcopenia is a unique syndrome characterized by poor bone density and decreased muscle mass, strength, and/or functional capacity (87). The researchers revealed that osteosarcopenia dramatically raised the likelihood of fractures, falls, and mortality (88). Compared to those without osteosarcopenia, with sarcopenia alone, and those with osteoporosis alone, women with osteosarcopenia were more likely to have previously suffered a fracture (89). Therefore, the elderly people should be mindful of the risks associated with osteosarcopenia. The researchers investigated the efficacy of non-pharmacological (exercise and/or dietary) therapies on musculoskeletal measures and outcomes in osteosarcopenic individuals and found that RT can boost gains in muscle mass, strength, and quality, as well as increase or maintain BMD in older osteosarcopenic adults (90). A study by Kemmler also showed that high intensity dynamic resistance exercise (HIT-DRT) on devices especially when combined with moderate protein supplementation was proven to be a safe, appealing, highly efficient and effective strategy for managing osteosarcopenia in older men with sarcopenia and osteoporosis (91). As far as muscle quality (MQ)parameters are concerned, intermittent exercise regimens with intervals of 6 months or longer should be substituted with largely continuous regimens (92). Consequently, suitable therapy routes involving moderate-to-high intensity supervised RT should be promoted in clinical settings for individuals with osteosarcopenia. For osteosarcopenia upstream prevention, current recommendations should emphasize large-scale RT programs that are aimed at increasing participation of older adults. These strategies may ultimately lessen the socioeconomic impact of this geriatric disease.

Bone fragility caused by osteoporosis is common in older persons and is associated with a higher of fragility fracture. However, osteoporosis may not be detected until the patient has suffered multiple fragility fractures. It is estimated that 319 million adults aged 50 years or more will be at significantly higher risk for osteoporotic fractures worldwide (93). Individuals who suffer fragility fractures are at higher risk of developing subsequent fracture at a different site. Based on a meta-analysis conducted by Kanis and colleagues, prior fractures are associated with an 86% increased risk of further fracture at any new site (94). Therefore, The International Osteoporosis Foundation offers a best practice suggestion for secondary fracture prevention, emphasizing the need to diagnose patients early, identify their future fracture risk, evaluate the patient in a reasonable timeframe, and then determine the next measure. Exercise approach is usually advised for persons who are deemed to be at low or moderate risk for osteoporotic fractures (95). According to the study, multimodal exercise can reduce the risk of falling in participants at high risk of primary osteoporotic fractures when compared with a control group (96). PRT can enhances physical function, life quality, and relieves pain. Current research suggests that PRT should be prescribed for those at risk of fracture, however determining the optimal frequency or intensity of PRT is difficult due to its heterogeneity and limitations. A hip protector is one of the many multifactorial interventions that can be used to prevent fall and fractures among patients living in high-risk residential settings. A systematic review found moderate quality evidence supporting a small reduction in hip fracture risk (97). Generally, Fractures of conservative treatment indicated the benefits of early initiation of exercise therapy and physiotherapy. Nevertheless, reliable data on the optimal duration and intensity of physiotherapy and use of orthoses remain lacking (98). A sufficient number of studies have not been conducted to determine whether exercise affects incident fractures, falls, or adverse events. High-quality randomized trials are required in the future to determine the safety and efficacy of exercise in reducing the incidence of fractures and falls, improving patient-centered outcomes (pain, function) in individuals with fractures (99).

Application of mesenchymal stem cells (MSCs) in the prevention and treatment of osteoporosis

During osteoporosis pathogenesis and treatment, MSCs play a vital role due to their multi-directional differentiation potential and self-renewal ability (100). On the one hand, a number of factors contribute to the pathogenesis of osteoporosis, including homing disorders, impaired osteogenic differentiation, senescence of MSCs, an imbalanced microenvironment (such

as transcription factors, signal pathways, and microRNAs), and disrupted immunoregulation (101). On the other hand, a number of preclinical studies have shown that MSC transplantation can enhance osteogenic differentiation, increase bone mineral density, and slow down osteoporosis progression (101). The latest techniques, such as gene modification (overexpressing osteogenic and angiogenic genes, knocking down bone destruction genes, modifying homing-related genes, causing MSCs to delay senescence), targeted modification, and co-transplantation, offer promising results for enhancing MSC therapeutic effectiveness (102). Despite this, it remains unclear which regulatory mechanisms and molecular markers can be used to assess MSC migration to the bone surface, which is crucial for bone formation and fracture healing. As a result, it is difficult to regulate MSC activity when managing osteoporosis and fractures. In addition, due to some safety concerns, the effectiveness of transplantation, and uniformity of manufacturing processes, no pertinent clinical study data have yet been reported in terms of clinical trial investigations on MSC for osteoporosis. Therefore, future studies ought to investigate the regulatory mechanisms of MSCs in the management of osteoporosis, and research should concentrate on the effectiveness of readily available and highly biocompatible autologous adipose stem cells in the osteoporosis therapy.

Strengths and limitations

Based on bibliometric and visual analyses, this study examined the progress and trends in global scientific research into osteoporosis rehabilitation therapy. With the CiteSpace and VOSview software, a comprehensive analysis and a visual literature network for co-occurrence and co-citation were performed. Moreover, researchers are now able to quickly grasp the present state of investigation, hot topics, and development trends in this area through visualization of the top ten references with the strongest citation bursts. In spite of this, limitations are unavoidable. First, we put a lot of emphasis exclusively on publications from solely WoS core databases, consequently, several crucial studies may be excluded. It would have been preferable to combine the findings with those from other databases (such as PubMed and Scopus). Notably, Web of Science is the most widely used database in scientometrics, and the majority of bibliometric tools can detect data from this database. Second, there was limited coverage of literature in the field of osteoporosis rehabilitation because only articles and reviews of English-language publications were included, which may have resulted in the omission of high-quality literature in other languages. Therefore, publication bias may be caused by these factors. Additionally, as osteoporosis rehabilitation has been a developing research field in recent years, some recently published, high-quality papers may have a low citation frequency due to their short publication time. There is therefore a discrepancy between the research results and the actual situation. Last but not least, the bibliometric analysis is only a tool, and the results may vary from what you see in real-world research.

Conclusion

During the last few years, the number of published studies on the rehabilitation of osteoporosis has increased significantly. Osteoporosis rehabilitation therapy will continue to receive an increasing number of publications. In conclusion, the study presented the first bibliometric and visual analysis of international research on osteoporosis rehabilitation utilizing the Web of Science database, CiteSpace and VOS view software, and displayed a relatively scientific and intuitive overview of osteoporosis rehabilitation research. We rigorously evaluated publishing data pertaining to the number of published articles, influential nations and institutions, authors and co-cited authors, published journals, and collaborative networks. In addition, we presented both historical and prospective insights into osteoporosis rehabilitation strategies, as well as information regarding major research hotspots, development trends, and frontiers. At present, the major modes and parameters of physical activity/exercise for osteoporosis (including WBV, weight bearing exercises, resistance training), targeted multicomponent training regimens,rehabilitation therapy for postmenopausal women, older women, children and men, osteoporosis related -sarcopenia and fractures, and mesenchymal stem cells are among the frontiers and hotspots of research. These areas indicate the development trend for future research and can serve as a guideline for future research. In summary, our findings may provide useful resources to scholars for understanding the present state and trend of studies on osteoporosis rehabilitation and providing references and suggestions for future research in this area.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

CH and SL: designing this study. LW: writing initial draft and revision. YLi and JH: reviewing and analyzing the literature. JJ and RW: rechecking the manuscript and providing suggestions for amendment. YLia: revising language and content. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.1022035/full#supplementary-material

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Interventions simultaneously promoting social participation and physical activity in community living older adults: A systematic review

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Background: In recent years, there has been a global trend toward an increase in life expectancy and the proportion of elderly people among the population. In this regard, it becomes important to promote active and healthy aging. Physical inactivity and social isolation are both risk factors of many chronic illnesses and highly prevalent in older adults. This challenges communities to develop interventions that reduce these risk factors among elderly populations. The main aims of this study were to summarize community-based interventions that aim to simultaneously promote social participation and physical activity in older adults and to examine their effects.

Methods: We performed a systematic review based on the PRISMA standards. Literature searches were conducted in six scientific databases in July 2021. Articles were included if they had an interventional design, focused on older adults living in the community and measured social participation and physical activity as an outcome. The data were summarized narratively due to the heterogeneity of studies and the variety of outcome measures.

Results: Overall, 46 articles published in English were included. The studies were grouped in (1) interventions with main focus on physical activity promotion; (2) social activities that included a physical activity component; (3) health behavior interventions/ health education interventions; (4) multicomponent interventions; (5) environmental interventions. The majority of the reviewed studies reported positive effects of interventions on physical activity and/or social participation. No study reported negative effects. Analysis of quantitative studies showed that multicomponent interventions have great positive effects on both outcomes. In qualitative studies positive effects were found regardless of intervention type.

Conclusion: This review summarizes the evidence about the effects of community-based interventions that aim to promote social participation and physical activity in older adults. Multicomponent interventions seem to be most suitable for simultaneous promotion of physical activity and social participation. However, high variability in measurement methods used to assess

both social participation and physical activity in the included studies made it difficult to compare studies and to indicate the most effective.

Systematic review registration: www.crd.york.ac.uk, identifier: PROSPERO [CRD42021268270].

KEYWORDS

older adults, community-based intervention(s), physical activity, social participation, physical activity promotion

Introduction

Physical activity and social participation are both vital components of healthy aging. However, many older adults are less physically active (1) and integrated in their social surroundings than adults younger than 65 years (2). Thus, improving our understanding of how to simultaneously increase both physical activity and social participation among adults is important for promoting health in old age. This is especially relevant when considering demographic shifts which will result in the world's population of older people to double by 2050 (3), and with it, the burden of disease among older adults (4).

Regarding physical activity, there are irrefutable health benefits for older people to stay active (5). Based on such evidence, the World Health Organization has issued guidelines on physical activity and sedentary behavior for older people in 2020 (6). These guidelines state that individuals over the age of 65 years should engage in 150–300 min of moderate or 75–150 min of vigorous physical activity. Despite these recommendations, more than 50% of older people (age 80 years and older) worldwide remain physically inactive, with progress in increasing physical activity having largely plateaued in recent years (7).

A review of reviews suggests that interventions conducted among community dwelling older people can result in increases in physical activity (8). Farrance et al. (9) demonstrated that community-based exercise programs can result in long-term adherence rates of 70%. There is also some, albeit limited, evidence that volunteer-lead physical activity interventions can result in positive health outcomes for older people (10). Furthermore, among the same population, eHealth interventions have also shown to be effective in increasing physical activity levels (11). For community dwelling older adults receiving home care, however, the results of interventions to increase physical activity remain inconclusive (12). Altogether, these findings indicate the potential of community-based interventions for increasing physical activity of older adults.

In addition to physical activity, social participation also plays an important role in the health of older individuals. Currently there are overlapping definitions and operationalizations for the concepts of social participation, social capital, social support. Levasseur et al. reviewed and analyzed definitions of social participation within aging literature and suggested defining social participation as a "person's involvement in activities that provide interaction with others in society or the community" (13). Based on this definition, social capital and social support can be considered as consequences of successful social participation, while the absence of social participation can lead to feelings of isolation and loneliness.

Studies have demonstrated that being less socially isolated (14) and belonging to social groups (15) results in important health benefits. In this regard, Steffens et al. reports the effects of a feeling of belonging on mortality as being similar to the effects of physically activity (15). Face-to-face interactions have also been positively linked to the mental health of older adults (16).

Regarding interventions aimed at decreasing feelings of loneliness and increasing social participation, several reviews have provided evidence of their effectiveness. Nevertheless, the results reported in these reviews are inconclusive: Dickens et al. (17) reported that most interventions targeted at reducing loneliness among older people report at least one positive outcome. In 2005, a review by Cattan et al. revealed that social and educational interventions are suitable to decrease feelings of loneliness among older people (18). A review of interventions to increase social capital by Coll-Planas et al. (19), however, concluded that similar interventions did not reduce feelings of loneliness among older people, although high-quality trials showed positive effects on mental health within this target group. In contrast, Franck et al. (20) reported that three out of five trials were able to reduce loneliness among older adults receiving home care.

Social participation and physical activity among older adults may mutually reinforce each other. A review performed by Lindsay Smith et al. (21), shows that older adults who report receiving more social support (from family members) report higher levels of leisure-time physical activity than their counterparts receiving less support. Pels and Kleinert (22) concluded from their review that physical activity can contribute to a reduction in feelings of loneliness among older adults.

However, ways to simultaneously promote social participation and physical activity among this population

group are still unclear. Until now, no systematic review has summarized the literature on interventions aiming to promote both simultaneously. It is currently unclear which types of interventions would optimize the effects of increased social participation and physical activity among older people. In addition, it is uncertain what types of interventions communities should offer to optimize these effects among community-dwelling older adults.

This review therefore sets out to investigate the effects of interventions aiming to simultaneously promote physical activity and social participation among community dwelling older adults. It focuses on studies that have been conducted within real-world community settings, to investigate the effectiveness of these interventions, and thus increase the external validity of the review's findings.

Methods

Study design and background

This review was commissioned by the Federal Centre for Health Education (Bundeszentrale für gesundheitliche Aufklärung; BZgA), Germany. The results of the review are intended to support the participatory project "Aging in Balance" ("Älter werden in Balance"; https://www.aelter-werden-in-balance.de). In the project, researchers and project officers from communities collaborate to establish structures for health and physical activity promotion for older people. It is the intention of this project to improve service offers for citizens and exchange good practice in this field. The results of this review are meant to provide guidance to communities on which services they should offer to increase social participation and physical activity among older people. Methods used to conduct this review were aligned to reach this objective by focusing on trials that were able to investigate effectiveness (by conducting the trial in real-world settings) rather than efficacy (by doing randomized controlled trials conducted in laboratory or field setting) (23).

This review was conducted according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement guidelines (24). The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (www.crd.york.ac.uk) on August 18, 2021, with the registration number CRD42021268270.

Eligibility criteria

Inclusion and exclusion criteria were formulated based on the PICO approach (25). Only articles from peer-reviewed journals published in English or German that fulfilled the criteria described in the Table 1 were eligible.

Information sources and search strategy

A systematic search was performed on PubMed, CINAHL, SPORTDiscus, PsycINFO, Scopus, and Web of Knowledge in July 2021. By discussion with the research team members and project officers from communities of the project "Aging in Balance", a comprehensive search strategy was developed using the PICO approach (25) with a combination of keywords in the categories study sample, intervention, and outcomes.

The search formula was as follows:

("old people" OR "older people" OR elderly OR elders OR aging OR aging OR "old men" OR "old women" OR "older persons" OR "older adults" OR seniors)

AND ("physical activity" OR "physical activities" OR sport OR training OR exercise OR exercises OR fitness OR stretching OR flexibility OR strength OR resistance OR balance OR endurance OR aerobic OR mobility OR walking OR cycling OR yoga OR pilates OR dancing OR swimming OR jogging OR hiking OR "tai chi" OR taichi OR taijiquan OR gardening OR "qi gong" OR qigong)

AND (Intervention OR programme OR program OR trial)

AND ("social interaction" OR "social interactions" OR "social participation" OR "social support" OR "social network" OR "social networks" OR "social isolation" OR "social activity" OR "social activities" OR "social engagement" OR "social involvement" OR "social inclusion" OR "social life" OR loneliness OR "interpersonal communication" OR "interpersonal interaction" OR "interpersonal interactions" OR "interpersonal relationship" OR "interpersonal relationships" OR "community involvement" OR "community participation" OR "community life").

Study selection

Two reviewers independently screened and selected relevant articles using the Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia; www.covidence.org). The first stage consisted of screening titles and abstracts. Afterwards, full texts of potentially relevant articles were reviewed. If the title and/ or abstract indicated that the study fulfilled the eligibility criteria or did not provide sufficient information, both reviewers screened the full texts for eligibility. When necessary, Supplementary material were also assessed for additional information. Disagreements between the reviewers were discussed in the research team until a consensus was reached.

Data extraction

Data of included studies were extracted and summarized by one researcher, with verification by another reviewer,

TABLE 1 Eligibility criteria.

	Inclusion criteria	Exclusion criteria
P–population	Study should include only older adults (the average age of the sample should be above 65 years) or in mixed age populations results for older adults are reported separately. Participants were freely living in the community (either at home or in places of residence that, on the whole, do not provide residential health related care or rehabilitative services).	Participants lived in places that provide residential health related care or rehabilitative services (e.g., nursing homes).
I–intervention	All kinds of interventions that simultaneously promote social participation and physical activity by bringing at least two people together in public spaces.	Intervention did not take place in public spaces. Intervention focused only on patients with specific disease, or carried out as part of rehabilitation, or performed by medical staff. Intervention included only instructor/therapist and one participant.
C–comparison	No inclusion criteria.	No exclusion criteria.
O–outcome	Study included subjective or objective measurement of social participation (e.g., loneliness, social isolation, social support, participants' opinions of changes in their social participation during intervention). Study provided exercise classes that increased overall time of physical activity or included subjective or objective measurement of physical activity or any kind of outcome that constitutes a measure of physical performance that is sought to improve by PA/exercise (e.g., strength, mobility, participants' opinions on changes in their PA level during intervention).	Study did not measure outcomes of social participation. Study that did not provide additional physical activity and did not measure physical activity or any kind of outcome that constitutes a measure of physical performance that is sought to improve by PA/exercise (e.g., strength, mobility).
S, study type	Intervention quantitative and quantitative studies (e.g., effectiveness trials undertaken in real-world implementation settings, quasi-experimental studies, post-intervention).	Study had a cross-sectional design.

in order to reduce bias and error. Extraction included the following items: general study information (authors, year of publication, country), intervention description (name, type, duration, frequency, length of session, description of control conditions), sample characteristics (age, special conditions, functional status, activity status, language skills, sample size, mean age, proportion of females), type of collected data (quantitative, qualitative or mixed), quantitative (questionnaire, test, etc.) and/or qualitative (interview, focus groups) methods of measuring social participation and physical activity/fitness, results on effects of interventions on social participation and physical activity/fitness level.

Risk of bias assessment

The methodological quality of each study was assessed with the QualSyst tool- developed by the Alberta Heritage Foundation for Medical Research (26). This tool was chosen because it assists in the evaluation of intervention studies with different designs, including both qualitative and quantitative studies. Quantitative studies were evaluated according to the following 14 criteria: objective, study design, method of subject/comparison group selection, subject characteristics, intervention allocation, blinding, outcome measure definition, exposure measure definition, sample size, analytic methods, estimate of variance, control for confounding, reporting results and conclusions. For qualitative studies the tool provided the following ten criteria: objective, study design, context, connection to theoretical framework, sampling strategy, data collection, data analysis, verification procedure, conclusions, and reflexivity. Depending on the degree to which the specific criteria were met, each item was scored as "yes" = 2, "partial" = 1, or "no" = 0. If an item was not applicable to the study it was marked "N/A" and excluded from the summary score. The summary score (range: 0–1) indicates the risk of bias, with a higher score indicating higher quality and thus less risk of bias.

Data synthesis and analyses

Before data analyses, the included interventions were grouped into five different intervention types that were defined based on a discussion with project officers from communities of the project "Aging in Balance": (1) interventions which primarily focused on physical activity promotion; (2)

TABLE 2 Definition of intervention types.

Type	Description
1) Physical activity/exercise interventions	Interventions with the main focus on offering participants physical activity or exercise. Increased social participation might have been an additional outcome, however interventions did not provide any additional social activities.
2) Social activity interventions	Interventions provided some types of social activities which naturally included some physical activity, but participants did not receive any direct instructions to increase physical activity/exercises.
3) Health education interventions	Interventions included only lectures or consultations on how to improve health by increasing physical activity level and social participation. No exercise or social activities were offered to participants.
4) Environmental interventions	Interventions consisted only of changes in the built environment in a way that it can increase physical activity and social participation for the residents of a community.
5) Multicomponent interventions	Interventions which combined two or more components from the interventions described above. For example, exercise sessions were combined with additional social activities.

social activities that included physical activity; (3) health education interventions; (4) environmental interventions; (5) multicomponent interventions. The criteria for classification are presented in Table 2. Associations between interventions and changes in social participation and physical activity/fitness level were analyzed for each type.

The level of evidence within each type of interventions was summarized narratively due to the heterogeneity of studies and the variety of intervention contents and outcome measures, which prevented a quantitative meta-analysis. For the quantitative studies, we used an approach of summarizing results from studies with different designs that has been suggested by Sallis et al. (27) and also been used by Lindsay Smith et.al (21) in a systematic review with a similar topic. Using this approach, each study was rated as + or –, depending on if a statistically significant positive or negative effect of an intervention was found, and as 0 if no statistically significant associations were found. Ratings were assigned separately for effects on social participation and physical activity/fitness level. Overall ratings for quantitative studies in each category were calculated as "0" (No association; 0–33% of the findings supported the association), "?" (indeterminate association; 34–59% of the findings supported the positive or negative association), "+" or "–" (positive or negative association; 60–100% of the findings supported the association).

Results

Study selection process

Electronic searches across the six databases identified 11,900 records, 7,935 remained after removing duplicates. The titles and abstracts were assessed for relevance based on eligibility criteria, resulting in 262 papers retrieved for full text review. After the full text screening, 56 papers met the inclusion criteria. Of these articles, 46 were written in English or German (languages spoken by at least two members of the research team) and included in the analysis. The selection process is presented in a PRISMA flow-diagram (see Figure 1). Characteristics of the included studies are shown as a structured table (see Table 3) and as a narrative summary (see Appendix 1).

Characteristics of included studies

The 46 papers in this review included reports from 45 studies [McKay et al. and Franke et al. analyzed the same data with different methods (28, 29)]. The included articles were published between 2002 and 2021. Sixteen studies were conducted in North American countries, 12 in Asian countries, ten in European countries, four in Brazil, two in Australia, and one in New Zeeland. There was a total of 16,285 participants across 45 studies, ranging from six (30) to 11,701 (31) per study. The majority of participants were females. There were four studies which consisted solely of female participants, and in 18 studies females made up 75% or more of the sample. Meanwhile, just one intervention was designed exclusively for men (32) and only one further study consisted of more men than women (33). This review included 29 quantitative studies, nine qualitative studies, and seven mixed-methods studies. The way social participation and physical activity were measured and analyzed varied widely between studies.

Measurements of social participation

Out of the studies which used quantitative methods, 32 applied different self-reported questionnaires to assess post-intervention changes in social participation. In one study,

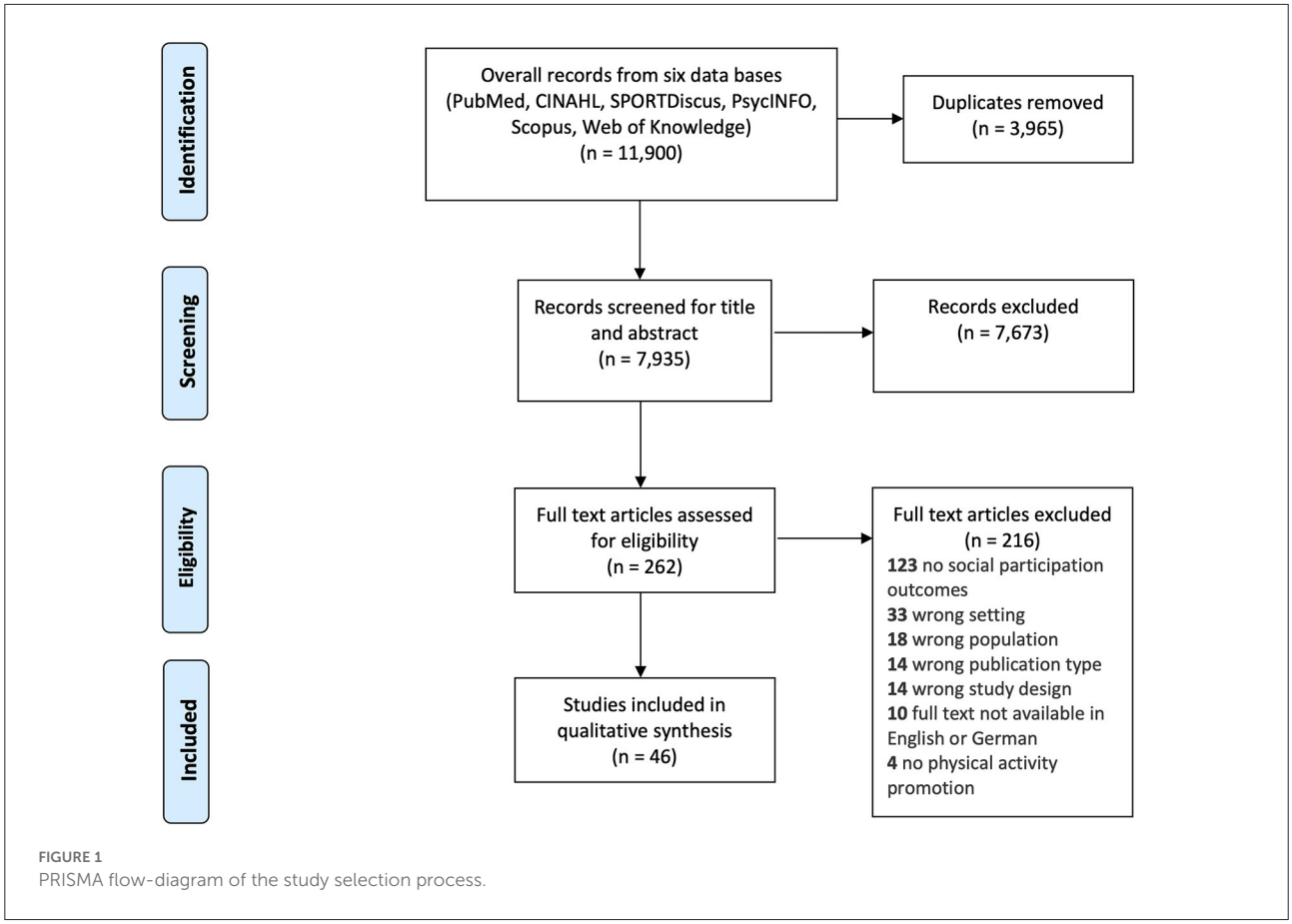

FIGURE 1
PRISMA flow-diagram of the study selection process.

researchers counted the number of participants engaged in social interaction before and after changing the built environment (34). From studies using qualitative methods, nine performed interviews and three conducted focus groups to let participants describe their experiences and perceived changes in social participation during the interventions.

Measurements of physical activity/fitness

The most common methods of measuring a change in physical activity/fitness level, among the studies which employed quantitative methods, were functional fitness tests (21 studies) and self-reported physical activity questionaries (12 studies). Two studies used accelerometers to objectively assess time spent on physical activity and two studies used pedometers to objectively measure daily steps. Nine studies used interviews and two organized focus groups to gather participants experiences with changes in their physical activity/fitness level. Eight studies engaged participants in extra physical activity without measuring changes in physical activity levels.

Risk of bias assessment

The average quality score of included studies was 0.77 (0.76 for quantitative studies and 0.78 for qualitative studies) with a range of 0.41–0.95. In most of the quantitative studies, the research question, objective, analysis, and results were sufficiently described and the study design was appropriate. The main sources of bias were related to randomization, blinding of investigators, confounding, and subject selection. The quality of some quantitative studies suffered from poor sample representativeness or lack of a control group. In all qualitative studies, the context of study was well-described, and the conclusions were supported by results. The research question, design, and connection to a theoretical framework were also sufficiently presented in the majority of the studies. The main sources of bias for qualitative studies were related to sampling strategy and absence of reflexivity on how researcher's personal characteristics and methods could have impacted obtained data. Quality scores of the individual studies are reported in Table 3.

Effects of community-based interventions on social participation and physical activity outcomes

The majority of the reviewed quantitative studies reported interventions having a statistically significant positive effect on social participation (23 studies) and physical activity (18 studies). All qualitative studies showed positive effects on perceived social participation and on the physical activity/fitness levels of the participants. There were no studies which reported negative effects.

The studies were grouped as (1) interventions which primarily focused on physical activity promotion; (2) social activities that included physical activity; (3) health education interventions; (4) environmental interventions; (5) multicomponent interventions. The results of quantitative studies by intervention types are presented in the Table 4.

Interventions focused on physical activity promotion

Of the included studies, 21 described interventions which focused primarily on providing different types of physical activity, and also measured intervention effects on social participation among older individuals. Studies included a total of 1,722 participants. Most of the studies (13 studies) used quantitative methods, five used qualitative methods, and three used mixed methods. During the interventions, participants performed different types of physical activity including walking, dancing, tai chi, fall prevention training, aquatic training, volleyball, and others (see Table 3).

Positive effects of the physical activity interventions on physical activity and fitness outcomes were observed and reported in 70% of the quantitative studies (see Table 4). The effects of the interventions on social participation, however, were not as obvious (53.3% of quantitative studies reported positive associations). In the qualitative studies, participants reported that involvement in the programs gave them the opportunity to get out and be among other people with similar experiences (32, 35), feel more social engagement and social support (36, 37), be more socially connected (38, 39), and expand their communication beyond the group exercise (39). In the participants' opinion, physical activity programs also helped them to improve their physical performance in everyday life (e.g., strength, endurance, balance, coordination) (32, 35, 37, 39, 40).

Social activities that included a physical activity component

Six of the reviewed studies, including 580 participants, presented the results of interventions which focused on performing different social activities with a physical activity component. These activities included social farming, community gardening, a choir program, dance evenings, outdoor adventure activities, environmental volunteering, and social activities in city parks.

From the four studies that used quantitative methods, three (75%) reported positive effects of the interventions on social participation outcomes; only one study, however, reported positive effects on physical activity/fitness outcomes (33). Qualitative analysis showed that participants noticed improvements in their social participation and felt that the interventions helped them to become more physically active (33, 41, 42).

Health behavior interventions/health education interventions

Two studies, including a total of 534 participants, examined interventions that promoted physical activity and social participation solely through lectures or consultation. McKay et al. and Franke et al. reported the results of the health promotion program "Choose to Move", which included consultations with active coaches, motivational meetings, and telephone support (28, 29). Mendoza-Ruvalcaba et al. described the results of "the Vital Aging" program to promote active aging through teaching basic knowledge about aging, and promoting healthy lifestyles (43). McKay et al. and Mendoza-Ruvalcaba et al. collected quantitative data and Franke et al. used a mixed methods approach. The results showed that the effects of health education interventions on social participation and physical activity/fitness outcomes are rather unclear. While the "Choose to Move" program showed positive effects on both social participation and physical activity, the "Vital Aging" program had no effect on either of these outcomes.

Environmental interventions

Schmidt et al. presented the results of the environmental intervention "Move the Neighborhood" a program based on a participatory research approach, which aimed to increase the use of neighborhood open spaces to promote active living through social interaction and physical activity (34). Together with landscape architects, local older adults explored and developed ideas on how to improve neighborhood open spaces. Renovations were later implemented based on the results of this collaboration. To evaluate the effects of renovations on older adults, authors used a mixed methods approach. They gathered data on the amount of older people engaged in social interaction and physical activity in renovated areas and conducted qualitative interviews with older people to see how these renovations affected social interaction. The environmental intervention study showed that renovating the neighborhood open spaces had some positive effects on social participation and physical activity.

TABLE 3 Studies overview.

References	Country	Intervention	Number of participants	Gender composition	Data structure	Methods of measuring social participation	Methods of measuring PA/fitness level	Effect on social participation	Effect on PA/fitness	Quality (quant./qual.).
Physical activity promotion interventions										
Arnett et al. (36)	USA	PA program to reduce falling risk	120	79.2% female	Mixed	Open-ended survey	Functional fitness tests	Yes	Yes	0.91/0.65
Barbosa et al. (53)	Brazil	Aquatic training program	28	89.3% female	Quantitative	Self-reported questionnaire	–	No	-	0.59
Barraagan (38)	USA	Fitness program	55	Only females	Qualitative	Focus group	–	Yes	–	0.85
Bidonde et al. (35)	Canada	Fitness program	9	Only females	Qualitative	Semi-structured interview	Semi-structured interview	Yes	Yes	0.90
Brustio et al. (54)	Italy	Dance training program	163	75.5% female	Quantitative	Self-reported questionnaire	Functional fitness tests	Yes	Yes	0.77
Carrapatoso et al. (40)	Portugal	Walking	19	84.2% female	Mixed	Semi-structured interview	• Functional fitness tests • Self-reported questionnaire • Semi-structured interview	Yes	Yes	0.68/0.85
Cedergren et al. (55)	USA	Volleyball program	222	79.7% female	Quantitative	Self-reported questionnaire	–	Yes	–	0.91
Chan et al. (56)	China	Tai Chi	48	76% female	Quantitative	Self-reported questionnaire	–	Yes	–	0.88
Dionigi (37)	Australia	Resistance training	10	60% female	Qualitative	Interview	Interview	Yes	Yes	0.70
Ehlers et al. (57)	USA	Dance, or strength/stretching/ stability, or walking, or walking plus (with nutrition supplements)	247	68.4% female	Quantitative	Self-reported questionnaire	–	Yes	–	0.88
Figureira et al. (58)	Brazil	PA program (walking, hydrogymnastics, strengthening, and stretching)	70	62.5% female	Quantitative	Self-reported questionnaire	–	Yes	–	0.54
Frei et al. (59)	Switzerland	Walking groups	29	75.9% female	Mixed	• Self-reported questionnaire. • Structured interview	• Accelerometer • Functional fitness tests. • Structured interview	No	Yes	0.86/0.90
Gomeñuka et al. (60)	Brazil	Nordic walking and free walking	1	72.7% female	Quantitative	Self-reported questionnaire	Functional fitness tests	Yes	Yes	0.92
Kohut et al. (61)	USA	Cardiovascular exercise or strength/flexibility/balance exercise	87	65% female	Quantitative	Self-reported questionnaire	Functional fitness tests	No	Yes	0.88

(Continued)

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TABLE 3 (Continued)

References	Country	Intervention	Number of participants	Gender composition	Data structure	Methods of measuring social participation	Methods of measuring PA/fitness level	Effect on social participation	Effect on PA/fitness	Quality (quant./qual.).
Komatsu et al. (39)	Japan	Low intensive exercise program	26	57.7% female	Qualitative	Focus group	Focus group	Yes	Yes	0.95
Liu and Tsui (62)	China	Tai Chi	122	87% female	Quantitative	Self-reported questionnaire	• Functional fitness tests. • Self-reported time spent on exercise	No	No	0.92
Maki et al. (63)	Japan	Walking groups	150	70.7% female	Quantitative	Self-reported questionnaire	• Functional fitness tests. • Pedometer	No	Yes	0.77
McAuley et al. (64)	USA	Walking or stretching	174	71.8% female	Quantitative	Self-reported questionnaire	–	Yes	–	0.88
Streber et al. (65)	Germany	Multimodal PA program	87	78.2% female	Quantitative	Self-reported questionnaire	Pedometer	No	No	0.73
Wang (66)	USA	Yoga	18	88.9% female	Quantitative	Self-reported questionnaire	Functional fitness tests.	No	No	0.50
Wickman et al. (32)	Denmark	Floorball	37	only males	Qualitative	Semi-structured interview	Semi-structured interview	Yes	Yes	0.55
Social activities that included a physical activity component										
Austin et al. (30)	USA	Community gardening	6	50% female	Quantitative	Self-reported questionnaire	Functional fitness tests	Yes	No	0.41
Boyes (41)	New Zeeland	Outdoor adventure activities	80	63% female	Qualitative	Semi-structured interview	Semi-structured interview	Yes	Yes	0.70
Vadineia da Silva et al. (42)	Brazil	Dance evenings	12	66.7% female	Qualitative	Interview	Interview	Yes	Yes	0.70
Gagliardi et al. (67)	Italy	Social farming	73	63% female	Quantitative	Self-reported questionnaire	Self-reported time spent on exercise	Yes	No	0.80
Gagliardi et al. (33)	Italy	Environmental volunteering and social activities in city parks	19	42.1% female	Mixed	Self-reported questionnaire. Interview	• Self-reported questionnaire • Interview	Yes	Yes	0.75/0.85
Johnson et al. (68)	USA	Choir program	390	76.4% female	Quantitative	Self-reported questionnaire	Functional fitness tests	Yes	No	0.83
Health behavior interventions/ health education interventions										
Franke et al. (29)	Canada	Health promotion program	452	77% female	Mixed	Self-reported questionnaire. Qualitative survey	Self-reported PA questionnaire	Yes	Yes	0.86/0.85
McKay et al. (28)	Canada	Health promotion program	458	77% female	Quantitative	Self-reported questionnaire	Self-reported PA questionnaire	Yes	Yes	0.91
Mendoza-Ruvalcaba and Fernández-Ballesteros (43)	Mexico	Health education	76	only females	Quantitative	Self-reported questionnaire	Self-reported PA questionnaire	No	No	0.62

(Continued)

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TABLE 3 (Continued)

References	Country	Intervention	Number of participants	Gender composition	Data structure	Methods of measuring social participation	Methods of measuring PA/fitness level	Effect on social participation	Effect on PA/fitness	Quality (quant./qual.).
Environmental interventions										
Schmidt et al. (34)	Denmark	Renovation of neighborhood open spaces	10	74.2% female	Mixed	• Observing number of people engaged in social interaction. • Interview	Observing number of people engaged in PA	yes	yes	0.64/0.85
Multicomponent interventions										
Ahn et al. (69)	South Korea	Health education + exercise + social activities	33	Only females	Quantitative	Self-reported questionnaire	Functional fitness tests	Yes	Yes	0.77
Cardenas et al. (70)	USA	Sport + social activities	444	52% female	Quantitative	Self-reported questionnaire	Self-reported questionnaire	Yes	Yes	0.91
Hopman-Rock and Westhoff (71)	Netherlands	Health education + exercise	390	82% female	Quantitative	Self-reported questionnaire	Self-reported questionnaire	Yes	Yes	0.88
Huang et al. (72)	Taiwan	Tai Chi + cognitive-behavioral intervention	186	58.6% female	Quantitative	Self-reported questionnaire	Functional fitness tests	Yes	Yes	0.92
Hwang et al. (73)	Canada	Health education + fitness program to reduce falls + walking groups + socialization activities	16	94% female	Qualitative	Semi-structured interview	Semi-structured interview	Yes	Yes	0.90
Kamegaya et al. (74)	Japan	Exercise + leisure social activities	52	90.4% female	Quantitative	Self-reported questionnaire	Functional fitness tests	No	No	0.77
Kim et al. (75)	South Korea	Health education + exercise + group activities	39	89.7% female	Quantitative	Self-reported questionnaire	Functional fitness tests	Yes	Yes	0.69
McMahon et al. (76)	USA	Fall-reducing exercise + motivational support	30	93.3% female	Quantitative	Self-reported questionnaire	• Self-reported questionnaire • Accelerometer • Functional fitness tests	Yes	Yes	0.77

(Continued)

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TABLE 3 (Continued)

References	Country	Intervention	Number of participants	Gender composition	Data structure	Methods of measuring social participation	Methods of measuring PA/fitness level	Effect on social participation	Effect on PA/fitness	Quality (quant./qual.).
McNamara et al. (77)	Australia	Exercise + social activities	21	71% female	Mixed	Interview	Functional fitness test. Interview	Yes	Yes	0.55/0.60
Merchant et al. (78)	Singapore	PA + cognitive exercises + social activities	197	75% female	Quantitative	Self-reported questionnaire	Functional fitness tests	Yes	Yes	0.46
Ren et al. (79)	China	Health education + psychological intervention + Taijiquan exercise	121	N/A	Quantitative	Self-reported questionnaire	–	Yes	–	0.77
Seino et al. (31)	Japan	Exercise + social activities + improving community environment	11,701	51.4% female	Quantitative	Self-reported questionnaire	• Self-reported questionnaire • Functional fitness tests	No	No	0.79
Shvedko et al. (80)	UK	Walks + health education + social interaction	25	56% female	Qualitative	Focus group	Focus group	Yes	Yes	0.80
Yamamoto et al. (81)	Japan	Health education + exercise	31	56% female	Quantitative	Self-reported questionnaire	Functional fitness tests	Yes	Yes	0.75
Yeom and Fleury (82)	USA	Exercise + social support + education + motivational support	64	76.6% female	Quantitative	Self-reported questionnaire	• Self-reported questionnaire • Functional fitness tests	Yes	Yes	0.77

–, No outcome of the category was measured; quant., quantitative; qual., qualitative; PA, physical activity.

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TABLE 4 Summary of quantitative studies results.

Outcomes	Associations	Studies (first author, year, country)								Summary score
PA/exercise interventions										
Social participation	Mostly positive*	Cedergren, 2007, USA	Brustio, 2018, Italy	Figureira, 2012, Brazil	Gomeñuka, 2019, Brazil	Chan, 2017, China	Ehlers, 2017, US	McAuley, 2000, USA	Carrapatosoa, 2017, Portugal	? (53.3% positive associations)
	Mostly no association	Streber, 2017, Germany	Frei, 2019, Switzerland	Liu, 2014, China	Kohut, 2006, US	Maki, 2012, Japan	Wang, 2010, USA	Barbosa, 2018, Brazil		
PA/fitness	Mostly positive	Frei, 2019, Switzerland	Carrapatosoa, 2017, Portugal	Kohut, 2006, US	Brustio, 2018, Italy	Maki, 2012, Japan	Gomeñuka, 2019, Brazil	Arnett, 2019, US		+ (70% positive associations)
	Mostly no association	Streber, 2017, Germany	Liu, 2014, China	Wang, 2010, USA						
Social activities that included PA component										
Social participation	Mostly positive	Johnson, 2018, US	Gagliardi, 2018, Italy	Austin, 2006, USA						+ (75% positive associations)
	Mostly no association	Gagliardi, 2020, Italy								
PA/fitness	Positive	Gagliardi, 2020, Italy								0 (25% positive associations)
	Mostly no association	Johnson, 2018, US	Gagliardi, 2018, Italy	Austin, 2006, USA						
Health behavior intervention/Health education (lectures, counseling)										
Social participation	Mostly positive	McKay, 2018, Canada								? (50% positive associations)
	Mostly no association	Mendoza-Ruvalcaba, 2016, Mexico								

(Continued)

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TABLE 4 (Continued)

Outcomes	Associations	Studies (first author, year, country)										Summary score
PA/fitness	Mostly positive	McKay, 2018, Canada										? (50% positive associations)
	Mostly no association	Mendoza-Ruvalcaba,2016, Mexico										
Multicomponent												
Social participation	Mostly positive	Hopman-Rock, 2002, Netherlands	Ahn, 2014, South Korea	Kim, 2020, South	Cardenas, 2009, US	Ren, 2021, China	Huang, 2011, Taiwan	Yamamoto, 2020, Japan	Yeom, 2014, US	McMahon, 2016, US	Merchant, 2021, Singapore	+ (83.3% positive associations)
	Mostly no association	Seino, 2021, Japan	Kamegaya, 2013, Japan									
PA/fitness	Mostly positive	Hopman-Rock, 2002, Netherlands	Ahn, 2014, South Korea	Kim, 2020, South	Cardenas, 2009, US	Huang, 2011, Taiwan	Yamamoto, 2020, Japan	Yeom, 2014, US	McMahon, 2016, US	Merchant, 2021, Singapore		+ (81.8% positive associations)
	Mostly no associateon	Seino, 2021, Japan	Kamegaya, 2013, Japan									

*The associations were considered as positive only if reported results were statistically significant.
PA, physical activity.
0, No association (0–33% of the findings supported the association); ?, indeterminate association (34–59% of the findings supported the positive or negative association); +, positive association (60–100% of the findings supported the association) [cut-offs were suggested in (27)].

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Multicomponent interventions

Interventions which combined two or more different components from other approaches (physical activity/exercise, social activities, health education, environment changes) were classified as multicomponent: 15 such studies, with a total of 13,350 participants, were reviewed. All 15 included some form of exercise or physical activity. In addition, ten interventions included social group activities, six studies organized health education, five studies provided psychological or motivation support, and in one study improvements were made to the built environment.

Analysis of the quantitative studies showed that when compared to the other intervention groups, multicomponent interventions had a greater positive effect on both social participation outcomes (81.8% of studies) and physical activity/fitness outcomes (80% of studies). The results of the qualitative studies support this finding.

Discussion

This review has summarized evidence on the effects of community-based interventions which aimed to promote social participation and physical activity in older adults. It focused on trials conducted within the communities. To the best of our knowledge, this is the first review that focused on investigating the effectiveness, rather than efficacy, of intervention studies. While this approach led to the inclusion of some studies with lower scientific evidence, it also describes the interventions used in real-world conditions, in as much as possible. Based on this, we are able to form recommendations for communities (see below).

This review summarized results from various intervention study designs including pre- and post-test, retrospective, controlled trials and randomized controlled trials. A variety of intervention types were identified and allocated to the physical activity interventions, social activities that included physical activity, health education intervention, environmental interventions, and multicomponent interventions.

The majority of quantitative studies reported positive effects of interventions on social participation (68% of studies) and physical activity (67% of studies). All included qualitative studies reported that participants believed the interventions had had positive effects on their physical activity and social participation. It could be argued that this is due to the fact that quantitative measures might often be less sensitive to change. However, it could also be disputed that qualitative inquiry is more prone to socially desirable answers.

Our findings that interventions promoting social participation and physical activity can have positive effects on older adults are in line with findings of other reviews on similar topics (8, 17, 44). The classification of interventions into different types made it possible to identify approaches that more often reported statistically significant positive changes in physical activity and social participation of participants. Interventions that provided only physical activity/exercise activities often showed more positive effects on physical activity/fitness outcomes, rather than on social participation, which is in line with the findings from another review (45). The majority of interventions which focused on social activities had positive effects on social participation outcomes and nearly no effect on physical activity/fitness levels. The effect of health education interventions is rather unclear. It was impossible to make a comparison regarding environmental interventions, since only one such study with a small number of participants (ten older adults) has been identified. Further research needs to be done on these types of interventions in the future. In agreement with the review from Zubala et al. (8), we found that in quantitative studies on multicomponent interventions, more than 80% reported statistically significant effects on both social participation and physical activity/fitness outcomes – the highest result among all intervention types. This is in line with principles of ecological perspectives on health behavior change (46).

We observed a high variability in measures on physical activity and social participation outcomes across trials. This finding is in line with previous reviews on similar topics (17, 44) and this fact prevents comparisons between studies and interventions. This heterogeneity allowed us to summarize data only narratively and prevented a quantitative meta-analysis.

The methodological quality of the studies was also very heterogeneous, which has previously been noted in other reviews on similar topics (18, 44). The methodological quality of the reviewed studies was limited due to a lack of appropriate control conditions, consideration of cofounders and poor sample representatives (small number of participants, high loss to follow-up). There were many trials that reported on a small number of participants. In quantitative studies, randomization, confounding, and subject selection were often poorly described. In qualitative studies, authors often did not reflect on how the personal characteristics of researchers and their methods could have impacted the obtained data. Blinding of the participants was often not implemented as it is in general complicated for physical activity interventions. From the 23 studies where blinding of investigators was potentially possible, less than half (ten studies) used this opportunity and at least partly described the process. It is recommended that future studies find a way to blind at least investigators when it is possible.

More than 70% of participants in the reviewed studies were female and there seemed to be few interventions that particularly target males. Consequently, women seem to be overrepresented in the studies, even when considering that with 55% of the global population aged 65 years or over women comprise a majority of older persons worldwide (47). This might also be due to the fact that older women are much more likely to attend health prevention programs and community-based health screening

programs than older men (48, 49). In a study from Sims-Gould et al. male participants reported that knowing that other men are also participating in a program is an important and attractive feature (50). The development and evaluation of programs which are more geared toward men or which are of more interest to a male audience, such as the "Men's Sheds" (51), can be suggested as a direction for future research.

The included studies did not specifically address minorities and socially disadvantaged groups or report data regarding potential health disparities (52). Thus, it remains unclear whether these interventions are suitable to prevent health inequalities or, on the other hand, if they might potentially widen the health gap between advantaged and disadvantaged groups of older people.

Guidance to communities

Our main findings can be framed as recommendations to project officers working in communities to provide services to older people. Considering the findings of our review and the varied effectiveness of the different types of interventions to increase social participation and physical activity, certain (although preliminary) conclusions can be drawn:

- Health behavior and health education interventions that predominantly rely on lecturing and counseling do not work well. This type of interventions should only be conducted when there are special occasions that warrant this.
- Physical activity/exercise interventions increase physical activity, and social activities interventions increase social participation. Depending on the aim, one can choose which of the two to conduct accordingly.
- Physical activity/exercise interventions are more likely to increase social participation than social activity interventions are to increase physical activity. Due to the additional health benefits that come through physical activity/exercise interventions, these interventions might be a "best buy" for older people who are not too frail to participate in a physical activity program.
- Multicomponent interventions that combine social and physical activities had the highest rate of statistically positive results in comparison with other types of interventions. Services which are able to combine these different types of activities (e.g., health education, physical activity, and environmental measures) may be most beneficial.
- Specific efforts are required to reach minority or socially disadvantaged populations to prevent health inequalities and pursue health equity. Additionally, interventions specifically addressing the needs and interests of men are needed to attract this target group.

The decisive factors in choosing the type of intervention are undoubtedly the resources existing in the community and the characteristics of the population living in it. However, we recommend that communities take other factors into account that may generally contribute to or, conversely, hinder the implementation and promotion of such interventions. Organizers should consider in advance: the strategies for attracting participants to the program, the availability of the program venue, and the number and the necessary number of staff to conduct regular classes (50).

Strengths and limitations

To the best of our knowledge, this is the first review focused on the effectiveness of interventions aiming to simultaneously promote physical activity and social participation among community-dwelling older people. The systematic search of relevant studies, with various study designs, was conducted in six electronic databases, and the methodological quality (risk of bias) was evaluated for all included studies. We see it as a strength of our study, that we were able to include 45 trials and draw some, although limited, conclusions regarding the effectiveness of different types of interventions.

We faced certain difficulties when conducting the review. From the outset, it was decided that an effectiveness review would need to be conducted, rather than an efficacy review (23). We were thus interested in trials that had been conducted in real-world settings, with free-living populations. This turned out to be difficult to determine for some studies, since the contexts within which trials were conducted and the recruitment of participants were sometimes ambiguously described.

Distinguishing between physical activity/exercise, social activities including physical activity, health education, and multicomponent interventions in the analysis was challenging, and for some interventions might have resulted in classifications that could be disputed. This was partially due to the fact that, like in other health behavior reviews, interventions were sometimes described only cursorily. This type of classification can also be regarded as being somewhat arbitrary. A dance class for example could, depending on one's perspective, be classified as an exercise intervention, a social activity, or a multicomponent intervention. We attempted, however, to describe the content of the intervention since it was our intention to provide project officers with some guidance on what to do. Additionally, most trials did not focus on minority or socially disadvantaged populations. This limits the generalizability of our findings.

This systematic review focused only on the effects of the interventions and did not provide information on the implementation process, such as how participants were recruited, drop-off rates, or protentional challenges. It could be recommended to focus on implementation effectiveness in further research.

Conclusions

This systematic review sheds light on the effectiveness of community-based programs promoting physical activity and social participation for older people. Notwithstanding the large variability in study designs and measurements, overall, the findings from this review show that among the existing interventions there are some that can simultaneously increase physical activity and improve social participation among older people. The evidence also highlights multicomponent interventions' higher probability to show positive effects. The analyzed studies allowed for the formulation of some recommendations for communities who aim to promote physical activity and social participation in older adults. Further research on the effectiveness of interventions is recommended, especially in the field of rarely studied interventions, such as environmental interventions.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

AT and VH conducted the literature search. AT, KA-O, and VH performed abstract/title screening, full-text selection, and data extraction. DM participated in the quality assessment. AT and KA-O analyzed data and summarized results. AT and KA-O with support from DM prepared a first draft of the manuscript. VH, AB, CC, CR, and AR critically revised the draft. AR supervised this work. All authors contributed to conceptualization of the study and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.1048496/full#supplementary-material

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Relationship between knee joint discomfort, self-management behavior, and quality of life in the middle-aged and elderly people in China: A cross-sectional study

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Background: The aim of this study was to describe the knee joint discomfort, self-management behavior, and quality of life (QoL) in the middle-aged and elderly people in China and to clarify the relationship between the knee joint discomfort, self-management behavior, and QoL.

Methods: It is a cross-sectional study and in this study, a stratified multistage random sampling method was used to collect data on the three factors such as knee joint discomfort, self-management behavior, and QoL among the middle-aged and elderly people in the Hunan Province. Spearman's correlation analysis was used to test the relationship between the knee joint discomfort, self-management behavior, and QoL.

Results: The results of the present study showed that among them, the prevalence of knee pain was the highest (52.1%), followed by knee weakness (42.5%), numbness (41.8%), cold feeling (40.0%), tenderness (38.3%), and distension feeling (37.5%). Average score of self-management of knee joint discomfort in the middle-aged and elderly people was 2.14 ± 0.67. The level of self-management in each dimension ranged from high to low as emotional management, daily management, symptoms management, and information management. The average scores of physical component summary (PCS) and mental component summary (MCS) were 42.85 ± 5.34 and 43.62 ± 8.43, respectively. The occurrence, frequency, and severity of discomfort symptoms were positively correlated with the symptoms management, daily management, information management, and self-management behaviors, and negatively correlated with the emotional management, PCS and MSC, except for the occurrence of discomfort symptoms ($P < 0.05$).

Conclusion: Knee joint discomfort was prevalent in the middle-aged and elderly people. In addition, they displayed a low level of self-management behavior and poor QoL. The middle-aged and elderly people faced knee discomfort symptoms, the more frequent and severe symptoms, the higher level of symptom management, daily management, and information management, and the lower level of emotional management and QoL.

KEYWORDS

knee, self-management, quality of life, middle-aged and elderly, China

Introduction

By the end of 2018, China's elderly population over the age of 60 years had exceeded 240 million, accounting for 17.9% of the total population (1). Globally, joint disease, which becomes more pronounced with age, is the leading cause of disability in the middle-aged and older people (2). Osteoarthritis (OA) is a debilitating common joint disease that affects an estimated 302 million people worldwide (3–5). Large epidemiology studies have found that the hands, knees, and hips are the most commonly affected joints (6). In particular, the knee joints, which bear all the weight of the body, are the most frequently troubled joints (7). With acceleration of the aging process in China, the incidence of knee OA (KOA) is only 2% for those below 45 years of age, 30% for those between 45 and 60 years of age, and 68% for those over 65 years of age (8).

On the basis of recent studies, it is brought to light that KOA is the most common cause of knee discomfort among middle-aged and older adults (9). Knee discomfort is a subjective sensation that may vary significantly depending on the patient and the patient's health condition. In fact, knee discomfort is characterized by severe pain, stiffness, swelling, and loss of normal joint function (10). Previous studies have mainly focused on the severe stage of knee discomfort, such as obvious joint symptoms of KOA and perioperative acute pain of knee replacement (4), while there were a few investigations on the early stage of knee discomfort. In addition, there is a dearth of appropriate multidimensional self-assessment tools to accurately evaluate the characteristics of various symptoms of knee discomfort in the middle-aged and elderly people.

Given the increasing demands for improved health outcomes, self-management behaviors of the middle-aged and elderly people cannot be ignored (11). Evidence shows that adequate self-management behaviors have been linked to preventing or reducing health risks and optimizing the quality of life (QoL) (7). In the present study, older people were more susceptible to knee joint discomfort (12). Despite abundant literature on the effectiveness of self-management programs (13, 14), the paucity of epidemiology data on self-management behaviors and QoL among the middle-aged and elderly people in China appeals for drawing up more population-based surveys. At present, there are no assessment tools or related studies on the self-management of knee joint discomfort in the middle-aged and elderly people in China.

To sum up, the research on the knee joint discomfort of middle-aged and elderly people is still insufficient and many more research works are needed on this subject. The middle-aged and elderly people are the most common groups experiencing knee joint discomfort, and a considerable segment of this population eventually develops clinical diseases. Before the evolution of symptoms, it is important to understand the current status of knee discomfort symptoms and self-management in the middle-aged and elderly population. It is also imperative to provide management recommendations for the prevention or alleviation of knee discomfort. At the same time, it is even necessary to provide a theoretical basis and practical reference for the next exploration of how to effectively implement symptoms management measures for middle-aged and elderly people with knee discomfort.

In this study, we sought to provide overall estimates for the prevalence of knee joint discomfort, self-management behaviors, and QoL among middle-aged and elderly people in China. "The middle-aged and elderly" refers to individuals aged 45 years and above. Additionally, the relationship between knee joint discomfort, self-management behaviors, and QoL was analyzed, hoping to fill the vacancy and provide evidence for policymakers.

Materials and methods

Study design

A cross-sectional study design was adopted from 15 January 2020 to 31 May 2020. The study was conducted in two cities of "Changsha" and "Zhangjiajie" in the Hunan Province, China.

Setting

Two cities (states) were randomly selected from among 14 cities and states in the Hunan Province, namely Changsha City

and Zhangjiajie City. The participants had lived in the city for at least 6 months.

Participants

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) Age of the participant should be ≥45; (2) the participant should be a community resident in the Hunan Province of China for >6 months; (3) the participant should possess normal communication skills; and (4) the participant should agree to take part on a voluntary basis and should have signed an informed consent form.

The exclusion criteria were as follows: (1) The participant had a history of knee surgery and (2) the participant expressed the inability to participate or is unwilling to cooperate with the investigation.

Sample size calculation

The minimum sample size was calculated by the equation $n = t^2pq/d^2$, which was equal to 7,968. Considering a dropout rate of 20%, the target sample size was 9,562. Eventually, 10,000 individuals who met the inclusion criteria were included and 9,993 questionnaires were returned. In this study, 9,640 valid questionnaires were collected.

Sampling procedure

The stratified multistage random sampling method was used to collect samples. First, two cities (states), namely Changsha City and Zhangjiajie City, were randomly selected from among the 14 cities (states) in the Hunan Province; then, one district (county), respectively, namely Kaifu District and Sangzhi County, was randomly selected from each of the selected cities (states) by further stratification; finally, two communities, namely Dongfeng Road Community ($N = 1{,}620$) and Qingshuitang Community ($N = 1{,}724$), and two townships, namely Zhuyeping Township ($N = 3{,}234$) and Furong Village Township ($N = 3{,}415$), were randomly selected from among the selected districts (counties). The total sample size selected by simple random sampling stands at $N = 9{,}993$. Figure 1 shows the flowchart for screening the subjects in this study.

Instruments

The survey tools consist of four parts, including General Information Questionnaire, Self-Rating Scale for Knee Joint Unpleasant Symptoms, Self-management Behavior Scale for Knee Joint Discomfort, and the 12-item Short Form Health Survey.

Demographic characteristics

The questionnaire was formulated based on demographic characteristics of the middle-aged and elderly people, including age, gender, BMI, ethnicity, educational level, marital status, dwelling state, source of finance, monthly income, residence, smoking, and alcohol drinking.

Self-Rating Scale for Knee Joint Unpleasant Symptoms

Self-Rating Scale for Knee Joint Unpleasant Symptoms in the middle-aged and elderly people was used to measure the knee joint discomfort. It was developed by our research team in 2020 (15), based on the middle-range theory of unpleasant symptoms (16). As the study was conducted in China, the scale was designed in Chinese and translated into English as given in the present manuscript. This scale consists of two dimensions, subjective symptoms (items 1–14) and self-examination signs (items 15–21), with 21 items. Subjective symptoms are evaluated from three aspects: incidence, frequency, and severity. In addition, self-examination signs are assessed from two sides: incidence and severity. The frequency is divided into four grades: rare, sometimes, frequent, and continuous, from 1 to 4, respectively. The severity is divided into mild, moderate, severe, and unbearable, with four grades ranging from 1 to 4. The content validity index (CVI) for each item ranges from 0.777 to 1.000, the average CVI for all items is 0.891, and the total scale has a Cronbach's alpha of 0.949, the half-reliability is 0.888, and the test-retest reliability is 0.914 (15).

Self-management Behavior Scale for Knee Joint Discomfort

Self-management behavior for knee joint discomfort was measured using the Self-management Behavior Scale for Knee Joint Discomfort developed by Peipei et al. (17) for the middle-aged and elderly. This scale consists of 27 items in four dimensions: symptoms management (ten items), daily management (nine items), emotion management (four items), and information management (four items). Each item is scored from 1 to 5 points (1 = none, 2 = few, 3 = sometimes, 4 = often, and 5 = always), and the total scores range from 27 to 135. A higher total score indicates better self-management skills. The CVI of each item ranges from 0.833 to 1.000, and the average CVI of all items is 0.964. The Cronbach's alpha of the total scale is 0.946, the split-half reliability is 0.894, and the test-retest reliability is 0.876 (17).

The 12-item Short Form Health Survey

The QoL was assessed using the 12-item Short Form Health Survey (SF-12) simplified from SF-36 by the Boston Institute of Health Education (18). It involves 12 items in

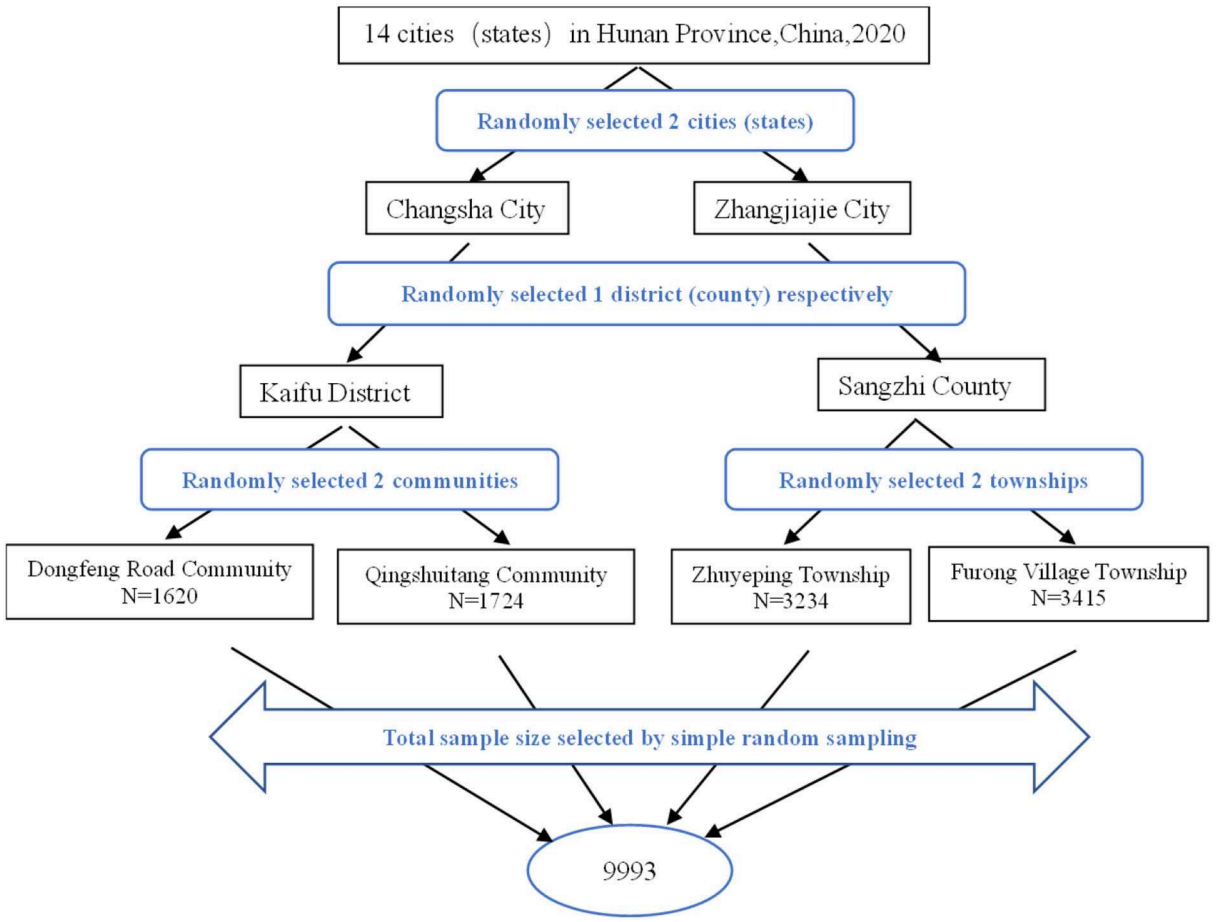

FIGURE 1
Flowchart for screening the subjects (N = 9,993).

eight dimensions: general health (GH), physical functioning (PF), role-physical (RP), bodily pain (BP), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). Physical component summary (PCS) can be obtained by calculating the score of GH, PF, RP, and BP; SF, RE, MH, and VT add up to mental component summary (MCS). The score ranges from 0 to 100 (0 = worst, 100 = best), and a score equal to or >50 is normal. And the higher the score, the better the subjective feeling of the respondents and the better the quality of life. The total scale of Cronbach's alpha is 0.760–0.860, and Cronbach's alpha of each dimension is 0.700–0.778 (19).

Data collection procedure

Before conducting the study, the study proposal and questionnaire were reviewed and approved by the Medical Ethics Committee of the Xiangya Hospital of Central South University. Members of the research team who received unified training visited different communities or townships. The training was provided to each local collector on methodology, survey tools, data collection, ethical issues, and how to supervise the data collection process. The purpose, benefits, and risks of participation in the research were also explained to potential participants. Participants were informed that their participation was voluntary and they had the right to withdraw at any time. After obtaining the consent of the participants, the questionnaire was answered under one-on-one guidance. Items difficult to understand were explained by the researcher to ensure consistency in the interpretation of each item. Each questionnaire took about 15–20 min to fill. All questionnaires were completed anonymously and the answers of participants did not involve any personal assessment. The information provided by the participants was confidential and the survey would not cause any harm to the participants. The completed questionnaires were assured of completeness and consistency during the survey period. The collected data were entered into the database and rechecked. Initially, 9,993 middle-aged and elderly people consented to participate in the study and received the questionnaires. Of these, 353 were ultimately excluded from

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TABLE 1 Demographic characteristics of the middle-aged and elderly people ($n = 9,640$).

Variable	*n* (%)	Mean ± SD
Age (years)		
45–50	3,485 (36.2)	58.99 ± 12.00
51–60	2,038 (21.1)	
61–70	2,312 (24.0)	
71–99	1,805 (18.7)	
Gender		
Male	4,559 (47.3)	
Female	5,081 (52.7)	
BMI (kg/m^2)		
<24	6,480 (67.2)	23.25 ± 5.96
24–27.99	2,062 (21.4)	
≥28	1,098 (11.4)	
Ethnicity		
Han Chinese	4,979 (51.6)	
Ethnic minorities	4,661 (48.4)	
Educational level		
Elementary school and below	3,775 (39.2)	
Junior high school	3,256 (33.8)	
Technical/high school	1,216 (12.6)	
Diploma/bachelor degree	1,247 (12.9)	
Master degree and above	146 (1.5)	
Marital status		
Unmarried	348 (3.6)	
Married	8,355 (86.7)	
Divorced	211 (2.2)	
Widowed	26 (7.5)	
Dwelling state		
Solitary	773 (8.0)	
Living with family	8,442 (87.6)	
Living in a nursing home	155 (1.6)	
Others	270 (2.8)	
Source of finance		
Salary	5,582 (57.9)	
Others	4,058 (42.1)	
Monthly family income (RMB)		
<1,000	2,248 (23.3)	
1,000–3,000	4,041 (41.9)	
3,001–5,000	2,036 (21.1)	
5,001–10,000	945 (9.8)	
>10,000	370 (3.8)	
Residence		
Urban	2,915 (30.2)	
Countryside	6,725 (69.8)	
Smoking		
Smoker	2,227 (23.1)	
Non-smoker	7,414 (76.9)	
Alcohol drinking		
Drinker	3,453 (35.8)	
Non-drinker	6,187 (64.2)	

BMI, body mass index; BMI, weight (kg)/height^2 (m).

the analysis due to incomplete or missing data. In total, 9,640 questionnaires were eligible for data analysis in the study, resulting in a response rate of 96.5%.

Statistical analysis

In this research, IBM SPSS Statistics 23.0 was used for statistical analysis. Descriptive statistics were used for presenting demographic characteristics, knee joint discomfort, self-management behavior, and quality of life in the middle-aged and elderly. Categorical variables are expressed as absolute frequencies (percentages), while continuous variables are expressed as mean ± SD (standard deviation) or median (interquartile range, IQR), as appropriate. The Kolmogorov-Smirnov test was used to check the normal distribution of continuous data. Spearman's correlation analysis was used to test the relationship between the knee joint discomfort, self-management behavior, and QoL. All *P*-values < 0.05 were considered statistically significant.

Results

Demographic characteristics of the middle-aged and elderly

The demographic characteristics of the middle-aged and elderly people are shown in Table 1. The average age of the middle-aged and elderly people was 58.99 ± 12.00 years, and an overwhelming number of them were female (52.7%). The BMI was mostly <24 kg/m^2 (67.2%) and as regards ethnicity of the study participants, the Han Chinese were predominant and occupied 51.6% of the total number of study participants, while the other ethnic minorities occupied 48.4%. As regards the educational level of the participants, the elementary school

TABLE 2 Prevalence of knee joint discomfort among the middle-aged and elderly people ($n = 9,640$).

Knee joint discomfort	*n* (%)	Frequency was "frequent and continuous" (*n*, %)	Severity was "severe and unbearable" (*n*, %)	Frequency (mean ± SD)	Severity (mean ± SD)
Subjective symptoms					
3. Pain	5,022 (52.1)	916 (9.5)	569 (5.9)	1.94 ± 0.74	1.59 ± 0.75
13. Weakness	4,096 (42.5)	577 (6.0)	328 (3.4)	1.78 ± 0.75	1.45 ± 0.68
2. Numbness	4,032 (41.8)	542 (5.6)	269 (2.8)	1.82 ± 0.71	1.43 ± 0.65
1. Cold feeling	3,854 (40.0)	433 (4.5)	196 (2.3)	1.78 ± 0.70	1.40 ± 0.64
5. Tenderness	3,696 (38.3)	610 (6.3)	346 (3.6)	1.86 ± 0.75	1.50 ± 0.72
4. Distension feeling	3,616 (37.5)	465 (4.8)	304 (3.2)	1.79 ± 0.71	1.47 ± 0.69
14. Muscle cramps	3,509 (36.4)	512 (5.4)	351 (3.7)	1.80 ± 0.75	1.50 ± 0.76
6. Stiffness	3,382 (35.1)	503 (5.3)	263 (2.8)	1.80 ± 0.75	1.45 ± 0.68
12. Heaviness	3,220 (33.4)	464 (4.8)	251 (2.6)	1.80 ± 0.75	1.46 ± 0.68
8. Snapping	3,197 (33.2)	424 (4.4)	193 (2.0)	1.75 ± 0.75	1.39 ± 0.64
7. Friction feeling	3,150 (32.7)	455 (4.7)	215 (2.2)	1.79 ± 0.74	1.42 ± 0.65
9. Instability	2,956 (30.7)	399 (4.1)	254 (2.7)	1.75 ± 0.75	1.46 ± 0.70
10. Noose feeling	2,365 (24.5)	278 (2.9)	224 (2.4)	1.69 ± 0.75	1.44 ± 0.71
11. Skin temperature arise	2,320 (24.1)	254 (2.6)	143 (1.5)	1.69 ± 0.73	1.39 ± 0.65
Self-examination signs					
15. Full knee extension	1,663 (17.3)	/	156 (1.7)	/	1.52 ± 0.74
16. Full knee flexion	1,486 (15.4)	/	178 (1.8)	/	1.59 ± 0.77
17. Claudication	1,455 (15.1)	/	202 (2.1)	/	1.63 ± 0.78
18. Swelling	1,440 (14.9)	/	186 (2.0)	/	1.61 ± 0.75
20. Protuberance	1,192 (12.4)	/	143 (1.5)	/	1.59 ± 0.77
19. Deformity	1,163 (12.1)	/	127 (1.3)	/	1.53 ± 0.75
21. Muscle atrophy	1,104 (11.5)	/	149 (1.6)	/	1.59 ± 0.78

and below level of education accounted for 39.2%. The great majority of them were married (86.7%) and lived with family members (87.6%). The source of finance mainly came from salary earnings (57.9%) and the average family income per month stood at 1,000–3,000 RMB (41.9%). As regards residence, most of the people lived in the countryside (69.8%), while the number of urban dwellers was comparatively less. A portion of the population had smoking (23.1%) and alcohol drinking (35.8%) habits. While the majority of the participants were non-smokers (76.9%) and non-drinkers (64.2%), the number of drinkers stood at 35.8%.

Knee joint discomfort of the middle-aged and elderly people

As shown in Table 2, the prevalence of knee pain was the highest (52.1%), followed by knee weakness (42.5%), numbness (41.8%), cold feeling (40.0%), tenderness (38.3%), and distension feeling (37.5%). Knee pain was the most frequent and continuous subjective symptom (9.5%) and 5.9% of the middle-aged experienced severe and unbearable pain.

Knee joint discomfort self-management and quality of life

As shown in Table 3, the average score of self-management of knee joint discomfort in the middle-aged and elderly people was 2.14 ± 0.67. The emotion management was the highest, followed by daily management, symptoms management, and information management. The average scores of PCS and MCS were 42.85 ± 5.34 and 43.62 ± 8.43, respectively.

Correlations of major study variables

The correlations of major study variables among middle-aged and elderly people are shown in Table 4. The results of the study showed that the occurrence, frequency, and severity of discomfort symptoms were positively correlated with symptoms management, daily management, information management, and self-management behaviors, and negatively correlated with emotional management, PCS and MSC, except for the occurrence of discomfort symptoms ($P < 0.05$).

Discussion

Knee joint discomfort was prevalent in the middle-aged and elderly people

To our knowledge, this is the first quantitative study to provide the overall prevalence of knee joint discomfort in the middle-aged and elderly people in China. For knee joint discomfort, there are not enough articles available to discuss, except the main focused symptom of "pain." Previous literature related to the word "discomfort" was reviewed; however, questionnaires are commonly used to study "pain" rather than "discomfort" in most of the publications (20). Actually, pain is just one of the symptoms of knee joint discomfort. In this study, more than half (52.1%) of 9,640 middle-aged and elderly populations in Hunan province had pain. Furthermore, the frequency that ranged from frequent to almost continuous was 9.5%, and the severity that ranged from severe to unbearable was 5.9%, indicating that more than half of the middle-aged and elderly suffered from knee joint pain, and some of them had even severe symptoms of knee joint pain. We explored with other symptoms, not limited to the highest incidences of "pain." They included knee weakness (42.5%), numbness (41.8%), cold feeling (40.0%), tenderness (38.3%), and distension feeling (37.5%). This suggests that middle-aged and older adults often experience multiple knee discomfort symptoms. Healthcare workers and middle-aged and elderly people themselves should pay more attention to the health care of the knee joint, not only in the management of its symptoms and health education, but also in gradually cultivating the awareness of nutrition and health care related to the knee joint.

Additionally, we found that some symptoms had a high incidence or frequency, but were not the most serious. For example, "Muscle cramps" vs. "Weakness" symptom. This inconsistency between different dimensions illustrates the importance of a comprehensive assessment of knee discomfort symptoms. Based on an overall assessment of knee discomfort symptoms in the middle-aged and older adults, interventions targeting high severity and frequency of symptoms are necessary for a better symptom management.

TABLE 3 Mean, standard deviation, minimum, and maximum of knee joint discomfort self-management and quality of life ($n = 9,640$).

	Mean	SD	Min	Max
Knee joint discomfort self-management	2.14	0.67	1.15	5.00
Symptoms management	1.96	0.81	1.00	5.00
Daily management	2.05	0.90	1.00	5.00
Emotion management	3.12	0.53	1.00	5.00
Information management	1.83	0.92	1.00	5.00
Quality of life	/	/	/	/
PCS	42.85	5.34	17.46	62.68
MCS	43.62	8.43	9.99	68.53

Middle-aged and elderly people had a low level of self-management behavior

In our research, we found that the average score of self-management of knee joint discomfort in the middle-aged and elderly people was at a low level (2.14 ± 0.67). The literature describing the self-management behavior of knee joint discomfort among elderly people in China is scarce. In terms of dimension, we found that the elderly strived for an optimal emotion management. However, their coping skills in daily management, especially information management and symptoms management, were lacking. Patients in a study by Miller et al. (21) reported that they attempted to adjust their lifestyle to reduce knee joint symptoms. Conceivably,

TABLE 4 Correlations of major study variables ($n = 9,640$).

Variable	Symptoms management	Daily management	Emotion management	Information management	Self-management	PCS	MCS
Occurrence	0.465**	0.340**	0.013*	0.296**	0.409**	−0.324*	−0.300*
Frequency	0.596**	0.402**	−0.089**	0.372**	0.499**	−0.578**	−0.571**
Severity	0.598**	0.400**	−0.100**	0.377**	0.498**	−0.382**	−0.390**

*$P < 0.05$.
**$P < 0.01$ (2-tails).

those with knee discomfort seek information on their own initiative, using a variety of sources, such as multimedia platforms and peers, to gain control of their condition (11). Therefore, in order to increase their knowledge on how to self-manage problems to improve their QoL (22), health professionals should ensure that the elderly with knee joint discomfort receive individualized self-management plans and lifestyle advice. Our study may provide some insight into the design and implementation of future self-management interventions.

Middle-aged and elderly people appeared to have poor QoL

This study demonstrated that the QoL of middle-aged and elderly people was very poor, with average scores of PCS and MCS (42.85 ± 5.34) and (43.62 ± 8.43), respectively, which were significantly lower than those given in the study by Hu et al. (23) (68.57 ± 24.21) and (74.17 ± 22.96) for patients with hypertension in the rural areas of Lianyungang City. Additionally, the QoL in our study appears to be higher than the level of elderly population in the study by Palo et al. (24) on knee OA patients in India and the study by Choojaturo et al. (22) in Thailand. In large epidemiology studies, OA has been reported as the major common cause affecting function and QoL in older adults worldwide (6). Although many health policies and countermeasures have been adopted, the QoL of elderly people remains very disagreeable in both developed and developing nations (25, 26). In our research, 69.3% of the elderly lived in rural areas and the majority of them had a low knowledge level and socioeconomic status (SES). In reality, these factors may in some way become barriers to adequate access to health services. There is already evidence to suggest that individuals with lower SES have poorer QoL (27). These situations raise important questions about what factors, if any, can improve healthcare accessibility and QoL for elderly people.

Relationship between knee joint discomfort, self-management behavior, and QoL

This study indicated that middle-aged and elderly people had knee discomfort symptoms, the more frequent and severe the symptoms, the higher level of symptom management, daily management, and information management, and the lower level of emotional management and QoL. The correlation between the variables suggests the importance and necessity of knee self-management in the middle-aged and elderly people. This fact also indirectly indicates that different degrees of knee discomfort symptoms may be related to self-management behaviors, and the results are also consistent with the interpretation of clinical phenomena. The correlation between different levels of knee discomfort symptoms and self-management behaviors may also be explored in later studies.

Strengths and limitations

Our study has several strengths. First, although previous studies have been conducted on knee OA, to the best of our knowledge, this is the first study to look at the prevalence of knee joint discomfort and the level of self-management behaviors and QoL among the middle-aged and elderly people in the Chinese population. As the aging process accelerates and the life expectancy increases, there is a need to study China's middle-aged and older populations because of the significant differences in culture and healthcare system compared to other countries. Second, the scales used in this study were specifically designed to measure the symptoms and self-management of people with knee discomfort, which contributed to the validity and reliability of the results. Moreover, the validated scale can be used as a theoretical basis for developing and observing the effects of self-management programs in the future. Third, the collected data were analyzed using reliable statistical methods, and the results may provide theoretical support for future knee management interventions.

Some limitations need to be addressed. First, the study was just conducted in the Hunan province of China, which might limit the generalizability of the results. Further research is needed to increase the sample size and extend the finding to populations in other parts of China. Second, recall bias may exist due to the long span of time. Last, our study is a cross-sectional investigation; cross-sectional study designs may not be able to determine the causal relationship between the variables of interest.

Conclusion

Knee joint discomfort was prevalent in the middle-aged and elderly people. In addition, they have a low level of self-management behavior and poor QoL. This study indicated that the middle-aged and elderly people had knee discomfort symptoms, the more frequent and severe the symptoms, the higher level of symptom management, daily management and information management, and the lower level of emotional management and QoL. It is necessary to conduct a further study, such as on in-depth coping strategies used by middle-aged and elderly people themselves experiencing knee joint discomfort, to

increase their self-management skills and improve their quality of life.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Research Ethics Board of the Xiangya Hospital of Central South University. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

MS designed the study, participated in the data processing and statistical analysis, and wrote the initial draft of the manuscript. PZ, BZ, and QZ participated in the designing of the study, administration of the questionnaire, and discussed the analytical results. YZ provided important feedback on the manuscript, participated in the designing of the study, and provided important feedback on the manuscript. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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A study on the factors influencing old age identity among the Chinese elderly

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Background: Old age identity is the self-perception of when old age begins, reflects public age values and acceptance of aging. Not all elderly people aged 60 and above identify with their old age status. The aging society in the traditional sense may not be "aging". Therefore, redefining old age is crucial. Different from Western countries, China is a country with a long-standing culture of respect for the elderly and filial piety norms, and the influence of the cultural background on the old age identity is worthy of attention.

Data and method: Data were drawn from the 2014 China Longitudinal Aging Social Survey (CLASS). A total of 7400 participants answered questions about old age identity. Based on old age identity, we obtained two other types of indicators of perceived old age: elderly group identity and aging degree. For the continuous variable old age identity and aging degree, an OLS linear regression model was established. A binary logistic regression model was established for the binary variable elderly group identity.

Result: The average old age identity of Chinese people aged 60 and above is 70 years. Health status, psychological status, behavior, socioeconomic status, and some demographic characteristics significantly affect the old age identity of the Chinese elderly.

Conclusion: The traditional Chinese cultural background of respect for the elderly and the norms of filial piety have an impact on the old age identity of the Chinese elderly through family intergenerational support. The various forms of support provided by children to the elderly can help them achieve a positive age identity—enter old age later, raise the likelihood of identification with non-elderly groups, and reduce aging degree. The number of children of the elderly, the children's economic conditions and care support for grandchildren have negative effects. A positive old age identity can help the elderly improve their self-esteem.

KEYWORDS

old age identity, age values, intergenerational support, respect for the elderly, social identity

Introduction

China—along with most countries in the world —are facing severe aging problems. The increase in the elderly population will not only increase the support burden of young people, but also lead to major challenges for employment, the social security system, health care system, etc (1–3). Statistics from the United Nations show that in 2017, the world's elderly population aged 60 and above accounted for 13% of the total population, and more than 100 countries and regions have entered an aging society; China's elderly

population aged 60 and above is about 226 million, equivalent to nearly a quarter of the world's elderly population, accounting for 16% of China's population (4). However, this is only based on the statistics of the elderly at the age of 60 as the benchmark for old age. In the past 30 years, the average life expectancy in China has increased from 67.9 to 76.5 years (5). As life expectancy increases, individuals also change their perceptions of when they enter old age (6, 7) and may reassess their own perceptions of aging (8). Older people do not necessarily consider themselves old (9, 10), and chronological age is no longer the only useful indicator for defining old age (11). There are also studies suggesting that 15 years of expected remaining lifespan should be used as a new standard for the definition of old age (12). Advances in longevity, healthy aging, and technological innovation have made today's elderly become a generation that actively contributes to society and the family, so it may be meaningless to define old age in a static, homogenous way (13).

According to the 2014 China Longitudinal Aging Social Survey, the average chronological age of 7,399 elderly people aged 60 and above is about 69 years, but the average self-perception of aging is about 70 years. China and many other countries still define the elderly as 60 years old and above, but based on the old age identity (the self-perception of when old age begins), China and other countries in the world still have room to maneuver in response to the challenges of aging. Not all Chinese elderly people aged 60 and above identify with their old age status. Therefore, the practical outcome of self-identity of old age may be that the actual scale of the elderly would be reduced, and the aging society in the traditional sense may not be "aging." In addition, China uses chronological age as the age reference for mandatory retirement. The Chinese government stipulates that the legal retirement age is 60 for men, 55 for women in white-collar jobs, and 50 for women in blue-collar jobs. Although there is no consensus on when a person ages, 60 or 65 years is the most commonly used eligibility age for pension plans, and therefore people associate retirement age with old age (14). In order to cope with the many challenges brought by an aging society, postponing the retirement age can ease the pressure on pensions and increase labor supply. However, based on the old age identity, postponing the retirement age may be more in line with the psychological expectations of the old age identities over 60, and bring certain negative psychological impacts to the old age identities below 60. Therefore, the policy significance of old age identity is reflected in the fact that it may affect public response and acceptance of relevant policies such as the gradual extension of retirement age. When adjusting the retirement age, referring to old age identity will help improve the flexibility of the policy.

The old age identity of the Chinese elderly can reflect the age values and the acceptance of aging of the contemporary Chinese public. Paying attention to the old age identity of the Chinese elderly has great practical and policy significance for actively responding to the aging society. We believe that redefining old age is crucial. Combined with the existing research on the influencing factors of old age identity, we found that there are three shortcomings: the construction of old age identity is based on a single index, the influencing factors rarely involve cultural background, and the significance of old age identity to the elderly is not highlighted. Therefore, this paper addresses the following questions:

RQ1: What is the characteristic of the old age identity of the Chinese elderly?

RQ2: What factors influence the old age identity of the Chinese elderly, especially whether cultural background factors have a significant impact?

RQ3: What is the significance of old age identy for the elderly, why do some elderly people tend to enter old age later?

Answers to these questions will help identify differences in the old age identities of various types of elderly people, thereby providing greater flexibility for the formulation of public policies involving retirement and old-age security. This study takes China as an example, based on demographic correlates, socioeconomic status, health status, psychological status, behavior and major events, combined with the traditional Chinese cultural background of respect for the elderly and filial piety norms, to focus on the influence of family factors, especially family intergenerational support, on the old age identity of the Chinese elderly. Based on the social identity theory of social psychology (15–18), we empirically analyzed the significance of old age identity for the elderly, that is, whether positive old age identity helps the elderly improve self-esteem.

Literature review

Old age identity is the self-perception of when old age begins. Kaufman and Elder proposed five dimensions of age identity, including subjective age (the age you feel like most of the time), other age (the age other people think you are), desired age (the age you want to be), desired longevity (the age you hope to live to) and perceived old age (the age at which you become old) (8). Diehl et al. emphasized that age identity originated from the role identity theory of sociology and the social identity theory of social psychology in their seminal theoretical reflections on the awareness of aging (8, 15, 19, 20). Individuals explicitly and consciously report their age identities to ensure that they belong to the most appropriate identity, from among the diverse social role identities represented by the various age classes (21, 22). Age identity is the core of social identity (15), and individuals belong to certain social groups according to their age identities as group members. Therefore, consistent with Goffman's definition of identity and with overall sociological and social-psychological theory, age identity is primarily seen as a person's subjective sense of age based on their social experiences and identification with a particular age group (19, 23).

There is accumulating evidence that age identity relates to a wide array of physical and mental health outcomes, including mortality, functional status, morbidity and loneliness (24, 25). Age identity has a better effect than chronological age in predicting cognitive aging patterns (26). In recent years, the influence of age identity on workplace performance has received much attention in the field of psychology (27–29). The fact that subjective age identity influences the ability as well as the motivation to act or perform (30), makes it a vital personal characteristic to explore in the domain of economic behaviors (31).

As age identity shows amazing predictive power in different domains, more studies have begun to focus on the factors influencing age identity. Most studies on the factors influencing age identity are based on four types of potential related factors proposed by Barak & Stern: (a) biological and physiological correlates (i.e., objective health status or self-perceived health); (b) demographic correlates (i.e., gender, marital status, socio-economic status, etc.,); (c) socio-psychological correlates (i.e., life satisfaction, emotional health, morale etc.,); and (d) behavioral correlates (i.e., consumer behavior, leisure-time activities, etc.) (32). Health is an important factor influencing age identity (33, 34), and those with more positive evaluations of cognitive and physical function tend to delay the onset of old age (35). Chronic diseases were positively correlated with subjective age (36). Barak and Rahtz found that there were no significant differences in subjective age and the likelihood of feeling older between men and women (37). Recent research has further demonstrated that the subjective age of young and middle-aged adults is not related to gender (38). Participants who reported higher levels of financial stress were perceived as older than their actual age to a greater extent (39). Based on 2471 investigators aged 40–79, Bergland et al. found that factors such as older age, physical health, mental health and higher personal accomplishment can significantly predict perceived subjective younger age (40). Grandparents are critical to the shaping of personal aging experiences, and grandchild care behaviors significantly influence age identities of the elderly (41, 42).

Recent research provides empirical support for views of aging from a life-course perspective, emphasizing that childhood starvation experience predict older subjective age and that parental death is associated with lower old age identity (43). Barrett and Gumber examine the impact of aging body reminders on age identity, such as everyday body problems and body repairs (44). While most studies have considered age identity to be a relatively stable variable, Hughes and Touron offer a novel account of how daily life offers a variety of situational contexts and experiences that directly impact the age a person feels at a given moment (45). It has also been found that retirement intentions positively predicted subjective age (46), while personality traits with higher scores such as extroversion, openness, agreeableness and conscientiousness were associated with a younger subjective age (47). The closest study to this paper is Liu et al., who focused on examining the impact of social engagement behaviors on the old age identities of the Chinese elderly and found that political engagement behaviors of the elderly help delay the onset of old age (11).

Most studies on age identity focus on subjective age identity and old age identity. However, there are still three insufficiencies in the studies on the influencing factors of old age identity: First, it is difficult to explain the profound connotation of old age identity with a single research index. Most studies only conduct empirical analyses based on continuous variables measured by age identity, but ignore that age identity also reflects identity with a specific age group, furthermore, continuous variables derived from age identity measures can be combined with chronological age to perform mathematically more complex analyses (48). The second limitation is the lack of cultural background factors. Age identity is based on the understanding of individuals' cognitions and experiences in the sociocultural context (24). By contrasting American and German age identities, Westerhof and Barrett emphasized that gerontological theory and research should incorporate the cultural context (49). Third, the significance of old age identity for the elderly is not highlighted in the empirical analyses. Most studies on age identity ignore the process of self-perception and meaning formation (19), and deciding how respondents feel about a particular age remains a challenge (50). We therefore ask the question: do the elderly achieve self-enhancement through a positive age identity?

In view of the insufficiencies of existing studies, we advance the research on the influencing factors of old age identity from the following three aspects.

First, on the basis of old age identity, we combine the theoretical connotation of age identity and draw on the mathematical processing technology of Rubin and Berntsen to predict subjective age identity (the age you feel like most of the time) (48). Using the same mechanism, we can logically deduce the question of old age identity (the self-perception of when old age begins), and obtain two other types of indicators of perceived old age: elderly group identity and aging degree.

Second, we combine the traditional Chinese cultural background of respect for the elderly and incorporate family factors such as family intergenerational support into the analysis of the factors influencing the old age identity of the Chinese elderly. Age discrimination is a universal feature of European countries (51); a number of older people in the world may suffer from disrespect, and only a few can maintain the respect of younger generations through unusual achievements (52, 53). However, China is a society with a traditional culture of respect for the elderly (54), which is also reflected in other East Asian countries, such as Japan and South Korea (55, 56). China is a country with very close two-way support between parents and children. Family intergenerational support such as financial, emotional, and domestic support provided by children to the elderly is considered a behavior of respect for the elderly

(54), which is also in line with Chinese traditional filial piety norms (57). The elderly often also provide care and support for their grandchildren.

Third, to provide a new perspective to the study of the factors influencing the old age identity of the elderly, based on the social identity theory of social psychology, this paper empirically analyzes the significance of old age identity to the elderly, that is, the way in which a positive old age identity can help the elderly improve their self-esteem. Social identity is defined as an individual's psychological process of obtaining emotional experience and sense of worth as a member of a specific social group (16). Social identity theory argues that through appropriate intergroup social comparison, positive social identity can be obtained, for example, enhancing self-esteem (15, 17, 18). To some extent, age identity may serve the purpose of compensation and self-enhancement (58–60). For the elderly, the importance of this self-enhancement is even greater than that of health and socioeconomic status in predicting age identity (49).

Materials and methods

Data

Data were drawn from the 2014 China Longitudinal Aging Social Survey (CLASS). CLASS is a nationwide and continuous large-scale social survey project, specifically implemented by the China Survey and Data Center of Renmin University of China. By regularly and systematically collecting the social and economic background data of the elderly in China, CLASS can grasp the various problems and challenges faced by the elderly in the aging process, evaluate the actual effects of various social policy measures in improving the quality of life of the elderly, and provide important theoretical and factual basis for solving the problem of aging in China. The first nationwide baseline survey was carried out in 2014, and an elderly person aged 60 and above was selected from the sampled households for interview, and a total of 11,511 resident questionnaires were completed. A total of 7,400 participants answered questions about old age identity. Of the 4,111 participants who did not answer questions about old age identity, 2,015 were unable to answer these questions due to lower cognitive functioning or poor understanding of the questions. Compared to those who completed the study, those who were excluded from the study were older, had lower levels of education and income, and a higher proportion were female residents of rural areas. According to the needs of the research, we retain a total of 6,788 samples of elderly people whose age was between 40 and 100 and had 1–5 children. After eliminating the missing values of the variables, the final sample size was 6,033.

Measures

Based on four types of potential related factors proposed by Barak and Stern (32), and combined with the traditional Chinese cultural background of respect for the elderly, we built a predictive model of old age identity among the Chinese elderly, including seven dimensions: demographic correlates (age, gender, marital status, ethnicity, extent of solitude, residence), socioeconomic status (educational achievement, pension income, occupation type), health status (self-assessed health, chronic diseases), psychological status (life satisfaction, emotional status), behavior (economic behavior, political behavior, public welfare behavior), major events (major sad events, major happy events), and family factors (the number of children, children's economic conditions, care support for grandchildren, emotional support provided by the children, financial support provided by the children, domestic support provided by the children).

Old age identity

Old age identity not only reflects the specific age identified by individuals, but also, combined with the chronological age (CA), can further reflect the differences in the aging degree of individuals and the identity with a particular age group. Compared with previous studies, we use three types of indicators to interpret and enrich the profound connotation of old age identity, which is conducive to the in-depth study of the factors influencing age identity. Details as follows: First, CLASS2014 asked the respondents "At what age do you think you are old?". This is the respondents' self-perception of when old age begins, and we measure old age identity accordingly. Second, Rubin and Berntsen introduced three measures of subjective age identity, subjective age (SA); absolute difference between subjective age and chronological age (SA - CA); and relative difference between subjective age and chronological age (SA - CA) / CA (48). Drawing on Rubin and Berntsen's mathematical processing techniques for subjective age identity, we use two methods to measure the aging degree, absolute difference between chronological age and old age (CA - OA), and relative difference between chronological age and old age (CA - OA) / OA. For example, if old age identity is 60 years old and chronological age is 70 years old, aging degree is 10 years old or 16.7%; if old age identity is 65 years old and chronological age is 75 years old, aging degree is 10 years old or 15.4%. Third, based on the social identity theory, old age identity reflects identity with a particular age group. When a nominal elderly person over 60 years old answers the self-perception of when old age begins, it also represents their own judgment on the identity of an age group, that is, whether they belong to the elderly group or not. This is something that cannot be measured by the index system of Rubin and Berntsen, and is also the focus of this study.

Therefore, elderly group identity can be expressed as two groups: the non-elderly group (OA > CA), and the elderly group (OA ≤ CA).

Demographic correlates

Demographic correlates include age, gender, marital status, ethnicity, extent of solitude, and residence. Age is a continuous variable, and gender (male = 1, female = 0), marital status (married = 1, not married = 0), ethnicity (Han Chinese = 1, non-Han Chinese = 0), extent of solitude (live alone = 1, do not live alone = 0), residence (urban = 1, rural = 0) are set as categorical variables.

Socioeconomic status

Socioeconomic status includes educational achievement, pension income, and occupation type. Occupation type is a categorical variable measured by respondents' most recent primary occupation (whether currently working or previously working), agricultural jobs (including farming, animal husbandry and fishing) = 0, or non-agricultural jobs = 1. Educational achievement and pension income are continuous variables. Educational achievement is measured by years of education (illiterate or never attended primary school = 0, primary school = 6, junior high school = 9, high school/technical secondary school = 12, junior college and above = 15). In China, an individual's pension type is related to his or her occupational background, including basic pension for urban employees, retirement pension for government agencies and institutions, social pension for urban residents and social pension for rural residents. CLASS2014 asked the respondents about the above pension income, the unit is 1,000RMB.

Health and psychological status

Health status includes the categorical variables of self-assessed health and chronic diseases. Psychological status includes life satisfaction and emotional status. The measure of chronic disease was: 1 if there is a chronic disease, 0 otherwise. In this paper, referring to the practice of Bordone et al. (13), self-assessed health and life satisfaction were set as two-category variables. The measure of self-assessed health was: healthy (relatively healthy, very healthy) = 1, unhealthy (generally unhealthy, relatively unhealthy, and very unhealthy) = 0. The measure of life satisfaction was: satisfaction (relatively satisfied, very satisfied) = 1, dissatisfied (generally dissatisfied, relatively dissatisfied, very dissatisfied) = 0. CLASS2014 asked the elderly about their emotional status in the past week from the time of the survey, with questions such as "Did you feel lonely in the past week?", "Did you feel sad in the past week?", "Did you feel that you didn't want to eat in the past week?", and "Did you sleep poorly in the past week?", with the responses of often = 1, sometimes = 2, and never = 3. We added up the scores for the 4 questions about emotional status; the score range of emotional status was 4–12 points, the higher the score, the better the emotional status.

Behavior

Behavioral correlates include economic behavior, public welfare behavior, and political behavior. Economic behavior is measured by questions such as "Are you currently engaged in a paid job?", and scored as 1 if the answer is yes, and 0 otherwise. Political behavior is measured by questions such as "Have you participated in the voting of the local residents committee or village committee in the past 3 years?", with a score of 1 if the answer is yes, 0 otherwise. The measure of public welfare behavior is participation in public welfare activities in the past 3 months from the time of the survey. Public welfare activities are divided into seven categories: community security patrols, caring for other elderly members, environmental sanitation protection, mediation of disputes, accompanying chat, volunteer services requiring professional skills, and helping to take care of children from other families, with a score of 0 if the respondent has attended, but not in the past 3 months, or has never attended, 1 otherwise.

Major events

We considered two types of major events: One was major happy events, and the measurement standard was two major events of child or grandchild marriage, child or grandchild birth in the past 12 months since the time of the survey, with a score of 1 if the respondent experienced at least 1 event, 0 otherwise. The other was major sad events, and the measurement standard was based on nine major events of serious illness, natural disaster, death of spouse, death of child, death of other relatives and friends, financial loss, serious illness of family members, conflicts with relatives and friends, and accidents in the past 12 months since the time of the survey, with a score of 1 if the respondent experienced at least 1 event, 0 otherwise.

Family factors

The traditional Chinese culture of respect for elders stems from Confucian teachings of filial piety; filial piety essentially directs offspring to recognize the care and aid received from their parents and, in return, to pay respect for their parents (61). In Chinese society, adult children attach great importance to filial piety, and the dominant value of filial piety stipulates

that adult children assume the responsibility of caring for their aging parents (57). Combining the traditional Chinese cultural background of respect for the elderly and the norms of filial piety, this paper focuses on the influence of family intergenerational support on the old age identity of the Chinese elderly in relation to family factors. In addition to the three forms of support provided by children to their elders in line with filial piety, grandchild care support, number of children, and children's economic conditions are also included in family factors.

CLASS2014 asked about the financial support provided by the children to the elderly respondents in the past 12 months from the time of the survey, including money, food or gifts, converted into a range of monetary amounts for children to choose from, such as "not provided," "1∼199RMB," "200∼499RMB," etc. We used the median of the range of monetary amounts to approximate the financial support provided to respondents by each child. CLASS2014 counts financial aid for up to 5 children, therefore, the number of children in the empirical sample of this paper is 1–5, and children's financial support is the average monthly amount of money provided by all the children of the respondents. Children's housework support was measured by questions such as "how often did this child help you with housework in the past 12 months?", if the respondent answered "almost every day," a score of 1 was given, otherwise it was 0, other options included "at least once a week," "at least once a month," "several times a year" and "hardly ever." Children's emotional support was measured by questions such as "do you think this child does not care enough for you?", if the respondents answered "never," a score of 1 was given, otherwise it was 0, other options included "occasionally," "sometimes" and "often." CLASS2014 asked respondents how often they had looked after their grandchildren in the past 12 months since the time of the survey, with options including "from morning to night," "for some time each day," "at least once a week," "several times a month," "about once a month," "rarely," or "not." If the respondent had at least one grandchild whose frequency of grandchild care is from morning to night or some time each day, the score for care support for grandchildren was 1, otherwise it was 0. The children's economic conditions was measured by questions such as "how do you think the child's financial condition is?", if the elderly answered "relatively difficult" or "very difficult" for all their children's financial situations, the score was 1, otherwise it was 0, other options include "basically adequate," "relatively well-off" and "very well-off."

Methods

In this study, an OLS linear regression model and a binary logistic regression model were used to empirically analyze the influencing factors of the three types of indicators of old age identity. For the continuous variable old age identity and aging degree, an OLS linear regression model was established, see model (1) and model (2). A binary logistic regression model was established for the binary variable elderly group identity, see model (3).

$$Y_1 = \alpha + \beta_1 X_1 + \cdots + \beta_k X_k + \varepsilon \quad (1)$$

$$Y_2 = \alpha + \beta_1 X_1 + \cdots + \beta_k X_k + \varepsilon \quad (2)$$

$$ln[P/(1-p)] = \alpha + \beta_1 X_1 + \cdots + \beta_k X_k + \varepsilon \quad (3)$$

Among them, Y_1 represents old age identity, P is the probability that the elderly identify themselves as belonging to the non-elderly group, X is the independent variable, α is the constant term, β is the coefficient to be estimated, and ε is the error term. For the estimation of the direction of the coefficient to be consistent, this paper sets Y_2 as the opposite number of the aging degree. Table 1 shows the descriptive statistics of the variables.

Results

Table 2 shows the old age identity of the Chinese elderly based on CLASS2014. Excluding the sample of respondents whose chronological age was missing (only 1), 7,399 respondents aged 60 and above participated in the survey on old age identity. The average chronological age of the participants was about 69.02 years, and the average old age identity was about 70.04 years. It can be seen that the average chronological age of the Chinese elderly is less than the average old age identity. However, through the elderly group identity, we found that the elderly who identified themselves as the elderly group (CA $\geq$ OA) accounted for 54%, the average chronological age was about 70.83 years, and the average old age identity was about 64.31 years; the elderly who belonged to the non-elderly groups (CA $<$ OA) accounted for 46%, the average chronological age was about 66.92 years, and the average old age identity was about 76.70 years. We believe that old age identity among Chinese elderly does reflect identity with a specific age group.

Due to space limitations, we select a few of the factors to compare the old age identity of the various categories of the Chinese elderly. We found that the average old age identity of male and female Chinese elderly members was almost the same, 70 years. However, the average old age identity of the Chinese elderly living in cities was 71.23 years, which is significantly higher than that of the Chinese elderly living in rural areas,

TABLE 1 Descriptive statistics of the variables.

Continuous variables	Average	Mean	Minimum	Maximum
Old age identity	70.05	9.77	40	100
Aging degree (absolute difference)	−1.04	10.44	−40	36
Aging degree (relative difference)	0	0.15	−0.4	0.9
Age	70.31	8.10	60	113
Educational achievement	5.63	4.72	0	15
Pension income	1.17	1.44	0	10.23
Emotional status	10.24	1.83	1	12
The number of children	2.76	1.20	1	5
Financial support provided by the children	0.31	0.43	0	5
Categorial variables	**Percentages (%)**			
	0		1	
Elderly group identity	53.63		46.37	
Gender	52.04		47.96	
Marital status	35.21		64.79	
Ethnicity	7.54		92.46	
Extent of solitude	86		14	
Residence	40		60	
Occupation type	48.28		51.72	
Self-assessed health	57.58		42.42	
Chronic diseases	25.32		74.68	
Life satisfaction	24.75		75.25	
Economic behavior	81		19	
Political behavior	54.16		45.84	
Public welfare behavior	79.86		20.14	
Major happy events	89.82		10.18	
Major sad events	71.23		28.77	
Children's economic conditions	88		12	
Care support for grandchildren	71.55		28.45	
Emotional support provided by the children	18.58		81.42	
Domestic support provided by the children	67.90		32.10	

which is 67.92 years. It was found that elderly people with better self-assessed health status have a higher average old age identity. The average old age identity of the elderly who self-assessed their health as unhealthy was 69.08 years, and the average old age identity of the elderly who self-assessed their health as healthy was 71.25 years. The higher the educational achievement of the elderly, the higher the average old age identity. The average old age identity of the elderly with an education level of primary school and below was 68.88 years, the average old age identity of the elderly with an education level of junior high school was 71.07 years, and that of the elderly with an education level of junior high school and above was 71.65 years. The average old age identity of the elderly who participated in public welfare behaviors was 70.51 years, and that of the elderly who did not, was 69.92 years. According to the T-values and significance results that the mean *T*-test report, we found that, except for gender, there are significant differences in old age identity among different categories of the Chinese elderly, however, these differences may be influenced by other variables. Therefore, it is necessary to establish a regression model to

TABLE 2 The old age identity of the Chinese elderly based on CLASS2014.

Variable		Sample	Average chronological age	Average old age identity	T-values
-		7,399	69.02	70.04	-
Gender	Male	3,966	68.91	70.13	−0.83
	Female	3,374	69.11	69.98	
Residence	Urban	4,768	69.41	71.23	−13.81***
	Rural	2,623	68.30	67.92	
Self-assessed health	Health	3330	68.37	71.25	−8.62***
	Unhealth	4,056	69.55	69.08	
Educational achievement	Primary school and below	4,243	69.64	68.88	−11.75***
	Junior high school and above	3,148	68.18	71.65	
Public welfare behavior	Participate	1,616	68.11	70.51	−2.06**
	Not participate	5767	69.27	69.92	

*$p < 0.1$, **$p < 0.05$, ***$p < 0.01$.

exclude the influence of other related variables, and to examine whether the independent effects of each variable on the old age identity of the Chinese elderly are significant.

Table 3 presents the empirical results of the factors influencing old age identity among the Chinese elderly.

First, among the demographic correlates, only age has a significant impact on the three indicators of old age identity. Increasing age causes the elderly to enter old age later, raise the likelihood of identification with the elderly group, and exacerbate aging degree. Gender, marital status, ethnicity, extent of solitude, and residence have no significant effects on the three indicators of old age identity. Studies have also shown that, in addition to the effect of chronological age, demographic correlates play a secondary role at best in the analysis of the impact of age identity (48, 62, 63). Socioeconomic status, educational achievement, pension income and occupation type, all have significant effects on the three indicators of old age identity. Higher years of schooling and higher pension income cause the elderly to enter old age later, raise the likelihood of identification with non-elderly groups, and reduce aging degree. Compared with agricultural work, non-agricultural work causes the elderly to enter old age later, raise the likelihood of identification with non-elderly groups, and reduce aging degree. This is consistent with earlier research conclusions that socioeconomic status can reflect different social experiences of older adults, while age identity is primarily viewed as a person's subjective sense of age based on their diverse social experiences (19). Socioeconomic status affects age identity; those with poorer socioeconomic status have older identities (64). Recent research has also shown that there is heterogeneity in how people feel about old age when it comes to education, for example, highly educated respondents were less likely to associate old age with loneliness and boredom than respondents with lower education levels (13).

Second, health and psychological status have a significant impact on the three indicators of old age identity. Better self-assessed health, no chronic disease, higher life satisfaction status, and better emotional status cause the elderly to enter old age later, raise the likelihood of identification with non-elderly groups, and reduce aging degree. Among the behaviors, political and public welfare behavior have a significant impact on the three indicators of old age identity. Participating in political elections and public welfare activities cause the elderly to enter old age later, raise the likelihood of identification with non-elderly groups, and reduce aging degree. Although work plays a central role in the formation of self-perception (14), economic behavior has no significant effect on the old age identity of the Chinese elderly, which is consistent with the findings of Liu et al. (11). In addition, neither of the two major types of events (happy or sad) had a significant effect on old age identity. Since CLASS2014 counts the major events experienced by the elderly in the past year, we speculate that the impact of major events experienced by the elderly may be time-sensitive, and may affect old age identity by acting on the psychology of the elderly in a short period of time.

Finally, in the context of the traditional Chinese culture of respect for the elderly, there are positive and negative effects of family-related factors on the three types of indicators of old age identity among the Chinese elderly. The financial, emotional, and domestic support provided by children to the elderly have positive effects. Children providing substantial financial support to the elderly, caring about them often, and helping them with housework often, enable them to enter old age later, raise the likelihood of identification with non-elderly groups, and reduce

TABLE 3 Empirical results of the factors influencing old age identity among the Chinese elderly.

Variable	Old age identity		Elderly group identity		Aging degree (relative difference)	
Demographic correlates						
Age	0.387***	(0.022)	−0.098***	(0.006)	−0.009***	(0.000)
Gender	−0.303	(0.248)	−0.001	(0.064)	−0.005	(0.004)
Marital status	−0.021	(0.331)	−0.078	(0.086)	−0.002	(0.005)
Ethnicity	−0.016	(0.525)	−0.021	(0.133)	0.002	(0.008)
Extent of solitude	0.424	(0.450)	0.002	(0.111)	0.003	(0.007)
Residence	0.114	(0.329)	0.091	(0.085)	0.002	(0.005)
Socioeconomic status						
Educational achievement	0.095***	(0.034)	0.032***	(0.009)	0.002***	(0.000)
Pension income	0.463***	(0.122)	0.112***	(0.031)	0.007***	(0.002)
Occupation type	1.453***	(0.355)	0.282***	(0.090)	0.021***	(0.005)
Health status						
Self-assessed health	1.296***	(0.248)	0.327***	(0.064)	0.018***	(0.004)
Chronic diseases	−1.250***	(0.288)	−0.273***	(0.071)	−0.014***	(0.004)
Psychological status						
Life satisfaction	1.006***	(0.288)	0.262***	(0.077)	0.015***	(0.004)
Emotional status	0.402***	(0.069)	0.086***	(0.018)	0.005***	(0.001)
Behavior						
Economic behavior	−0.172	(0.313)	−0.001	(0.082)	−0.002	(0.005)
Political behavior	0.499**	(0.234)	0.155**	(0.061)	0.007**	(0.003)
Public welfare behavior	0.675**	(0.282)	0.173**	(0.072)	0.009**	(0.004)
Major events						
Major sad events	−0.079	(0.261)	−0.062	(0.068)	−0.002	(0.004)
Major happy events	−0.354	(0.387)	−0.035	(0.104)	−0.004	(0.006)
Family factors						
The number of children	−0.416***	(0.123)	−0.114***	(0.031)	−0.006***	(0.002)
Children's economic conditions	−1.072***	(0.406)	−0.281**	(0.111)	−0.015***	(0.006)
Care support for grandchildren	−0.701***	(0.261)	−0.146**	(0.068)	−0.011***	(0.004)
Emotional support provided by the children	0.715**	(0.298)	0.127*	(0.077)	0.011**	(0.004)
Financial support provided by the children	0.651**	(0.298)	0.128*	(0.072)	0.008**	(0.004)
Domestic support provided by the children	0.530*	(0.277)	0.137*	(0.070)	0.007*	(0.004)
Constant term	36.932***	(1.723)	5.305***	(0.457)	0.516***	(0.025)
R^2/ Pseuto R^2	0.164		0.133		0.250	
Sample	6,033		5,553		6,033	

*$p < 0.1$, **$p < 0.05$, ***$p < 0.01$, values in parentheses are robust standard errors clustered to the individual level. The empirical results of the aging degree measured by absolute difference are consistent with the old age identity, hence they are not presented here, however, they are available upon request. Considering that the elderly with the same old age identity and chronological age may be in the transition stage between the elderly group and the non-elderly group, in order to highlight the difference in the influence of various factors on the identity of the elderly group, we excluded the elderly with the same old age identity and chronological age. There are a total of 480 samples in this part.

TABLE 4 The self-enhancement effect of old age identity among the Chinese elderly.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Elderly group identity	0.515*** (0.059)	0.543*** (0.086)						
Elderly group identity*Gender		−0.050 (0.113)						
Old age identity			0.030*** (0.003)	0.037*** (0.005)				
Old age identity*Gender				−0.013** (0.006)				
Aging degree (absolute difference)					0.030*** (0.003)	0.037*** (0.005)		
Aging degree (absolute difference)*Gender						−0.012** (0.006)		
Aging degree (relative difference)							2.064*** (0.233)	2.553*** (0.342)
Aging degree (relative difference)*Gender								−0.838** (0.425)
Control variables	control	control	control	control	control	control	control	control
R^2/Pseudo R^2	0.092	0.092	0.094	0.095	0.094	0.095	0.093	0.094
Sample	5,917	5,917	5,917	5,917	5,917	5,917	5,917	5,917

*$p < 0.1$, **$p < 0.05$, ***$p < 0.01$, values in parentheses are robust standard errors clustered to the individual level. Control variables include demographic correlates, socioeconomic status, health status, psychological status, behavior, major events, and family factors.

aging degree. Studies have shown that more than 50% of the elderly aged 64–74 years believe that the decline in physical health and loneliness are the main reasons for their aging (13). These intergenerational support behaviors of respect for the elderly and filial piety may greatly improve the material and spiritual life of the elderly, help improve their physical health, and reduce their loneliness, so that they may harbor a more positive old age identity. The number of children of the elderly, the children's economic conditions and care support for grandchildren have negative effects. Larger numbers of children, financially disadvantaged children, and often caring for grandchildren cause the elderly to enter old age earlier, raise the likelihood of identification with elderly groups, and exacerbate aging degree. This paper argues that the elderly may devote more energy to raising a larger number of children, the difficult economic conditions of all children may bring psychological burdens to the elderly, and taking care of grandchildren often may also decline the physical health of the elderly. These effects may make it difficult for the elderly to demonstrate a more positive old age identity.

To test whether the elderly achieve self-enhancement through positive age identity, in this paper, a two-category proxy variable of self-esteem of the elderly is set up, and a logistic model is constructed. Based on the social identity theory of social psychology (15–18), we empirically analyzed the significance of old age identity for the elderly, that is, whether positive old age identity helps the elderly improve self-esteem. Up to now, the most widely used self-esteem scale (Rosenberg Self-Esteem Scale, RSE) is an assessment of an individual's overall feelings of self-worth and self-acceptance (65). Since CLASS2014 did not set up such self-esteem scales, this study only establishes the two-category proxy variable of the elderly's self-esteem through the question set by CLASS2014 namely: "I think I am still a useful person to society, is this statement consistent with the actual current situation of the elderly?". Set the answers "completely inconsistent," "relatively inconsistent," "general" to 0, and "more consistent" and "completely consistent" to 1. This question of CLASS2014 is more consistent with the evaluation indicators in RSE: "I feel that I am a valuable person" and "I have a positive attitude toward myself," which reflects the affirmation of the self-worth of the elderly. In addition, to be more precise, this question of CLASS2014 reflects a specific self-esteem (for a specific self-image, as opposed to the overall self-image) and state self-esteem (self-evaluation for the moment, as opposed to self-evaluation over a longer period of time) (66). Some studies have also pointed out that group classification under social identity theory is more likely to have an impact on state self-esteem that reflects current self-evaluation (67). Therefore, the setting of the proxy variable of elderly self-esteem in this paper has a certain representativeness.

Table 4 reports the self-enhancement effect of old age identity among the Chinese elderly. The empirical results show that the group identification of the elderly significantly affects their self-esteem. In order to improve self-esteem, the elderly

tend to identify themselves as belonging to the non-elderly group. This is consistent with the previous theoretical analysis. Through the social comparison between the non-elderly group and the elderly group, a positive social identity can be obtained, so as to achieve the purpose of self-enhancement. In addition, we further examined the effects of old age identity and aging degree on the self-esteem of the elderly. We found that in order to improve self-esteem, the elderly tend to enter old age later and have a lower aging degree.

However, male and females differently perceive things (68, 69). Recent research shows that gender moderated the relationships between social interaction activities and self-esteem, females reported higher levels of engagement in social interaction activities and self-esteem than their male counterparts (70). There may be some gender differences in the self-enhancement effect of old age identity. We further set the interaction terms between gender and the three indicators of old age identity to verify whether gender can moderate the influence of the three indicators of old age identity on self-esteem. The empirical results show that the positive influence degree of old age identity and aging degree on self-esteem of elderly women is significantly higher than that of men, but there is no significant gender difference in the influence of group identification of the elderly on self-esteem. Therefore, in terms of affirming the self-worth and realizing the purpose of self-enhancement, old age identity has more important significance for elderly women.

Discussion

For RQ1, according to CLASS2014, the average old age identity of Chinese people aged 60 and above is 70 years. More than 40% of Chinese elderly people aged 60 and above don't identify with their old age status. An earlier study assessed old age identity among 666 Midwesterners in the United States, and there appeared to be a consensus across all age groups that old age begins around age 74 years (8). There is a difference of nearly 10 years in contrast to Neugarten et al. finding that old age begins around age 65 years (71). A recent study assessed 126 Israelis aged 65 and above with an average old age identity of 69 years (72). Whether it is in different periods for a country or between different countries, there are certain differences in the way that old age identities are formed; we believe this may be related to changes in individual social experiences, increased life expectancy, and differences in sociocultural backgrounds across countries.

For RQ2, this study verifies that the traditional Chinese cultural background of respect for the elderly has a significant impact on the old age identity of the Chinese elderly. After controlling for the various influencing factors, there are positive and negative effects of family factors on the old age identity of the Chinese elderly. We found that the elderly who frequently cared for grandchildren entered old age earlier, were more likely to identify with the elderly group, and experienced an exacerbated aging degree. Our conclusions differ from Kaufman and Elder, who found that the elderly who like to be grandparents feel younger, believe that old age will appear later, and that positive interactions with grandchildren may lead to younger age identity (41). We speculate that this may be related to the frequency of grandchild care, and that the elderly who care for grandchildren on a daily basis may have lower levels of physical fitness, making it difficult to demonstrate a positive old age identity. In addition, from the perspective of cultural differences between China and the West, the majority of grandparents follow a norm of "non-interference" in intergenerational relationships and do not assume a central role in caring for, and rearing grandchildren (73). However, in contemporary rural and urban China, it is increasingly common for grandparents to play a major caregiving role. Childcare provided by grandparents could be interpreted as a family adaptive strategy to maximize the wellbeing of the whole family, by alleviating the mothers' burdens and enabling them to pursue economic opportunities, and also indicates a significant cultural emphasis on collective family interests over individual interests (74). Chinese grandparents who often provide childcare may regard this as a sign of entering old age.

For RQ3, based on the social identity theory of social psychology, from the perspective of the elderly affirming their own value, we prove that in order to improve their self-esteem, the elderly tend to identify themselves as belonging to the non-elderly group, have a lower aging degree, and enter old age later. Although the theoretical connotation of old age identity also includes sociological role identity theory, Hogg et al. argue that social identity theory is more advantageous in explaining psychological mechanisms, through critical comparison of role identity theory and social identity theory (75). Theorists in the aging field have suggested that the tendency of aging adults to maintain younger subjective age identities is a form of defensive denial by which they can dissociate themselves from stigma attached to growing old (76). Recent research suggests that adults may switch from an age-group identity to a generational identity to strategically avoid negative age stereotypes and protect their positive self-views (60, 77). We argue that maintaining a positive self-view may not be a form of defensive denial for the Chinese elderly. Under the background of traditional Chinese culture of respect for the elderly, the elderly enjoy many preferential treatments, such as free bus rides, free access to parks, and free museum visits. In fact, the elderly are highly respected in China, on the contrary, those who discriminate against and disrespect the elderly are condemned by moral public opinion and even punished by law in China.

China's one-child policy, established in 1979, has had a depressive effects on fertility rates, increasing the proportion of elderly people in China and causing profound economic and social problems (78). The generation that grew up under China's one-child policy will also tend to have a lower birth rate, which

will push China toward negative population growth and more serious aging population. The old age identity of the elderly in China has great practical and policy significance in coping with the challenges brought by an aging society. Based on the self-perception of the elderly on when old age begins, not all Chinese elderly people aged 60 and above identify with their old age status. The aging society may not be "aging," which may bring forth more high-quality elderly human resources. According to CLASS2014, the average old age identity of Chinese people aged 60 and above is 70 years. In fact, delaying the retirement age may benefit the elderly who show advantages in health, psychology and socioeconomic status, and may have a certain impact on the elderly who are disadvantaged in these areas. In order to actively respond to aging, the Chinese government should pay more attention to the health and psychology of the elderly, raise the level of pension income, encourage the elderly to actively participate in politics, public welfare, etc., and strategically adjust the old age identity of the Chinese elderly. Due to the traditional Chinese cultural background of respect for the elderly, family intergenerational support can also help the elderly to show a positive old age identity; creating an elderly-friendly society will thereby, also pave an effective path for active aging.

Since the implementation of the one-child policy in China in 1979, traditional family structure and care-giving patterns in Chinese society have been changed (78), and one-child families in urban areas have become mainstream (57). The traditional Chinese culture of respect for the elderly and the norms of filial piety make the elderly, their children and grandchildren gather the strength of intergenerational solidarity and present a close intergenerational relationship. The historically hierarchical intergenerational relationship is replaced by one that emphasizes mutual care and reciprocal exchanges, reflecting a contemporary renegotiated and reinterpreted "intergenerational contract," in which both generations make investments (79). The three-generation family structure between the elderly and their children and grandchildren enhances the age identity of the elderly through the supportive behavior of children even grandchildren to respect the elderly, however, the positive age identity that the elderly obtain also faces certain challenges. Under the four-two-one family structure (four grandparents, two parents, one child), adult children shoulder the burden of supporting both elderly parents (74), which undoubtedly brings more structural barriers to children providing support for their parents. However, other studies have shown that, although all the cultures studied share the value of elder respect, the extent to which elders are actively or passively respected, and the forms of respect shown most often would seem to vary by culture (54). Streib found that Chinese people's respect for the elderly is an automatic expression (80). Although social changes and changes in family structure may change the forms of respect for the elderly, the Chinese culture of respect for the elderly is deeply influenced by the Confucian filial piety ethics (54, 81). Values, norms, roles, and patterns of social interaction associated with respect for elders have persisted from generation to generation (53, 80). We have reason to believe that the traditional Chinese culture of respect for the elderly and the norms of filial piety will be well preserved, but the Chinese government should realize that the ability of children to perform filial piety must also be formally supported outside the family.

Conclusions

Old age identity is the self-perception of when old age begins, reflects public age values and acceptance of aging. Paying attention to the old age identity of the elderly in China has great practical and policy significance for actively responding to the aging society. Different from Western countries, China is a country with a long-standing culture of respect for the elderly and filial piety norms, and the influence of the cultural background on the old age identity is worthy of attention. Using the 2014 China Longitudinal Aging Social Survey (CLASS), this study focuses on the old age identity of the Chinese elderly and its influencing factors. Combined with the traditional Chinese cultural background of respect for the elderly and the norms of filial piety, we build a predictive model of old age identity among the Chinese elderly, including seven dimensions: demographic correlates, socioeconomic status, health status, psychological status, behavior, major events, and family factors.

By analyzing the theoretical connotation of the concept of old age identity and using mathematical processing techniques, we obtained two other indicators based on old age identity: elderly group identity and aging degree. We found that the empirical results on the influencing factors of old age identity are also applicable to elderly group identity and aging degree. Health status, psychological status, behavior, socioeconomic status, and some demographic characteristics significantly affect the old age identity of the Chinese elderly. As common influencing factors of age identity, these findings are consistent with the conclusions of previous studies. Increasing age causes the elderly to enter old age later, raise the likelihood of identification with elderly groups, and exacerbate aging degree. Higher years of schooling, nonagricultural work, and higher pension income cause the elderly to enter old age later, raise the likelihood of identification with non-elderly groups, and reduce aging degree. Better self-assessed health, no chronic disease, higher life satisfaction status, and better emotional status also delay their entry into old age, keep them identifying with the non-old age groups, and reduce aging degree. Participating in political elections and public welfare activities also have the same positive effects on the elderly.

Cultural background factors is novel about our study, we introduce for the first time that the traditional Chinese cultural background of respect for the elderly and the norms of filial piety have an impact on the old age identity of the Chinese

elderly through family intergenerational support, that haven't been addressed in previous studies. The various forms of support provided by children to the elderly can help them achieve a positive age identity. Children providing substantial financial support to the elderly, caring about them often, and helping them with housework often, enable them to enter old age later, raise the likelihood of identification with non-elderly groups, and reduce aging degree. The number of children of the elderly, the children's economic conditions and care support for grandchildren have negative effects. Larger numbers of children, financially disadvantaged children, and often caring for grandchildren cause the elderly to enter old age earlier, raise the likelihood of identification with elderly groups, and exacerbate aging degree.

In addition, based on the social identity theory of social psychology, we empirically analyzed the significance of old age identity for the elderly from the perspective of them affirming their own value. In order to maintain self-esteem, the elderly tend to identify themselves as belonging to the non-elderly group, have lower aging degree, and enter old age later. We also found that gender can moderate the influence of old age identity on self-esteem. In terms of affirming the self-worth and realizing the purpose of self-enhancement, old age identity has more important significance for elderly women.

We hope that our findings may add practical value among endeavors toward enhancing the quality of life for the elderly, worldwide.

Limitations and future work directions

There are a few limitations of this study. First, our study is based on a sample of Chinese elderly people aged 60 and above, which may render it difficult to generalize our findings. However, the identity of different age groups may have different behavioral responses, such as their devotion to the community (82). Of course, another study points out that the age identities of middle-aged and elderly people are independent, and it is necessary to conduct separate studies (72, 83). Second, our study only involves the Chinese cultural background of respect for the elderly, emphasizing the impact of family intergenerational support on the old age identity of the Chinese elderly. However, the 5,000-year-old culture in China is extensive, profound and has a long history. Not only is the behavior of respect for the elderly rich in content, but other cultural backgrounds in China may also have an important impact on the old age identity of the Chinese elderly, this can be a future work direction. Although we are the first to conduct a more comprehensive study on the influencing factors of old age identity among the Chinese elderly using survey data, we may have also ignored some important factors, to which we hope to pay special attention, in future studies. In addition, future work directions may consider quantifying the cultural background of each country as an influencing factor of age identity and carry out comparative analysis, which will help to understand the differences of age identity among countries.

Despite these limitations, we believe that our study significantly enriches existing conclusions about age identity. We theoretically analyzed the concept of age identity and logically deduced the question of old age identity, and obtained three types of indicators. We explained the profound connotation of old age identity, which has particular significance for studies on other dimensions of age identity. Although there have been many studies on the influencing factors of age identity, they have not empirically tested the role of the cultural background, our study deepens the influence of sociocultural background on age identity. Based on the social identity theory of social psychology, we also empirically verified that the elderly achieve self-enhancement by having an old age identity, which further highlights the significance of old age identities for the elderly.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

XY and QW: conceptualization and methodology. QW: writing–original draft preparation. XY: writing–review and editing. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Effects of different intervention combined with resistance training on musculoskeletal health in older male adults with sarcopenia: A systematic review

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Objectives: Nowadays, there is a significant increase in the elderly population in many countries around the world, and sarcopenia is one of the most common consequences of this with resistance training being one of the best treatments. Hence, this systematic review was conducted to determine what are the effects of different combinations of resistance training-based interventions on the musculoskeletal health of older male adults with sarcopenia

Methods: This systematic review was performed following the PRISMA 2020 guidelines. The search was performed between February and August 2022 in three electronic databases: Pubmed (MEDLINE), Web of Science (WOS) and Scopus employing different keywords combined with Boolean operators. Only 13 articles were included out of the initial 1,019.

Results: The articles studied the effects of resistance training combined with other interventions, 6 articles combined it with protein and vitamin supplementation, 4 with protein supplements only, while 3 combined it with aerobic training, finding beneficial results mainly on strength, functionality, and body composition.

Conclusion: Resistance Training combined with Aerobic Training or nutritional supplements has better effects than Resistance Training alone in older male adults with sarcopenia.

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KEYWORDS

sarcopenia, resistance training, older adults, men, protein supplementation, aerobic training, nutritional supplementation

1. Introduction

Currently, there is evidence of a significant increase in the elderly population in many countries of the world, including Spain. As a result, more and more people are becoming susceptible to the diseases associated with aging (1). According to the WHO, the percentage of people over 60 years of age is increasing worldwide, reaching 1 billion in 2019 and it is expected that by 2050 this number will increase to 2.1 billion (2). This has attracted the attention of multiple researchers, becoming one of the most relevant topics today, even considering aging as a global public health issue (3). Understanding the processes of aging will allow the development of new and better interventions that can alleviate the adverse effects that time brings on human beings.

Sarcopenia is one of the consequences of aging, consisting of a progressive loss of muscle mass with a consequent loss of strength, accompanied by a decrease in physical performance (4). In 2010 The European Working Group on Sarcopenia in Older People (EWGSOP) established a definition updated in 2018, which recognized sarcopenia as a muscular pathology characterized by the gradual loss of both, muscle mass and strength affecting the quality of life, with risk of disability and even death (5, 6). Additionally, since 2016 it is considered by the WHO as a disease (7). This pathology is present in 6–22% of people over 65 years of age, being this percentage higher when the subjects belong to home residences (14–38%), are hospitalized (10%) (7) or are over 80 years of age (8). Sarcopenia, in the same way as aging, has been considered a public health problema (9), with a higher prevalence in men than in women (11 vs. 2%) when the EWGSOP definition is used (10).

This disease has been associated with an increased risk of mortality, risk of falls, fractures and a marked decrease in physical capacity (11). Occasionally, it often occurs in association with nervous depression, mainly in men, where a direct relationship between nervous depression and muscle mass loss has been observed (12). To date, there is no pharmacological treatment that has been approved for use in humans; however, animal research in this field is promising (13). On the other hand, the implementation of non-pharmacological interventions based on exercise and nutritional interventions have shown favorable results (14).

Resistance training or strength training is one of the options for exercise-based interventions, in which the subject uses his or her body and strength to oppose an external resistance (resistance machines, free weights, elastic bands, etc.) or internal resistance (body weight) (15). Among the multiple effects of exercise in people with sarcopenia is the increase in strength and muscle mass, which improves the functionality of the individual, in addition to combating oxidative stress caused by the aging process (16–18).

During the last few years, a large amount of evidence and articles on physical exercise and its effects on sarcopenia have been published (19–21), however, these have mainly focused on the female population and have rarely considered complementary interventions that enhance the effects of exercise. There is a great need to establish a cost-effective treatment to mitigate the effects of sarcopenia, especially in men, who have a higher prevalence of this disease. For this reason, this study aims to determine what are the effects of different combinations of resistance training-based interventions on the musculoskeletal health of older male adults with sarcopenia.

2. Materials and methods

This systematic review was performed following the PRISMA 2020 guidelines (22). The protocol followed in this review was registered in the International Prospective Register of Systematic Reviews PROSPERO under code CRD42022354184.

2.1. Eligibility criteria

Articles were selected based on the following inclusion criteria: (i) studies that evaluated the effects of resistance training in older male adults diagnosed with sarcopenia. (ii) studies in which at least one of the groups studied had received an intervention based on resistance training combined with another type of intervention and that evaluated a variable related to muscle health. Gray literature was not considered, and no filter associated with date of publication, publishing country or language were applied.

2.2. Information sources

The search was performed between February and August 2022 in three electronic databases: Pubmed (MEDLINE), Web of Science (WOS) and Scopus. A snowball search was not performed to avoid non-reproducibility of the protocol used.

2.3. Search strategy

The search strategy was designed specifically for this study employing keywords combined with Boolean operators, resulting in the following search string: ("older adults" OR "older men" OR "elderly" OR "seniors" OR "aging" OR "elderly people" OR "Male older adult") AND ("Resistance training" OR "Endurance training") AND ("Musculoskeletal health" OR "strength" OR "Skeletal muscle index" OR "SKI" OR "muscular quality" OR "Bone mineral density" OR "BMD") AND ("Sarcopenia").

2.4. Selection process

The entire article selection process was carried out using the Rayyan QCRI application (23) (https://rayyan.qcri.org/welcome, accessed on 25 February 2022). Initially, two of the authors (M.d.C.C.-F. and A.A.-A.) were in charge of eliminating all the duplicate articles and then reviewing the titles and abstracts, choosing the articles that would be read in full text. Finally, two different authors (D.F.A.-R. and F.H.-C.) read the full text of the articles that met the eligibility criteria and blindly gave their verdict. When disagreements arose, a third author was in charge of solving them.

2.5. Data extraction

The main variable of this study was musculoskeletal health measured through strength, the skeletal muscle index, muscular quality, or the bone mineral density. Additionally, the authors, year and country of publication, the type of additional intervention employed, and the characteristics of resistance training were retrieved.

2.6. Assessment of methodological quality

The methodological quality of the selected articles was measured using the PEDro scale (24). This instrument consists of 11 items that can be answered as YES (1 point) or NO (0 points), the maximum score is 10 points since the first item is not used in the final score calculation. A score between 0 and 3 was considered "Poor" quality; between 4–5 "Fair", 6–8 "Good" and >9 "Excellent" (25).

3. Results

3.1. Selection of the studies

The raw search of the databases yielded a total of 1,019 articles, followed by a filter for duplicate articles that left 689 studies to be screened. Subsequently, 490 articles were excluded based on title and abstract review, only 199 full-text articles were reviewed, leaving a total of 13 articles (26–38) that met the inclusion criteria (Figure 1).

3.2. Methodological quality assessment

From the thirteen articles included in this study, it was possible to score nine (26–32, 35, 36) of them using the PEDro website, while 4 of the studies (33, 34, 37, 38) were evaluated manually. Two of the studies (29, 35) presented a fair methodological quality while the remaining 11 were between good (26–28, 30, 32–38) and excellent (31). The item that stood out the most was item 6, blinding the therapists, where only 1 of the studies (34) achieved it, additionally, only 4 of the studies (31, 34, 37, 38) blinded the subjects. Table 1 summarizes the evaluation of the methodological quality of the included studies.

3.3. Characteristics of the studies

All articles included in this review were randomized clinical trials. The studies were primarily conducted in Germany (27, 28, 30–32, 35, 36, 38), however, there were also studies from Iran (29, 33), Canada (34, 37) and Saudi Arabia (26). Publication dates ranged from 2015 to 2022, being 2020 the year with the highest number of publications, 6 in total (29–34).

In total, 571 older male adults with sarcopenia or osteosacorpenia participated were selected for inclusion in the studies, with an age range of 63 to 81 years. A total of 291 subjects were assigned to experimental groups that based their intervention on resistance exercise combined with another treatment, 263 participants were assigned to control groups while 17 received an intervention without resistance training. Table 2 presents the characteristics of the included articles.

3.4. Characteristics of resistance training-based interventions

Resistance training-based intervention protocols used to treat the subjects differed from study to study. Regarding duration, it varied from 8 weeks (26, 29, 33, 35) to 18 months (27), including interventions of 12 weeks (34, 38), 4 (37), 6 (30–32, 36), and 12 months (32). 8 studies (27–33, 36) determined volume based on the number of exercises and repetitions while 2 studies (26, 34) established it using sets and repetitions, 2 studies (35, 37) reported volume combining both forms in addition to quantifying the duration of the session and 1 study (38) established the volume from the duration of the session only. It is important to highlight that 6 of the studies analyzed (27, 28, 30–32, 36) followed exactly the same protocol, which was denominated The Franconian Osteopenia and Sarcopenia Trial (FrOST).

Only 2 studies (34, 35) included an intervention group that performed resistance training without any complementary intervention or used placebos, finding better results when they combined their resistance training protocol with some other intervention.

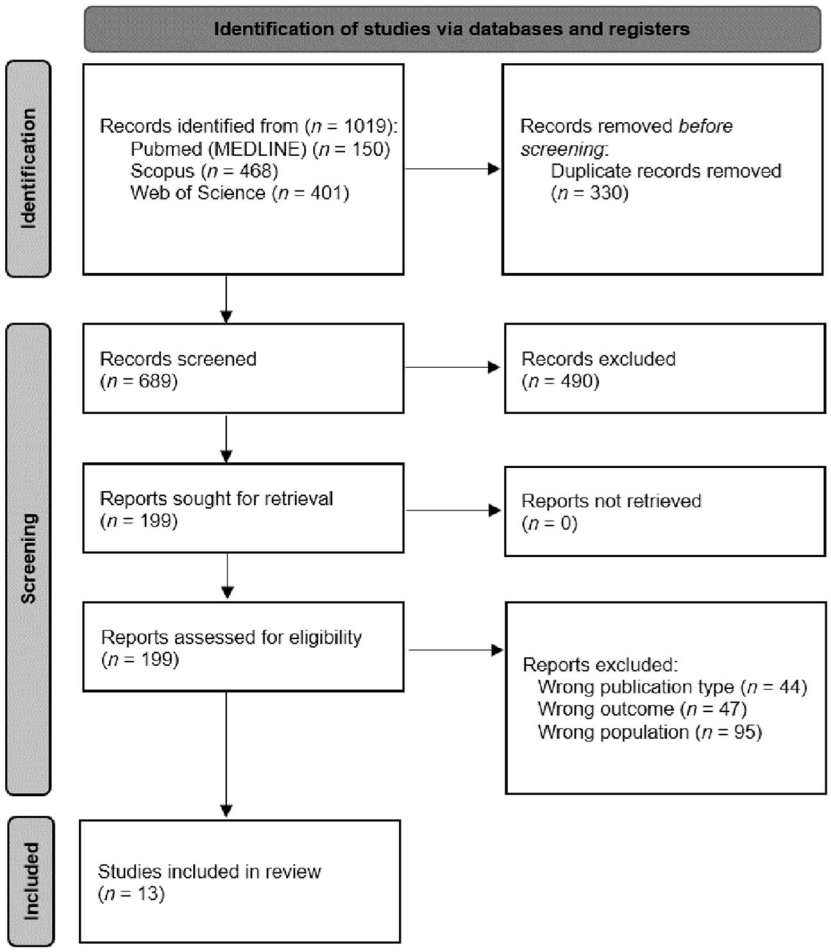

FIGURE 1
Flow diagram of the study selection process.

3.5. Effects of resistance training combined with protein and vitamin supplementation

Six of the studies (27, 28, 30–32, 36) analyzed in this review included as complementary treatment the use of protein and vitamin supplements; in addition, all employed the same protocol of high-intensity resistance training for IG compared with physical inactivity in CG. These similarities in the intervention protocols are due to the fact that all 6 articles are part of the FrOST.

Regarding protein and vitamin supplementation, it consisted of supplying all participants (GC and GI) with dietary protein, the GI was given 1.5 g/kg/day while the CG only received 1.2 g/kg/day, additionally, both groups received 800 IE/day of vitamin supplements. However, although all the studies are part of the FrOST, each one observed different variables and at different times, finding positive effects on the Skeletal Muscle Index (SMI) (28, 31, 32, 36), Bone Mineral Density at the lumbar and hip region (28, 31, 32), maximal hip and leg extensor strength (27, 28, 30, 32), handgrip strength (28, 31, 36), fat-free mass and abdominal and total body fat measured by DXA (30), prevalence of sarcopenia measured through z-score (31, 36), Gait velocity (31, 36) and, finally, muscle quality (27).

Two articles (27, 28), besides evaluating the pre and post intervention changes, conducted a 6 months follow-up of the patients to assess the effects that the detraining process has on this population. Kemmler et al. observed that 6 months after the end of the intervention a statistically significant and greater worsening was presented in the IG than in CG of SMI and hip extensor strength, which is partially consistent with the findings of Ghasemikaram et al. (27), who observed a significant worsening in maximal hip and leg extensor strength, however, when comparing both groups, the IG results were still better and presented statistically significant differences vs. CG.

TABLE 1 Methodological quality of the articles included.

item / authorship	1	2	3	4	5	6	7	8	9	10	11	Total
Nambi et al. (26)	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Ghasemikaram et al. (27)	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	7
Kemmler et al. (28)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Bagheri et al. (29)	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Kemmler et al. (30)	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	7
Kemmler et al. (31)	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9
Kemmler et al. (32)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Moghadam et al. (33)	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6
Nilsson et al. (34)	Y	Y	Y	Y	Y	Y	N	N	Y	Y	Y	8
Mafi et al. (35)	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Lichtenberg et al. (36)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Maltais et al. (37)	Y	Y	N	Y	Y	N	Y	N	N	Y	Y	6
Zdzieblik et al. (38)	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	7

Items: 1: eligibility criteria, 2: random allocation, 3: concealed allocation, 4: baseline comparability, 5: blind subjects, 6: blind therapists, 7: blind assessors, 8: adequate follow-up, 9: intention-to-treat analysis, 10: between-group comparisons, 11: point estimates and variability, Y, Yes; N, No. The eligibility criteria item does not contribute to the total score.

3.6. Effects of resistance training combined with protein only supplements

Four of the studies analyzed (34, 35, 37, 38) used specific supplementations based on different proteins in addition to resistance training. Nilsson et al. (34) used a protein compound called Muscle5 combined with a RT protocol based on low intensity exercises resisted by elastic bands and compared it with the same RT protocol but combined with a placebo, finding that when RT is combined with Muscle5 it generates better results in terms of fat-free mass, grip strength as well as press RM, functionality, muscle cross-sectional area and total lean mass. Mafi et al. (35) combined RT with Epicatechin, a flavonoid recognized for its ability to generate muscular mitochondria, reporting favorable effects on follistatin levels and maximal strength measured in chest and leg press; these effects were statistically significant when compared with the RT-only group and the CG (placebo). On the other hand, Maltais et al. (37), used as a complementary intervention to RT in the IG1 an Essential Amino Acids (EAA) supplement while for IG2 they used EAA from milk and compared them with a placebo based on flavored rice milk, finding that the RT groups had favorable results on the variables analyzed, however, there were no significant differences between the two IG which allowed them to conclude that RT is favorable for patients with sarcopenia regardless of the type of protein supplementation used, however, it is still important. Finally, Zdzieblik et al. used Collagen Peptides as an adjunctive intervention and observed significantly more pronounced changes in the IG in relation to fat-free mass, isokinetic quadriceps strength and fat mass, demonstrating that the combination of RT with Collagen Peptides is ideal for improving body composition in men with sarcopenia.

3.7. Effects of resistance training combined with aerobic exercise

Three of the studies (26, 29, 33) evaluated the effects of resistance training combined with aerobic training (AT). On the one hand, Bagheri et al. (29) and Moghadam et al. (33) studied the effects of these interventions by combining them in different ways in two IG. IG1 performed RT and then AT while in the IG2 this order was inverted, besides this, the other variables around the training prescription remained the same. On the other hand, Nambi et al. (26) only studied the combination of RT followed by AT.

The AT included a variety of exercises, two of the studies (29, 33) performed exercise on a fixed-speed cycle ergometer at an intensity of 70% for 30 min, while Nambi et al. (26) based their protocol on 30 min of aerobic activity comprising 20 min on the treadmill and 10 min on cycle ergometer, in this study they used aerobic exercise in the two groups analyzed, group 1 performed AT at low intensity (40–60% HRmax) while group 2 performed high intensity AT (60–80% HRmax).

Among the variables considered by the studies, it was found that resistance training combined with low-intensity aerobic training improved handgrip strength (26), quality of life (26), muscle mass (26, 29), musculoskeletal mass (33),

TABLE 2 Characteristics of the studies.

Author	*n* IG/CG	Age IG/CG	Intervention group: type, duration, volume, frequency, and intensity	Control group protocol	Duration and assessment	Outcomes
Nambi et al. (26)	38/38	63.2 ± 3.1	T: RT + AT	RT + High intensity AT	8 weeks	Handgrip strength; muscle mass; quality of life
		64.1 ± 3.2	V: RT: 3 sets-−10 repetitions/AT: 30 min		T0: baseline	
			F: 4 sessions a week		T1: 4 weeks	
			I: RT: 10 RM/low intensity AT: 40–60% HRmax/high intensity AT: 60–80% HRmax		T2: 8 weeks	
					T3: 6 months	
Ghasemikaram et al. (27)	21/22	79.6 ± 3.6	T: RT + protein, calcium, and vitamins supplementation	Life as usual + protein, calcium, and vitamins supplementatin	18 months	Muscle quality; maximum hip/leg extensor strength per unit of mid-thigh intra-fascia volume and per unit of thigh muscle mass
		80.8 ± 4.7	V: 12–14 exercises/session		T0: baseline	
			F: 2 times per week		T1: 18 months	
			I: high intensity		T2: 24 months	
Kemmler et al. (28)	21/23	77.8 ± 3.6	T: RT + protein, calcium, and vitamins supplementation	Life as usual + protein, calcium, and vitamins supplementatin	6 months	Skeletal muscle mass index; BMD; handgrip strength
		79.2 ± 4.7	V: 12–14 exercises/session		T0: baseline	
			F: 2 times per week		T1: 6 months	
			I: high intensity		T2: 12 months	
					T3: 18 months	
					T4: 6 months after the intervention	
Bagheri et al. (29)	IG1: 10	64.1 ± 3.3	T IG1: RT + ET	Life as usual	8 weeks	1RM estimation on lower limbs; VO2 max
	IG2: 10	63.8 ± 3.6	T IG2: ET + RT		T0: baseline	
	CG: 10	65.0 ± 3.9	V: RT: 6 exercises, 8–16 repetitions/ ET: 15–30 min		T1: 8 weeks	
			F: 3 times a week			
			I: RT: 75% of a RM/ET: 70% HRmax			

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TABLE 2 (Continued)

Author	*n* IG/CG	Age IG/CG	Intervention group: type, duration, volume, frequency, and intensity	Control group protocol	Duration and assessment	Outcomes
Kemmler et al. (30)	21/23	77.8 ± 3.6	T: RT + protein, calcium, and vitamins supplementation	Life as usual + protein, calcium, and vitamins supplementatin	6 months	BMD; STRENGTH OF LOWER Limbs
		79.2 ± 4.7	V: 12–14 exercises/session		T0: baseline	
			F: 2 times per week		T1: 28 weeks	
			I: high intensity		T2: 54 weeks	
					T3: 78 weeks	
Kemmler et al. (31)	21/23	77.8 ± 3.6	T: RT + protein, calcium, and vitamins supplementation	Life as usual + protein, calcium, and vitamins supplementatin	6 months	BMD; prevalence of sarcopenia; handgrip strength; gait velocity
		79.2 ± 4.7	V: 12–14 exercises/session		T0: baseline	
			F: 2 times per week		T1: 28 weeks	
			I: high intensity		T2: 54 weeks	
					T3: 78 weeks	
Kemmler et al. (32)	21/23	77.8 ± 3.6	T: RT + protein, calcium, and vitamins supplementation	Life as usual + protein, calcium, and vitamins supplementatin	1 year	BMD; SMI; maximum dynamic hip- and leg-extensor strength
		79.2 ± 4.7	V: 12–14 exercises/session		T0: baseline	
			F: 2 times per week		T1: 28 weeks	
			I: high intensity		T2: 54 weeks	
					T3: 78 weeks	
Moghadam et al. (33)	IG1: 10	64.1 ± 3.3	T IG1: RT + ET	Life as usual	8 weeks	BMI; 1RM estimation for all the exercises used in the resistance training; satellite cells related markers myogenic factor dietary intake
	IG2: 10	63.8 ± 3.6	T IG2: ET + RT		T0: baseline	
	CG: 10	65.0 ± 3.9	V: RT: 6 exercises, 8–16 repetitions/ET: 15–30 min		T1: 8 weeks	
			F: 3 times a week			
			I: RT: 75% of a RM/ET: 70% HRmax			

(Continued)

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TABLE 2 (Continued)

Author	*n* IG/CG	Age IG/CG	Intervention group: type, duration, volume, frequency, and intensity	Control group protocol	Duration and assessment	Outcomes
Nilsson et al. (34)	16/16	77.4 ± 2.8	T: HBRE + walking + Protein compound	Placebo + HBRE	12 weeks	BMD; hip-waist index; BMI; hear rate; arterial blood pressure; sarcopenia diagnosis; handgrip strength; 1RM on lower limbs; physical performance; muscle quality; physical activity; dietary intake
		74.4 ± 1.3	V: 3 sets/10–15 repetitions		T0: baseline	
			F: 3 sessions a week		T1: 12 weeks	
			I: low intensity HBRT/Walking: 5,000 steps on exercise days and 10,000 steps on rest days			
Mafi et al. (35)	IG1: 14	69.0 ± 2.4	T IG1: RT	Placebo	8 weeks	BMI; dietary intake; maximal muscle strength (leg and chest press); time up and go; physical activity level; follistatin; myostatin
	IG2: 15	69.0 ± 3.1	T IG2: RT + Epicatechin		T0: Baseline	
	IG3: 17	68.6 ± 3.1	T IG3: Epicatechin		T1: 8 weeks	
	CG: 16	68.0 ± 3.0	D: 55 min			
			V: 3 sets/8–12 repetitions/8 exercises			
			F: 3 sessions a week			
			I: 60–80% of 1RM			
			Epicatechin dosage: 1 mg/Kg/day			
Lichtenberg et al. (36)	21/22	77.8 ± 3.6	T: RT + protein, calcium, and vitamins supplementation	Life as usual + protein, calcium, and vitamins supplementatin	6 months	BMD; prevalence of sarcopenia; handgrip strength; gait velocity
		79.2 ± 4.7	V: 12–15 exercises/ 1–2 sets/7–18 repetitions		T0: Baseline	
			F: 2 times per week		T1: 6 months	
			I: High Intensity			

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TABLE 2 (Continued)

Author	*n* IG/CG	Age IG/CG	Intervention group: type, duration, volume, frequency, and intensity	Control group protocol	Duration and assessment	Outcomes
Maltais et al. (37)	IG1: 8	64 ± 4.8	T IG1: RT + EAA supplementation	Chocolate-flavored rice milk placebo	4 months	BMI; muscle mass; maxima muscle strength; physical activity level; dietary intake; walking speed; time up and go; chair stand: standing balance task; one leg stand
	IG2: 8	68 ± 5.6	T IG2: RT + EAAmilk + cowmilk		T0: Baseline	
	CG: 10	64 ± 4.5	D: 60 min		T1: 4 months	
			V: 9 exercises/3 sets/6–8 repetitions			
			F: 3 times a week			
			I: 80% of 1RM			
Zdzieblik et al. (38)	26/27	72.3 ± 3.7	T: RT + protein supplementation	Collagen peptides-based placebo	12 weeks	Body composition; muscular strength; sensory motor control; dietary intake
		72.1 ± 5.5	D: 60 min		T0: Baseline	
			F: 3 times a week		T1: 12 weeks	
			I: High Intensity			

IG, intervention group; CG, control group; T, type; D, duration; F, frequency; I, intensity; HRmax, maximum heart rate; HBRE, home-based resistance exercise; RT, resistance training; ET, endurance training; AT, aerobic training; RM, repetition maximum; BMI, body mass index; BMD, bone mineral density; SMI, structure model index; EAA, essential amino acids.

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total fat percentage (29), weight (29), el BMI (29), lower and upper limb power (29, 33), VO2Max (29, 33) and generated favorable modifications in the Satellite Cells related markers (33). Additionally, it was observed that low-intensity aerobic training is more effective than high-intensity training when combined with resistance training (26), irrespective of AT and RT order (29, 33).

4. Discussion

The objective of this systematic review was to determine the effects of resistance training when combined with different complementary interventions on musculoskeletal health in older male adults with sarcopenia. For this purpose, 13 articles were reviewed that included resistance exercise as the main treatment and employed other types of complementary treatments to enhance its effects. This review revealed robust evidence on the effects of resistance training when combined, mainly with aerobic exercise or with different nutritional supplementation, on variables associated with musculoskeletal health.

Regarding the quality of the included studies, it is possible to determine that the quality did not influence the observed results, since only one of the articles had a quality below Good and the results were homogeneous. Additionally, it is important to highlight that only one of the articles performed a blinded intervention, principally due to the fact that blinding an exercise-based intervention is a common problem reported in multiple reviews and studies (39, 40).

Resistance training is a widely used intervention for the treatment of patients with sarcopenia, due to the diverse effects it has on musculoskeletal health (16, 41, 42). However, due to the increasing number of people who suffer from this disease, it is necessary to develop interventions to obtain more and better results that also last over time, therefore, the effects of resistance exercise have been studied in combination with other types of intervention.

The implementation of protein supplementation either combined with vitamins (27, 28, 30–32, 36) or alone (34, 37, 38) along with RT showed favorable effects on multiple musculoskeletal health variables, mainly those associated with strength and body composition. These results may be due to the well-known important role of amino acids as substrates of protein synthesis and as mediators in physiological and metabolic processes (43). One of the conditioning factors of the effects of this type of supplementation is the origin of the protein, Poortmans et al. (44) that when RT is performed and accompanied by a whey protein-based supplement, the absorption process and its effects on protein synthesis are better than when other sources of EAA are used. However, although the studies analyzed did not all employ whey protein-based supplements (37), they all evidenced favorable results on the variables evaluated. Additionally, it is important to consider the negative effects of high protein intake on liver and colon health (43), therefore the doses prescribed to subjects should be correctly calculated.

Another complementary intervention to RT was AT, which has been shown to be better at modulating the immune system and inflammatory markers in older adults than other types of exercise (45). The results obtained in the studies analyzed in this review are congruent with those of several authors (46–48), who applied a similar protocol of RT combined with AT in prefrail or frail older adults, finding that it increased strength, muscle power and aerobic capacity. Although the order of the interventions was not a determinant of treatment success as demonstrated by Bagheri et al. (29) and Moghadam et al. (33), the intensity of the AT was. According to the findings of Nambi et al. (26), low-intensity AT was better than high-intensity AT when combined with RT, this is because during low-intensity exercise the oxidative capacity of the cell is stimulated and blood flow is increased (49), leading to significant differences in multiple variables, including strength, possibly due to the differences in energy metabolism that low-intensity AT produces.

With regard to the detraining process, two articles (27, 28) observed that after 6 months following the intervention, the effects obtained partially disappeared, decreasing about a third of what was gained, which agrees with the results of Padilha et al. (50), who after a 12-week intervention based on RT in older women observed that, although detraining negatively affects this population, it is not enough to reverse all the changes resulting from exercise. This can be attributed to the principle of stability of adaptation, which states that the longer the period of training time, the more stability it will create and the less susceptibility to failure it will present. Another possible explanation is related with the principle of reversibility of training, which establishes that once the exercise is interrupted, the benefits obtained and the adaptations generated are progressively lost; however, there is no specific time for this. The reversibility process depends on several factors such as: the duration of the training period, how significantly the subject's behavior changed, as well as intrinsic characteristics of the subject, such as age and genetics (51).

Likewise, it seems that the intensity of RT has no impact on its effects, since all studies obtained favorable results whether they used high (27, 28, 30–32, 36), moderate (26, 29, 33, 35, 37, 38) or low intensity (34). These results are partially in agreement with those of Steib et al. (52), which in their systematic review with meta-analysis determined that high-intensity RT is better than low-intensity RT in relation to strength; however, in terms of functionality there is no difference. Multiple studies have evidenced an association between strength and functionality (53, 54), which means that improvements in strength after a certain point do not necessarily mean improvements in functionality (55), therefore, different RT intensities could have similar effects on this variable.

Finally, this review presents several limitations that should be considered when interpreting the results. On the one hand, the great variety in the prescription of RT does not allow us to establish an ideal treatment protocol for older male adults with sarcopenia. In addition, due to the fact that 84.6% of the articles were published in Eurasia and, specifically, more than 60% of the articles were published in Germany, the results cannot be extrapolated to other populations such as Latin American or African populations. Also, because of the variety in the methodological quality of the articles and the lack of a specific PEDro score inclusion criteria, the quality of this systematic review may be affected.

5. Conclusion

Interventions based on RT have beneficial effects on different variables associated with musculoskeletal health in older male adults with sarcopenia. RT training can be used at any intensity as long as the objective is to improve functionality; additionally, when combined with AT, the AT should be low intensity to optimize results. Nutritional supplementation enhances the effects of RT, but by itself is not sufficient treatment for this population, and doses should be carefully adjusted to avoid potential health problems in the future. RT must be constant for maintaining the results obtained. Finally, RT is a cost-effective, low-risk strategy for treating sarcopenia, and is always recommended to be combined with another type of intervention, either aerobic exercise or nutritional supplementation to enhanced the effects.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

Conceptualization: MC-F and ML-N. Methodology: AA-A and FH-C. Performing literature review and synthesis of literature: MC-F, AA-A, and DA-R. Quality assessment: CR-L, FH-C, and AA-O. Writing—original draft preparation: MC-F, AA-A, and YC-C. Writing—reviewing and editing: FH-C, AA-O, YC-C, and DA-R. All authors have read and agreed to the published version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Country score tool to assess readiness and guide evidence generation of immunization programs in aging adults in Europe

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Objectives: Delaying of policies for immunization of aging adults, low vaccine uptake, and the lack of supportive evidence at the national level could diminish the value in health and economics of such programs. This study aims to develop a "country score tool" to assess readiness and to facilitate evidence generation for aging adult immunization programs in Europe, and examine the comprehensiveness, relevance, acceptability, and feasibility of the tool.

Methods: The tool was developed in two phases. First, a modified Delphi process was used to construct the tool. The process included a literature review, stakeholder consultations, and a three-round Delphi study. The Delphi panel included researchers, supra-national and national decision-makers of immunization programs recruited from five countries, using snowball sampling method. The consensus was predefined at the agreement rate of 70%. Pilot testing of the tool was conducted in the Netherlands, Germany, Serbia, and Hungary involving researchers in the field of health technology assessment. After assessing the countries' readiness, researchers evaluated four features, namely comprehensiveness, relevance, acceptability, and feasibility of the tool *via* an online survey that included 5-scale Likert questions. The percentages of affirmative answers including "agree" and "totally agree" choices were presented.

Results: The review identified 16 tools and frameworks that formed the first version of our tool with 14 items. Eight experts were involved in the Delphi panel. Through three Delphi rounds, four items were added, one was dropped, and all others were amended. The consensus was achieved on the tool with 17 items divided into decision-making and implementation parts.

Each item has a guiding question, corresponding to explanations and rationales to inform assessment with readiness scores. Eight researchers completed the pilot testing. The tool was rated as comprehensive (75%), relevant (100%), acceptable (75%), and feasible (88%) by participants.

Conclusion: Through a thorough and transparent process, a country score tool was developed helping to identify strengths, weaknesses, and evidential requirements for decision-making and implementation of immunization programs of aging adults. The tool is relevant for different European contexts and shows good comprehensiveness, acceptability, and feasibility.

KEYWORDS

immunization programs, aging, readiness, assessment, evidence, tool

1. Introduction

Burden of vaccine preventable diseases (VPDs) is threatening healthcare systems not only by an increasing number of aging people (50 years and older) but also through the age-related decline of the immune system (1, 2). An extreme burden was demonstrated with the COVID-19 pandemic when a sudden increase in cases, morbidity and mortality became an urgent problem (3). Besides COVID-19, other VPDs significantly impact on aging population. The issue is exemplified by European data with ∼40,000 deaths annually caused by influenza with 90% occurring among elderly (4), 73 hospitalizations per 100,000 seniors every year for community-acquired pneumococcal pneumonia (5), and almost a third of adults developing herpes zoster over lifetime (6).

As a preventive strategy, vaccination has been reported to be effective in limiting the severity, reducing morbidity and mortality of infections in aging population (7–9). Those health benefits enable them to contribute to nations' social and economic development as well as perform various valuable functions including childcare, providing financial and emotional support to families (10). Along with health and social benefits, immunization programs have been proved to be cost-effective (11–13). Despite those potential benefits in health, social and economic aspects, vaccines are underutilized in aging population characterized by delayed policy implementation and low vaccine uptakes. Less than two third of European countries had policies for pneumococcal vaccine and most countries had no vaccination policies against herpes zoster (14). Although influenza vaccination programs were in place all over Europe, only one country achieved the vaccine uptake target in 2018/2019 of 75% recommended by World Health Organization (WHO) (15, 16). During the same season, half of the countries had <35% of older people vaccinated against influenza; the lowest coverage was <1% (16). Therefore, countries need to strengthen their immunization programs for aging population by focusing on both decision-making and implementation aspects.

Required elements for both decision-making and strategies for implementation have been investigated among European countries. The most important component for making decision on vaccine introduction is evidence, including international literature and country-specific evidence (17). The former can be done by a standardized systematic approach using available supporting tools, for instance, GRADE and CAPACITI (18, 19). The latter element includes, but is not limited to, setting-specific evidence of the burden of disease and health economic evaluation. However, in many countries, there is no transparent guidance that presents various methodological requirements (17). It suggests a need for a holistic assessment to first identify the gaps in healthcare systems concerning aging adult immunization programs, and second, to identify methods for future research enabling decision-making and implementation (20). This assessment could be sufficiently defined by a concept of a "readiness assessment." By definition, readiness assessment can help to identify the potential challenges when implementing new processes within a current organizational context and affords the opportunity to remedy these gaps either before, or as part of, the implementation plan (21).

Although the two concepts of "decision-making" and "implementation" are commonly used across publications (22–24), they are poorly defined. That could be driven from the complexity and dynamic nature of introducing vaccines into different settings. A recent study identified key features of vaccine market access pathways across the European Union (EU) and the United Kingdom. They included horizon scanning, early advice, initiation of assessment, recommendations from advisory groups for vaccine introduction and funding, final decision, National Immunization Program (NIP) inclusion, and procurement (25). Drawing on that pathway, we defined decision-making as the process of generating recommendations to include

vaccines to the national immunization program and possibly reimbursed by National Immunization Technical Advisory Group (NITAG) and/or Health Technology Assessment Body (HTAB) (or equivalents); and implementation as the process of proceeding with the recommendations including resourcing, making final decisions of vaccine introduction, procurement, and sustainability.

Various published works exist that help to assess a country's readiness with regards to immunization programs; however, there are limitations in terms of target diseases, population, and transferability in different European contexts. First are readiness assessment tools for COVID-19 vaccine introduction, which might be though inapplicable for non-pandemic vaccines, given the special priority of resources for COVID-19 (26, 27). Second, a majority of guidelines and publications focus on vaccination of the general populations (28, 29), or specifically for children (30) or during pregnancy (31). Despite immunization programmes' common aspects, those of aging population have specific requirements including a need for adult vaccine working groups (22), evidence on potential gains from immunization, and relevant infrastructure to deliver immunization service to this population (20). Therefore, it is important to consider those existing guidelines as a foundation, but unique requirements for aging adults should be added to the assessment tool targeting this population. To partly fill in this gap, an "Evidence-Based Tool for Planning and Evaluating" was considered to be the first proposal up to 2021 aiming at improving coverage for the elderly by planning and monitoring vaccination strategies (32). However, the ability to support making policies and possibilities to generate evidence in immunization programs are not in scope of the tool. Additionally, the transferability of the tool to different European countries is limited when its development solely considered the Italian context.

All those gaps in the literature raise a need for a tool that can simultaneously assess countries' readiness and facilitate evidence generation to support decision-making and implementation processes of immunization programs in European countries targeting aging population. This work aims to (1) develop a country score tool, which can help to achieve those purposes and (2) to test the comprehensiveness, relevance, acceptability, and feasibility of the tool.

2. Materials and methods

The country score tool was developed in two phases (Figure 1). In phase 1, a modified Delphi process was used. This method concerns a group consensus strategy that systematically uses literature review, opinions of the research team (labeled steering group) and the judgment of experts within the research field to reach agreement (33, 34). Phase 2 involved pilot testing in four countries including the Netherlands, Germany, Hungary, and Serbia.

2.1. Phase 1: Tool development using a modified Delphi process

2.1.1. Development of an item pool and the first version of the tool

We conducted a comprehensive literature review in August 2021 to identify existing readiness assessment tools and frameworks for immunization programs with regards to decision-making and implementation in general populations and adult populations separately. Publications that specifically focused on aging population were separated from the adult-related search. To define aging population, the cut-off of 50-year-old and over was applied as suggested in published work regarding vaccination to promote healthy aging globally (35, 36). Details of the literature review including inclusion, exclusion criteria, and search strategy are presented in Supplementary material 1. All components and sub-components of the identified tools and frameworks were extracted for the development of an item pool. COVID-19 related aspects were excluded in the development process. This feature enables the tool to be used for non-pandemic vaccination programs in aging population in the future after the COVID-19 pandemic era.

We structured the tool along the two lines of decision-making and implementation. The foundation for item generation was set up based on (1) a published systematic review of 116 studies on national decision-making for the introduction of new vaccines and (2) WHO guidance on principles and considerations for adding a vaccine to a national immunization program (28, 30). Next, items in the item pool were linked to this foundation. Similar components were grouped, and new components were added. Disease-specific or vaccine-specific items were excluded from the item bank afterwards.

The structure of the tool was generated by integrating a checklist approach and a scoring approach. As a checklist, the country readiness tool presented each item in the item pool as a question supported by definitions and rationales (31). In addition, the readiness level in each item was defined by a scoring system of three values including 0, 1, and 2 (22). No weighting system was implied in order to provide flexibility for countries when using the tool according to particular infrastructures and the national priorities.

2.1.2. Stakeholder consultation

Consultation with stakeholders occurred in December 2021-January 2022 to first determine the relevance and importance of a set of components identified in the previous step, and to identify additional components. Participants were recruited from VITAL consortium comprising 17 public partners from 11 countries in Europe together with seven biopharmaceutical companies in a European project named Vaccines and InfecTious diseases in the Aging population (37).

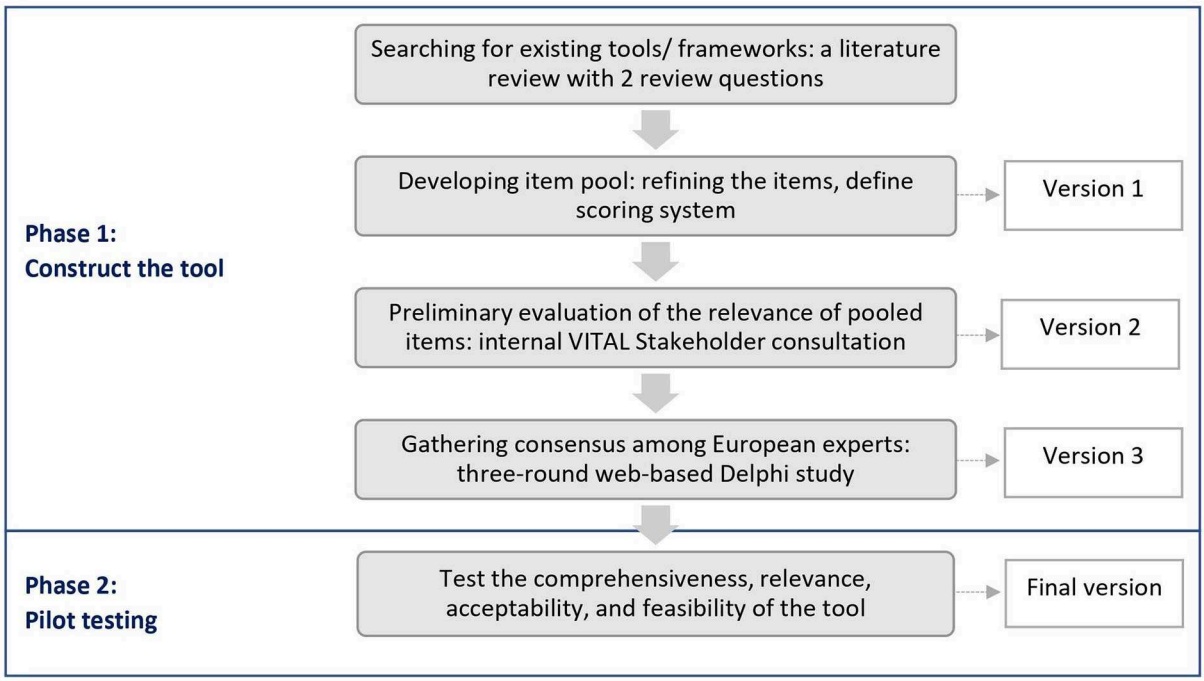

FIGURE 1
Development process of the country score tool.

All participants were provided with the first version of tool and asked for individual feedback before participating in an online meeting where all disagreements among individuals and suggestions for additional items were discussed. Polls were used during the meeting to support reaching agreements. The meeting was recorded and later transcribed *via* Microsoft Teams. The second version of the tool was generated according to the agreement.

2.1.3. Three-round Delphi study

Delphi panelists were non-VITAL members who have experience in one or more of the predefined fields/positions: (1) Ministry of Health; (2) NITAG (or equivalent); (3) Insurer; (4) HTAB (or equivalent); (5) Representatives of: Healthy aging, General practitioners (GPs), Pharmacists, Nursing homes; (6) World Health Organization; and/or (7) Researcher in related fields including, but not limited to, Infectious diseases, Immunization, Epidemiology, Health Economics and Public Health. Snowball sampling method was used to recruit participants. This method involves identifying index individuals and asking them to refer other persons suitable for the study (38). Responses were collected *via* a Qualtrics survey using Qualtrics software (39).

Figure 2 presents the item evaluation process following the three-round Delphi study. In the first and second rounds, panelists were required to evaluate all items and give their opinions if the item should be "included as is," "included with edits" or "dropped" from the tool; provide their suggestions for amendments, or for additional items or reasons for the exclusion. Consensus was predefined as a rate of agreement or disagreement above 70%. Items that reached the consensus value were included directly in the final version without further evaluation. Other items that did not reach the consensus or were subjects for edits or were newly added were transferred to the next round. Within 1 week after the evaluation period, panelists received the result and the survey link for the next round. Panelists who did not participate in one round were allowed to join the following round after he or she agreed with the current report.

In the third round, panelists were required to evaluate revised items resulting from round 2 by choosing "include the item" or "drop the item." Suggestions for edits or new items were not applicable. Consensus for inclusion was defined with a cut-off of 70%. The final result of the Delphi study was made available for all participants 2 weeks after the third round.

2.2. Phase 2: Pilot testing

An e-pilot test was conducted in four European countries: Netherlands (NL), Germany (GER), Serbia (SER), and Hungary (HU) to (i) test comprehensiveness, relevance, acceptability, and feasibility of the tool (40); (ii) finalize the tool; and (iii)

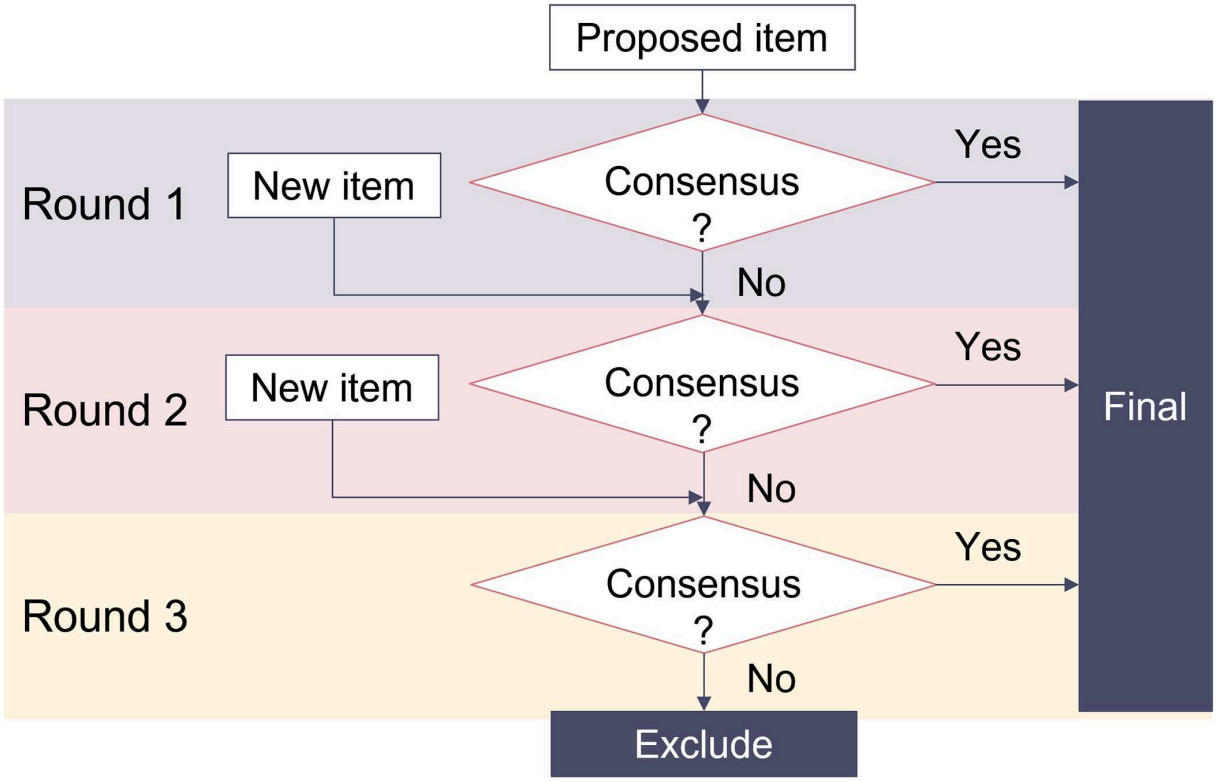

FIGURE 2
Item generation process through a three-round Delphi study.

present preliminary assessment of the countries' readiness. Tool version 3 (electronic version in excel) was tested in a small sample of the target audience—two researchers per country in the field of health economics/ health policy. These criteria were made based on considering the feasibility of the project and the ability of participant to assess different aspects of the tool rather than the importance of their roles in the topic area. Having a good understanding of various dimensions in the vaccine introduction process, starting from measuring the burden of diseases to financing and delivering the intervention, health economic/ health policy participants are a relevant proxy of the multidisciplinary audience of the tool. Snowball sampling method was used to recruit participants.

First, participants were asked to complete the readiness assessment in their countries and provide with corresponding evidence for their answers. Collected readiness scores were re-evaluated by the research team when conflicting answers existed between participants evaluating the same country. The final scores were determined based on provided evidence.

Second, participants took an online post-pilot assessment evaluating the tool followed on a five-point scale (strongly disagree, disagree, neutral, agree, and strongly agree) to determine the comprehensiveness, relevance, and acceptability of the tool. The feasibility of the tool was determined based on the ability to complete the readiness assessment and the ability to come up with one research idea that aimed to address identified problems based on the readiness scores. In addition, participants were also asked if they had any additional feedback to improve the abovementioned features and the tool as a whole. Based on the feedback, adaptation was followed to define the final version of the tool. Suggestions for major changes or inclusion of new items were inapplicable due to the extensive need for re-evaluation subsequently. Responses were collected *via* a Qualtrics survey (39).

3. Results

3.1. Phase 1: Tool development

3.1.1. Development of the item pool and the first version of the tool

From the literature review, 16 tools and frameworks were identified. After the data extraction process, an item pool was formed that included 65 items (Supplementary material 1). The first version of the tool included eight and six items in the decision-making and implementation parts respectively. Table 1 provides a summary of the item generation process throughout the whole process, from the development of the item pool until the pilot test.

3.1.2. Stakeholder consultation

Eleven members participated in the plenary meeting. All proposed items were evaluated to be relevant and important with some suggestions for edits. Overall, it was suggested to specify which vaccines to be used as criteria to assess the strength of current national immunization programs. Furthermore, experts pointed out the importance of having guidelines or strategies based on local evidence in the country with regards to vaccine acceptability among aging adults. The suggestion led to adding one item to the decision-making part.

3.1.3. Three-round Delphi study

The first round was completed by seven panelists. During the second and third rounds, all members completed the evaluation ($N = 8$). Description of the Delphi panel is presented in Table 2.

Availability of national guidance or communication campaigns for generating acceptance and demand for vaccines in aging adults, together with availability of healthy aging strategies, were considered to be important by 100% of panelists in round 1. In contrast, availability of alternative measures for prevention and control of VPDs in aging adults was suggested to be dropped by 14% of panelists in round 1, subjected for re-evaluation in the next rounds, and finally excluded. Moreover, the panel suggested and agreed on adding three items related to (1) basic requirements for NITAGs (or equivalent), (2) hard-to-reach groups (e.g., illiterate individual and migrants), and (3) healthcare professionals' involvement in providing vaccine recommendations to aging adults. Thirteen items that did not reach the consensus in round 1 were re-evaluated over round 2 and/or round 3. Generally, the panel suggested using universal terms to optimize the transferability of the tool in different contexts, given the diversity in policy and organizational setup of immunization programs among European countries. Furthermore, suggestions for rewording were proposed by panelists with regards to comprehensiveness of the tool as a whole and scoring system of each item that can cover all possibilities to assess readiness.

3.2. Phase 2: Pilot testing

3.2.1. Testing four features of the tool: Comprehensiveness, relevance, acceptability, and feasibility

Eight researchers participated and completed the readiness assessment and the post-pilot survey (Response rate 100%, $N = 8$). Table 3 shows the results of the post-pilot assessment in which a percentage of participants evaluating different features of the tool are presented.

The tool was evaluated to be comprehensive to capture all essential aspects of the readiness assessment by 75% of participants. In addition, 88% of participants perceived all components well-explained. All participants rated the tool to be relevant in their countries. In terms of acceptability, 75% of participants indicated their acceptance with time required and the future use of the tool. Moreover, 100% of participants suggested that the tool and the readiness results would be useful to their colleagues in health economics, and other fields including public health, epidemiology, and health politics. The feasibility of the tool was accepted by more than 85% of participants.

3.2.2. Final version of the tool

Participants of the pilot provided their feedback to redraft some of the sentences or provide more information for a better understanding on three items regarding existing vaccination programs (2 items) and healthy aging strategies. The final version of the tool consists of 17 items divided into decision-making and implementation parts. Each item has a guiding question, corresponding to explanations and rationales to inform assessment with readiness scores. Due to the large amount of information condensed in the tool, rationales and explanations of all items are presented separately in Supplementary material 2. The tool with guiding questions and readiness scores is presented in Table 4 of this manuscript.

The readiness of countries with regards to decision-making is assessed by the availability of sufficient infrastructure, fully functioning supportive groups and relevant strategies. First, the national surveillance system of VPDs should be in place to provide baseline epidemiological data on VPDs as well as to measure the impact of vaccines on disease incidences, morbidity, and mortality. Moreover, previously successful vaccine introductions for aging adults are indicative of the relevant infrastructure of the NIP for this target population. Second, the involvement of relevant stakeholders is crucial for countries to make decisions on vaccine introductions. While a NITAG (or equivalent) is a basic need for an NIP, the availability of adult vaccine workgroups is a specific requirement for aging adult immunization. Such groups could be in place as standalone groups or initiated by involving relevant experts into recommending bodies where vaccination of aging adults is considered. Third, national immunization strategies and healthy aging strategies covering aging adult vaccination serve as a foundation to direct new vaccine introductions given the many health issues and resource constraints that need to be tackled. Additionally, communication strategies, adjusted by local evidence on vaccine demand and acceptability, are needed to ensure high vaccine uptake. If the evidence is not available, corresponding studies at the local or national level need to be conducted to guide policies.

In alignment with the decision-making part, items in the implementation part of the tool further assess how countries have proceeded with vaccine recommendations and identify how the current system can facilitate future vaccine adoption

TABLE 1 Changes in the number of items during the item generation process of the country score tool.

Step	Decision-making					Implementation				
	Start	Progress			Finish	Start	Progress			Finish
		Drop	Add	Edit			Drop	Add	Edit	
Development of item pool*	38	0	0	38	8	27	0	0	38	6
Stakeholder consultation	8	0	1	8	9	6	0	0	6	6
Delphi round 1	9	0	1	7	10	6	0	1	6	7
Delphi round 2	10	0	0	5	10	7	0	1	4	8
Delphi round 3	10	1	0	0	9	8	0	0	0	8
Pilot testing	9	NA	NA	3	9	8	NA	NA	0	8

*In this step, items were dropped, edited or grouped together by the similarity leading to an increase in the number of items (Supplementary material 1).
NA, Not applicable.

TABLE 2 Description of the Delphi panel.

Stakeholder group*	Country				
	United Kingdom	Netherlands	Italy	Belgium	Hungary
Ministry of health	x				
National Immunization Technical Advisory Group (NITAG) or equivalent	x	x	x	x	x
Health Technology Assessment Body (HTAB)	x		x		x
Representatives of: Healthy aging, General practitioners (GPs), pharmacists, nursing homes	x				x
Researchers	x		x		x
World Health Organization	x				

*Panelists might have expertise/experience in more than one stakeholder group.

TABLE 3 The post-pilot assessment result.

Feature	Criteria	Results			
		Agree/ strongly agree	Neutral/ disagree/ strongly disagree	Yes	No
Comprehensiveness	The tool covers all essential components	75.0%	25.0%		
	All components of the tool are well-explained	87.5%	12.5%		
Relevance	All components of the tool are relevant	100.0%	0.0%		
Acceptability	Time needed to complete the tool is acceptable	75.0%	25.0%		
	Use the tool or its results in the future			75.0%	25.0%
	Recommend the tool or its results to colleagues			100.0%	0.0%
Feasibility	Ability to complete the readiness assessment			100.0%	0.0%
	Ability to come up with a research plan after completing the readiness assessment			87.5%	12.5%

for aging populations. By reviewing vaccine financing aspects, decision-makers might consider if expanding immunization financing mechanisms would be needed for the long-term financial sustainability of the NIP. Furthermore, a high level of government advocacy toward recommended vaccines plays an important role in increasing vaccine uptake. Healthcare professionals (HCP) are essential stakeholders who are actively involved in the care of aging adults being influential in commencing and completing vaccination schedules. The active involvement of this group contributes to the success of the NIP by increasing the uptakes of not only newly introduced vaccines but also routine vaccines. Other aspects, including centralization of vaccine invite/reminder/recall, easy access to supplies of vaccines and vaccine registries should be in place. Extra effort and resources need to be allocated to engage "hard-to-reach" aging adults to be vaccinated. They are often at high-risk for infectious diseases but face access barriers to vaccination due to various reasons, for instance, distance from vaccination centers, healthcare provider discrimination, and legal restrictions.

3.2.3. Readiness assessment results

Readiness scores for the four countries involved in the pilot testing are presented in Table 4. Although the scores cannot be considered as an official description of the readiness per country, the pilot assessment briefly reflects the current settings and performance of the national immunization programs in those countries. Overall, all countries demonstrated sufficient surveillance of at least three VPDs including influenza, pneumococcal disease, herpes zoster and/or pertussis. On the contrary, efforts to encourage hard-to-reach aging adults to be vaccinated were absent in all countries. In addition, availability of adult vaccine working groups and involvement of healthcare professionals were generally lacking. The Netherlands scored highly in items related to implemented vaccines including surveillance, local evidence of vaccine demand, and acceptability, the number of vaccines that have been introduced, and government advocacy to support vaccine introductions. However, supportive stakeholders, policies and strategies toward aging adult immunization programs were not fully in place. In contrast, Germany showed full preparations in those aspects which aligned with high scores in the item assessing the ease to vaccinate in the implementation part. Hungary was the only country of the four that did not have a NITAG. In addition, the country scored lowly in related items including having a national immunization plan, vaccine recommendations, and implementation in general. A similar pattern in implementation was seen in Serbia. There was no evidence on centralization of vaccine invite/reminder/recall in aging adults, together with active involvement of healthcare professionals. Although Serbia scored 0 in items related to existing immunization program and national guidance for communication, crucial stakeholders and national policy and surveillance systems were fully in place.

4. Discussion

This work has developed a tool to assess countries' readiness with regards to immunization programs in aging adults that can be used either before, or as part of the implementation process. Particularly, results from the readiness assessment can help to identify areas for improvement of the current programs as well as methodologies for future research to support decision-making and implementation of such programs in Europe.

In comparison with existing literature on this topic, our country score tool presents numerous unique features. First, unlike the purpose of other scoring systems such as archetype analysis aiming to categorize countries based on their characteristics (22), our tool serves as a readiness assessment which means that higher scores always indicate a higher level of readiness mentioned in the items. Second, although we propose a set of universal items that could be transferable among European countries, we consider each country to be unique. Thus, individual items in the tool are not necessarily equally important in all settings and subsequently no requisite labels are applied, which is opposite to the approach of a tool for planning and evaluating vaccination strategies in a published work (32). Additionally, the tool offers a great degree of flexibility for national authorities to specifically define the cut-offs of age for the national immunization programs considering the conceptualized cut-off of 50-year-old and over. Third, while some existing tools or guidance documents try to support countries in developing a comprehensive immunization program from zero (30, 41), our tool focuses on pinpointing important gaps in the current national immunization programs. By identifying those gaps, decision-makers can generate direct actions to strengthen current infrastructures and organizations such as setting up surveillance systems for common VPDs or forming working groups of aging adult vaccines. Fourth, aiming to not solely facilitate actions, our tool can help to go one step further to generate evidence needed for better decision-making. For that reason, the target audience of the tool is not only country-level decision-makers but also, researchers in different fields. Epidemiological research could be needed when countries score low in surveillance or having no evidence in monitoring vaccine coverage rates. In addition, when studies on vaccine demand and acceptability are lacking, behavioral research can help to generate tailored interventions or corresponding guidance to support implementation of the program. Furthermore, health economic research could be useful to address different gaps identified from the tool separately or simultaneously. For example, incorporating cost-effectiveness and value of information analyses can facilitate making well-informed policies regarding reimbursement of vaccination programs and setting priorities for future research.

In terms of content, our tool inherits from previous works to include well-known components aiming to support immunization programs; for instance: surveillance of VPDs, performance of existing programs, and public health priority

TABLE 4 The final version of the country score tool (*) and readiness scores in four pilot countries.

Domain	Guiding question	Readiness scores	NL	SER	HU	GER
Decision-making (9)						
1. Surveillance of vaccine preventable diseases (VPD)	1. Is national surveillance system of vaccine preventable diseases in aging adults in place (e.g., influenza, pneumococcal, herpes zoster and pertussis diseases)?	0 = No national surveillance system exists for any disease 1 = One or two diseases have national surveillance systems 2 = Three or more diseases have national surveillance systems	2	2	2	2
2. Vaccine acceptability among aging adults	2.1. In the last 5 years, have any studies been conducted on the demand and acceptability toward recommended/implemented vaccines in your country?	0 = None at both local and national/state levels 1 = Some studies at local level and/or less than one study (per vaccine) at the national/state level 2 = At least one study (per vaccine) at the national/state level	2	1	1	1
	2.2. Is national guidance or communication campaign available for generating acceptance and demand for vaccines in aging adults in your country?	0 = No guidance/campaign at the national level available 1 = National guidance/campaign available which was developed based on theory or adaptation 2 = National guidance/ campaign available which was developed based on the country's evidence of acceptability and demand	1	0	1	1
3. Performance of existing immunization programs in aging adults	3.1. Did your country introduce any vaccines for aging adults into the national immunization program?	0 = No vaccine in aging adults was introduced 1 = One vaccine in aging adults was introduced 2 = Two or more vaccine in aging adults was introduced	2	0	1	2
	3.2. If the answer to the above question is "yes," what are the vaccine coverage rates (VCRs) among aging population in the most recent year (according to the availability of data)?	0 = All VCRs $< 25\%$ OR the result is unknown OR the answer to question 3.1. is "No" 1 = VCRs ranges from 25 to 75% 2 = At least one vaccine reached VCR $\geq 75\%$	1	0	0	1
4. National immunization strategy	4. Is a National Immunization Strategy/Plan published which covered aging adult population?	0 = No immunization strategy publicly available 1 = Only pediatric immunization strategy publicly available 2 = National immunization strategy is published and covers both pediatric and adult vaccines	1	2	1	1
5. Stakeholders' involvement	5.1. Did your country establish a national immunization technical advisory group (or equivalent) that meets all basic World Health Organization (WHO) criteria in terms of membership and composition?	0 = No National immunization technical advisory group has been established 1 = National immunization technical advisory group has been established but has not met all criteria 2 = National immunization technical advisory group has been established and met all criteria	2	2	0	2
	5.2. Does national immunization technical advisory group (or equivalent) have adult vaccine workgroup(s)?	0 = No such working groups 1 = National immunization technical advisory group has no such working group, but is involved in other recommending bodies where vaccination in aging adults is approached and government is engaged 2 = Such working groups exist as part of a broader vaccine-specific working group or a standalone working group	0	0	0	2
6. The public health priority of diseases in aging adults	6. Is the publication of healthy aging strategies available in your country, and is immunization mentioned as a prevention measure?	0 = No healthy aging strategy publicly available 1 = Aging strategy available at the sub-national OR national level but does not mention adult vaccines 2 = Aging strategy available at the sub-national OR national level that mentions adult vaccines	1	1	1	2

(Continued)

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TABLE 4 (Continued)

Domain	Guiding question	Readiness scores	NL	SER	HU	GER
Implementation (8)						
1. Vaccine financing	1.1. How many vaccines in aging adults have been recommended by the national immunization technical advisory group (or equivalent) in your country?	0 = None or one vaccine has been recommended 1 = Two vaccines have been recommended 2 = More than two vaccines have been recommended	2	1	0	2
	1.2. If the national immunization technical advisory group (or equivalent) in your country recommended vaccines for aging adults, how many of them have been implemented (full/partial reimbursement) within 5 years after the recommendation or up to the current moment (depends on which point comes first)?	0 = <25% recommended vaccines have been implemented 1 = From 25 to 75% recommended vaccines have been implemented 2 = More than 75% recommended vaccines have been implemented	1	2	0	2
2. Advocacy	2. What is the level of governmental advocacy toward recommended vaccines for aging adults in the past 5 years in your country?	0 = No evidence of governmental advocacy toward recommended vaccines for aging adults 1 = At least one form of advocacy has been developed and involved one or two sectors 2 = At least one form of advocacy has been developed and involved multiple sectors (≥3) promoting aging adult vaccines	2	1	0	1
3. Access to vaccines	3. How easy it is to get vaccinated as an aging adult in your country in terms of location, provider, and requirement for vaccination appointment?	0 = Difficult to get vaccinated: only available at one provider with some limitations regarding required appointment or location 1 = Somewhat complicated: available at more than one provider (e.g., general practitioners—GPs, public health centers) but still some limitations regarding required appointment and location 2 = Easy to get vaccinated: available at GPs and/ or other providers (e.g., pharmacies, specialty physicians, long-stay facilities) without required appointment	1	2	1	2
4. Vaccine registry	4. What is the level of national/state vaccine registry for aging adults?	0 = No registry 1 = Sub-national or by individual health systems/providers/insurers 2 = Centralized	1	2	2	1
5. Active recommendation from healthcare professionals and reminder/recall centralization	5.1. What is the level of healthcare professionals' involvement in providing vaccine recommendations to aging adults and how is it monitored?	0 = No evidence of active involvement of healthcare professionals 1 = Active involvement of healthcare professionals is encouraged and monitored at sub-national level or by individual health systems/providers/ insurers 2 = Active involvement of healthcare professionals is encouraged and monitored at the national level	1	0	0	0
	5.2. What is the level of centralization of vaccine invite/reminder/recall in aging adults?	0 = No evidence: aging adults receive no reminder/recall 1 = Decentralized or mixture: some vaccinations have centralized reminder/recall, but some do not (aging adults only receive reminder/recall from healthcare professionals) 2= Centralized: auto-dial phone calls/ postcards/ text messages are provided for all recommended vaccines in aging adults	1	0	1	1
6. Hard-to-reach population	6. How much effort is being made to engage "hard-to-reach" aging adults (e.g., illiterates, migrants) to vaccinate?	0 = No additional effort at either local or national/state level 1 = Interventions/ strategies toward those groups have been implemented at local level but not yet at national/state level 2 = Interventions/strategies toward those groups have been implemented at national/state level	0	0	0	0

*This table only includes guiding questions and readiness scores in the tool; rationales and explanations of all items are presented separately in Supplementary material 2. NL, Netherlands; SER, Serbia; HU, Hungary; GER, Germany.

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of diseases (22). In addition, conducting research addressing the attitudes toward vaccines was considered crucial before the introduction of any vaccines to identify if low initial acceptance will exist or reasons for anti-vaccine sentiments (30). Nevertheless, it is important to turn knowledge into action. Therefore, one item was added to our tool to assess the availability of national guidance or communication campaigns for generating acceptance and demand for vaccines in aging adults. Regarding implementation, one novel item, relating to hard-to-reach populations, was suggested to be added and finally reached the consensus after the Delphi study. The item suggests to clearly define this population to inform strategy, planning, and resource determinations for target interventions to remove existing barriers to vaccinate (42). Besides confirmatory findings, contradictory judgments were found in this project. First, the item related to alternative measures for prevention and control of VPDs was excluded from our tool although it was considered as one of the criteria for decision-making in existing guidelines (30, 43). Those measures include, but are not limited to, treatment with antibiotics, antiviral therapies, or other medicines which could have a synergy with immunization programs. However, it might be irrelevant to include that aspect in the readiness assessment because those alternatives should be in place regardless of the availability of vaccines. Second, the involvement of healthcare workers by providing vaccine recommendation to aging adults was not initially included in the tool because of a non-significant association between this factor and vaccination coverage rates (VCR) of influenza in the elderly (44). However, considering that the success of one vaccination program is not necessarily comparable with others, the item was added by the Delphi panel.

Regarding the development process of the tool, the modified Delphi process provided many advantages. Firstly, the Delphi technique was an appropriate method when there was a lack of agreement, incomplete knowledge, uncertainty or lack of evidence (45). Compared to the conventional design, a modified Delphi approach allowed an active involvement of a steering group that performed a literature review in the problem area instead of open-ended discussion in the initial Delphi round (34). That helped to provide a comprehensive item pool for the following steps. Moreover, the internal VITAL stakeholder consultation was organized as an extra effort to ensure that comprehensiveness, relevance, and transferability of the tool were considered at the early phase of the development process. In addition, during the Delphi study, the use of a web-based platform allowed for anonymity and the inclusion of international experts. Additionally, predefined consensus criteria and a transparent procedure helped to reduce bias related to opinions of the steering group which was recognized as a disadvantage of the given study design (34). Furthermore, the comprehensiveness, relevance, and potential transferability of the tool were preliminary indicated in the pilot which has not been done in the development of existing tools. Finally, readiness scores of the four pilot countries showed that countries with higher scores including Germany and the Netherlands, had more vaccines being scheduled in the national immunization programs for aging adults, as well as higher vaccine coverage rates. That is indicative of the face validity of the tool.

Despite the thorough process, the study has some limitations which are primarily related to the small sample size in the Delphi study. There is no standard size of the panel members. It depends on the complexity of the topic and heterogeneity of the panel (34). With a similar topic, a Delphi panel of 8 participants was considered to be sufficient (32). The second limitation concerns the pilot testing with regards to the choice of countries, selection criteria for participants, and the sampling method. We selected four countries—partners of the VITAL project based on a convenience sampling approach. However, this set of four might be unrepresentative for European countries in general, and therefore might hamper the generalization of our findings. Regarding the selection criteria, although national authorities and researchers are both primary target audience of the tool, the inclusion of solely researchers can ensure the feasibility of the project but might affect the accuracy of the readiness assessment. Furthermore, the snowball sampling method could potentially introduce bias as the readiness assessment for one country might be performed by people working in the same organization. However, the difference between answers of two participants per country indicated that bias was unlikely to happen. The difference could be explained by the fact that not all of participants had strong background and experience in immunization. That suggests the ease to use of the tool when non-experts in the field could independently complete the tool with a reasonable level of accuracy. The third limitation comes with regards to the inclusions of items of the tool. Although the development process was evidence-based, the item inclusions could be subjective as indirect consequences of expert opinions from previous works and directly from our Delphi study. Therefore, it is uncertain that the effort spent to fill all gaps would always result in better decision-making. Future research should attempt to quantify the impact of individual items on the outcome of immunization programs measured by vaccine coverage rates. Besides, we suggest future research moving forward with the implication of the tool. First, it is important to conduct comprehensive field testing by using the tool in the appropriate target audience, being decision-makers, advisors and experienced researchers in immunization programs of aging adults across the majority of European countries. Second, digitalizing the tool could facilitate the usage of the tool on a large scale. Subsequentially, collection of readiness assessment data in many countries could help to quantify the association between readiness scores of individual item and vaccine coverage rates. Therefore, a precisely evidence-based readiness assessment could be developed to better inform decision-making at the

national or even supranational level with regards to aging immunization programs.

5. Conclusion

Decision-making and implementation of immunization programs in aging adults in European countries need to be strengthened based on a holistic assessment and using relevant evidence. Our extensive consultations and iterative development process have resulted in an innovative tool that serves as a readiness assessment and simultaneously helps to identify methodologies for future research to support decision-making and implementation of such programs. The tool is considered to be comprehensive, relevant, acceptable, and feasible in four countries. This indicates the transferability and applicability of the tool in Europe. We suggest future effort of this work to focus on digitalizing and comprehensive field testing of the tool across the majority of Europeans countries. Moreover, additional studies should be conducted to quantify the impact of individual items in the readiness assessment on vaccine coverage rates.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

According to the Dutch Law on Medical Research Involving Human Subjects (WMO), ethical approval is not required for research that does not involve participation by patients or use of patients' data (46). All expert participants gave informed consent before they took part in the study.

Author contributions

TP conducted the literature review and wrote the first draft of the manuscript. JvdS, EB, and TP contributed to the development of the item pool, organized stakeholder consultation, Delphi study, and pilot test. MP has made a direct and intellectual contribution to the first version of the tool, and the stakeholder consultation. BN, TÁ, CW, DS, and NN substantially contributed to the final version of the tool. All authors read, edited, and approved the final manuscript.

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Conflict of interest

MP reports grants and personal fees from various pharmaceutical industries, all outside the submitted work. EB is an employee of and holds shares in the GSK group of companies. TP was employed by Asc Academics.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2022.1080678/full#supplementary-material

SUPPLEMENTARY MATERIAL 1
Literature review and the item pool.

SUPPLEMENTARY MATERIAL 2
Supportive part of the country score tool.

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Balance ability and all-cause death in middle-aged and older adults: A prospective cohort study

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Objective: The present study aimed to explore the relationship between balance ability and all-cause death in middle-aged and elderly people and to provide a basis for formulating a balanced training plan for middle-aged and older people in China.

Methods: Based on data from the China Health and Retirement Longitudinal Study (CHARLS) carried out in the years 2011, 2013, 2015, and 2018, 18,888 participants aged 45 years and above were included. Cox proportional hazard models were designed to evaluate the effect of balance ability on death events.

Results: The present study found that there was an association between balance ability and death among middle-aged and older people. Multivariate Cox proportional hazard regression model analysis showed that the risk of death decreased by 10% (*HR* = 0.90,95% CI: 0.85–0.95) for every second increase in balance ability. With balance ability <10 s as the reference group, the adjusted *HRs* were 0.61 (0.44–0.85) among middle-aged and elderly people. The death density of balance ability of <10 s was 73.87 per thousand person-years higher than that of ≥10 s. There was no interaction between balance ability and chronic disease, overweight, and obesity ($P > 0.05$).

Conclusion: The risk of all-cause death in middle-aged and older people increased with the decrease in balance ability and showed no statistical significance between chronic disease, overweight, and obesity, as corroborated by the present study.

KEYWORDS

balance ability, death, overweight, obesity, chronic disease, elderly

1. Introduction

Balance ability is a complex body function that is coordinated by multiple systems, and the peak value decreases with age in adults (1). A variety of causes, such as somatosensory imbalance (2), brain damage (3), spinal cord injury (4), and decreased skeletal muscle mass (5), lead to impaired balance in the elderly. Chronic non-communicable diseases are referred to as chronic diseases, and mainly refer to hypertension, diabetes, stroke, etc., (6). It is predicted that, by 2030, death from chronic

diseases would increase to 62.7% by way of lost tax revenue and 51.6% by way of additional payment benefits (7). Being overweight and obese are both chronic diseases and major causes of other chronic diseases (8). Chronic diseases have an impact on the relationship between balance ability and death (9). Previous studies on balance ability have focused on the elderly population aged 51–75 years (9, 10) and were mainly focused on the relationship with falls (11, 12). Studies showed that the decline in physical function begins early in life (13), and more and more studies are using physical indicators as predictors of death (14). It has been indicated that successful 10-s one-legged stance (10-s OLS) performance might be able to predict survival (9). Balance ability is a low-cost screening tool to prevent adverse outcomes (1). However, participants with vestibular disease were unable to perform 10-s OLS and those with decreased muscle strength in both legs were limited. The present study uses the balance ability developed by the China Health and Retirement Longitudinal Study (CHARLS), a semi-tandem stand test, to explore the association between balance ability and death. The study aimed to provide a reference for early intervention of balance ability in middle-aged and older people and improve their adverse outcomes.

2. Manuscript formatting

2.1. Ethics statement

The Ethical Review Committee at Peking University (IRB 00001052-11014) approved CHARLS for the biomarker sample collection.

2.2. Study population

This study includes 24,805 participants who were 45 years of age and above as per the CHARLS of 2011–2018. In Figure 1, this study also excluded participants below the age of 45 years from all analyses (n = 1,597). Participants who did not have balance ability measures (n = 3,818) for that year were excluded, resulting in a final sample size of 19,390 participants. Additionally, participants who did not have body mass index (BMI) measures were excluded (n = 512).

2.3. Exposure

Interviewers measured balance ability, which refers to the number of seconds in which a participant can semi-tandem stand for 10 s without moving or holding anything. If the participant could semi-tandem stand for 10 s, then 10 s was recorded (15, 16). Otherwise, specific seconds were recorded, which is a continuous variable. The present study generates binary variables based on the median of balance ability.

2.4. Outcome

The death information for each participant and the outcome variable were obtained from death registration and certification by asking their relatives or community managers in 2013, 2015, and 2018, or at the end of follow-up (March 31, 2019). Death events were identified as "1" and survival and censorship as "0." The survival time was calculated according to the outcome (censored participations' survey year counted as survival time).

2.5. Covariates

According to our conceptual framework, low socioeconomic position and health status are strong determinants of all-cause death. Sociodemographic status includes age, gender, marital status, *hukou*, and education. Education is classified into five categories (no formal education, primary school, middle or high school, and college or above). The term *hukou* includes agricultural *hukou* and non-agricultural *hukou*. Health-related factors include self-reported smoking, drinking alcohol (never, former, or current), self-reported diseases (hypertension, diabetes, cancer, stroke, and memory diseases), activities of daily living (AOLs) / instrumental activities of daily living (ADLs/IADLs), and body mass index (BMI).

2.6. Statistical analysis

For summary statistics, the present study employed means and standard deviation (SDs) to describe continuous variables conforming to the hypothesis of normal distribution. Categorical variables were described by the frequency with percentage. Based on the baseline characteristics of balance ability, we deemed the chi-square (χ^2 test), analysis of variance (ANOVA), or Mann–Whitney U-test as appropriate. Assuming missing at random, incomplete observations were imputed with multivariate imputation *via* classification or regression trees. Ten imputed data sets were generated and pooled using R 4.2.1.

To examine the association between balance ability and death events of all causes, Cox proportional hazards models were used to calculate hazard ratios (*HR*s) with 95% confidence intervals (CIs). The risk of death was calculated based on a specific balance. Three models were designed and compared for middle-aged and elderly people. Model 1 was adjusted for age and gender. Model 2 is based on Model 1 with supplementary adjustment of marital status, household registration, education, smoking, drinking, and BMI. All covariates (15 covariables)

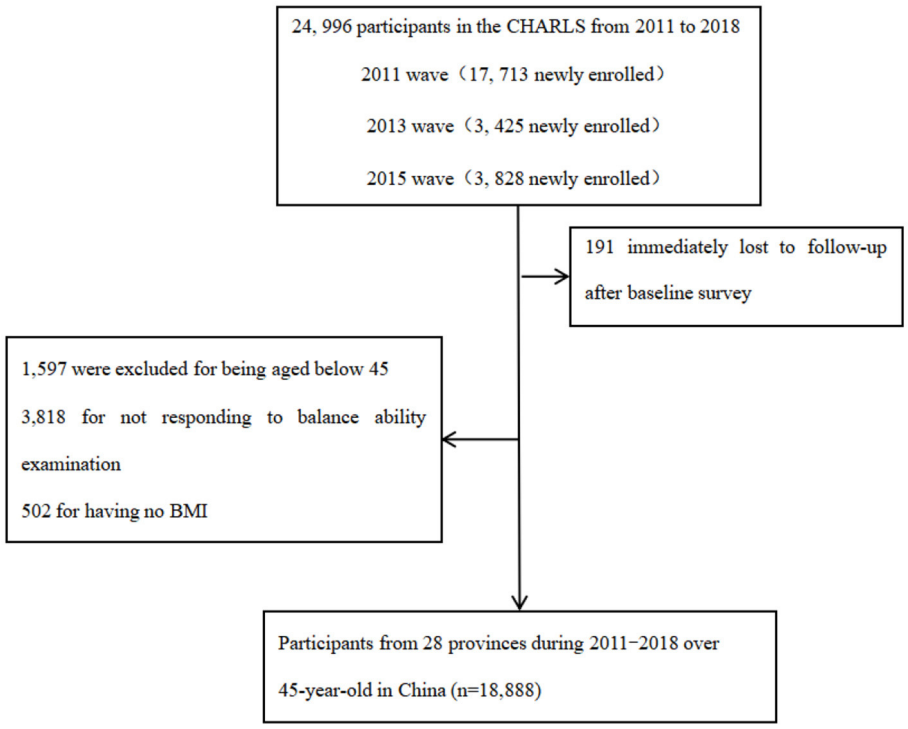

FIGURE 1
Flowchart of sample selection.

were included in Model 3. Chronic disease status and overweight and obesity were analyzed interactively between balance ability and death to study their effects. An interaction analysis was performed to examine the potential association between balance ability and death and to determine whether the results were regulated by chronic diseases, overweight, and obesity. Finally, we performed the sensitivity analysis by repeating all analyses using an original data set without multiple interpolations.

3. Results

3.1. Patient characteristics

A total of 18,888 eligible middle-aged and older people took part in this study, including 9,226 men and 9,650 women, with 57.9 ± 9.6 years of age (Figure 1). During the follow-up, 1,329 (7.0%) middle-aged and older people had died, and the median follow-up time was 7 years (Table 1). In total, there were 10,256 participants with non-overweight and obesity and 8,632 participants with overweight and obesity. There were 7,554 participants with a non-chronic health condition and 11,334 participants with chronic diseases.

3.2. Multivariate Cox proportional hazards regression models between balance ability and death risk

After adjusting for confounding factors such as demography and health behavior, the risk of death decreased by 10% (HR = 0.90,95% CI: 0.85–0.95) for every second increase in balance ability. After adjusting for confounding factors, the risk of death in middle-aged and older people with balance ability ≥10 s was reduced by 40% (HR = 0.61,95% CI: 0.44–0.85). The death density of middle-aged and older people with a balance ability of <10 s was 73.87 per thousand person-years higher than those ≥10 s (Table 2).

3.3. Stratified analysis of the association between balance ability and death risk

In the overweight and obese group and the non-overweight and obese group, for every second increase in balance, the risk of death in the population decreased by 16 and 7%, respectively (*HR* = 0.84,95% CI: 0.76–0.92; *HR* = 0.93, 95% CI: 0.86–0.99). For those persons with the balance ability <10 s as the control group, the risk of death of ≥10 s decreased by 55 and 35% in the overweight and obese and the non-overweight and obese,

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TABLE 1 Baseline characteristics of 18,888 participants according to death.

Baseline characteristics	Total sample (n = 18,888)	Survival (n = 17,559)	Death (n = 1,329)	*P*	*SMD*
Age, mean (SD)	57.86 ± 9.60	57.14 (9.14)	67.34 (10.52)	<0.001	1.035
Gender, *n* (%)				<0.001	0.301
Men	9 226 (48.9)	8,394 (47.8)	832 (62.7)		
Women	9 650 (51.1)	9,154 (52.2)	496 (37.3)		
BMI, mean (SD)	23.9()	23.98 (3.97)	22.17 (4.14)	<0.001	0.445
Married, *n* (%)				<0.001	0.397
No	16 739 (88.6)	15,745 (89.7)	994 (74.8)		
Yes	2 149 (11.4)	1,814 (10.3)	335 (25.2)		
hukou, *n* (%)				<0.001	0.122
Agricultural	13,745 (78.5)	1,2667 (78.1)	1078 (82.9)		
Non-agricultural	3,775 (21.5)	3,553 (21.9)	222 (17.1)		
Education				<0.001	0.363
No formal education	7,789 (44.0)	7,037 (42.9)	752 (57.7)		
Primary school	3,936 (22.2)	3,642 (22.2)	294 (22.6)		
Middle or high school	5,572 (31.5)	5,333 (32.5)	239 (18.3)		
College or above	395 (2.2)	377 (2.3)	18 (1.4)		
Smoking, *n* (%)				<0.001	0.352
Never	6,032 (32.0)	5,511 (31.4)	521 (39.3)		
Formal	1,547(8.2)	1,339 (7.6)	208 (15.7)		
Current	11,279(59.8)	10,681 (60.9)	598 (45.1)		
Drinking, *n* (%)				0.004	0.101
Never	5,037 (26.7)	4,657 (26.6)	380 (28.7)		
Formal	1,624 (8.6)	1,541 (8.8)	83 (6.3)		
Current	12,194 (64.7)	11,331 (64.6)	863 (65.1)		
History of comorbidities, *n* (%)					
Hypertension	3,931 (20.8)	3,517 (20.0)	414 (31.2)	<0.001	0.257
Diabetes	971 (5.1)	855 (4.9)	116 (8.7)	<0.001	0.154
Stroke	301 (1.6)	252 (1.4)	49 (3.7)	<0.001	0.143
Cancer	186 (1.0)	157 (0.9)	29 (2.2)	<0.001	0.105
Memory disease	203 (1.1)	168 (1.0)	35 (2.6)	<0.001	0.127
ADL, *n* (%)				<0.001	0.360
No	16,752 (88.7)	15,738 (89.6)	1,014 (76.3)		
Yes	2,136 (11.3)	1,821 (10.4)	315 (23.7)		
IADL, *n* (%)				<0.001	0.399
No	15,824 (83.8)	14,915 (84.9)	909 (68.4)		
Yes	3,064 (16.2)	2,644 (15.1)	420 (31.6)		
No	12,432 (65.8)	11,538 (65.7)	894 (67.3)		

(Continued)

TABLE 1 (Continued)

Baseline characteristics	Total sample ($n = 18,888$)	Survival ($n = 17,559$)	Death ($n = 1,329$)	*P*	*SMD*
Yes	6,456 (34.2)	6,021 (34.3)	435 (32.7)		
Balance ability, mean (SD)	10.0 (0.5)	9.97 (0.41)	9.85 (0.96)	<0.001	0.165
Balance ability, *n* (%)				<0.001	0.171
<10 s	156 (1.0)	117 (0.7)	39 (2.9)		
≥10 s	18,732 (99.0)	17,442 (99.3)	1,290 (97.1)		

SD, standard deviation. (A) *P*-values are based on chi-square (χ^2) or analysis of variance (ANOVA) or Mann-Whitney *U*-test. (B) Measured in the subpopulation of 18,888 participants. (C) Missing data instances: 12 for gender, 1,196 for educational level, 30 for smoking, 33 for drinking, and 1,368 for *hukou*.

TABLE 2 Construction of Cox proportional hazards model for balance ability to death.

Outcomes death of all causes	Cases, no	Incidence rate, per 1,000 person-years	*HR* (95% CI)		
			Model 1	Model 2	Model 3
Balance ability (continuous)	18,888	27.06	0.88 (0.84–0.93)*	0.89 (0.84–0.94)*	0.90 (0.85–0.95)*
Balance ability (binary)					
<10 s	156	100.32	1.00	1.00	1.00
≥10 s	18,732	26.45	0.52 (0.38–0.72)*	0.57 (0.41–0.79)*	0.61 (0.44–0.85)*

HR, hazards ratio.
Model 1 was adjusted for age and gender.
Model 2 was adjusted as model 1 plus *hukou*, body mass index (BMI), education, marriage, drinking, and smoking.
All 16 items were entered simultaneously in model 3.
* means $P < 0.05$.

respectively (*HR* = 0.45,95% CI: 0.23–0.88; *HR* = 0.67, 95% CI: 0.46–0.97). There was no interaction between overweight and obesity and continuous balance ability (*HR* = 0.91, 95% CI: 0.81–1.02), as well as binary balance ability (*HR* = 0.70, 95% CI: 0.33–1.50) (Table 3).

In the chronic disease group, for every second increase in balance ability, the risk of death decreased by 12% (*HR* = 0.88,95% CI: 0.82–0.94). For those people with a balance ability <10 s as the control group, the risk of death in the chronic disease group was reduced by 45% (*HR* = 0.55,95% CI: 0.38–0.79). There was no statistical significance in the predictive effect of continuous balance ability and binary variables on the survival of the non-chronic disease group (*HR* = 0.90,95% CI: 0.83–1.04; *HR* = 0.80,95% CI: 0.39–1.65). There was no interaction between chronic disease and continuous balance ability (*HR* = 0.95,95% CI: 0.84–1.08), as well as binary balance ability (*HR* = 0.76,95% CI: 0.34–1.68) (Table 4).

Sensitivity analysis was performed on 18,888 middle-aged and older people without multiple interpolations, and the results are given in Table 5.

4. Discussions

We found that the risk of death decreased significantly, as the number of seconds of balance maintenance increased. After adjusting the covariates, this relationship still existed. Higher balance ability was independently related to the decrease in death risk in middle-aged and older people. The death density of middle-aged and older people whose balance ability <10 s was higher than that of those people with a balance ability ≥10 s. Consistent with a cohort study of 1,085 elderly people in Japan, standing balance predicts all-cause mortality and was independently associated with all-cause mortality (14). The poor balance ability of middle-aged and older people can be traced back to many possible reasons. With increasing age, the muscles of the vestibular-evoked responses will be delayed, resulting in a decline in balance ability (17). Multiple systems were affected by chronic inflammatory states and oxidative imbalances (18). When middle-aged and older people stood with their eyes open, the force area of the feet mainly depended on the transmission information of the plantar proprioception and the muscle strength of the lower limbs to maintain the posture (19). At this time, it is more likely to have problems such as reduced information transmission efficiency of the plantar mechanoreceptor, low utilization rate, flat proprioceptive information, and weak relative strength, which finally lead to a decline in balance ability (20).

The present study found that chronic disease, overweight, and obesity had no significant effect on the association between balance ability and death. A total of 152 studies found that being overweight or obese were associated with plantar sensitivity, lower sensitivity, and decreased postural stability observed in obese people (21). Balance control impairment in individuals

TABLE 3 Cox risk proportional model of death risk among participants who were overweight and obese or not.

Subgroup	Cases, no	Non-overweight and obesity (n = 10,256)			Cases, no	Overweight and obesity (n = 8,632)			*HR* (95% CI) for interaction CI)
		Model 1	Model 2	Model 3		Model 1	Model 2	Model 3	
Balance ability (continuous)	1,0256	0.91 (0.85–0.97)*	0.92 (0.86–0.99)*	0.93 (0.86–0.99)*	8 632	0.83 (0.76–0.92)*	0.83 (0.75–0.91)*	0.84 (0.76–0.92)*	0.91 (−081–1.02)
Balance ability (binary)									0.70 (0.33–1.50)
<10 s	104	1.00	1.00	1.00	52	1.00	1.00	1.00	
≥10 s	10,152	0.56 (0.38–0.80)*	0.62 (0.43–0.90)*	0.67 (0.46–0.97)*	8 580	0.43 (0.22–0.84)*	0.44 (0.23–0.86)*	0.45 (0.23–0.88)*	

Model 1 was adjusted for age and gender.
Model 2 was adjusted as model 1 plus *hukou*, education, marriage, drinking, and smoking (excluded BMI).
All 15 items were entered simultaneously in model 3.
* means $P < 0.05$.

TABLE 4 Cox risk proportional model of death risk among participants with chronic disease or not.

Subgroup	Number	Non-chronic disease status (n = 7,554)			Number	Chronic disease status (n = 11,334)			*HR* (95% CI) for interaction CI)
		Model 1	Model 2	Model 3		Model 1	Model 2	Model 3	
Balance ability (continuous)	7,554	0.91 (0.82–1.02)	0.93 (0.83–1.04)	0.93 (0.83–1.04)	11 334	0.87 (0.81–0.93)*	0.86 (0.81–0.92)*	0.88 (0.82–0.94)*	0.95 (0.84–1.08)
Balance ability (binary)									0.76 (0.34–0.168
<10 s	37	1.00	1.00	1.00	119	1.00	1.00	1.00	
≥10 s	7,517	0.70 (0.34–1.43)	0.79 (0.39–1.63)	0.80 (0.39–1.65)	11 215	0.47 (0.33–0.67)*	0.50 (0.35–0.73)*	0.55 (0.38–0.79)*	

Model 1 was adjusted for age and gender.
Model 2 was adjusted as model 1 plus *hukou*, body mass index (BMI), education, marriage, drinking, and smoking.
All 11 items were entered simultaneously in model 3 (excluded five chronic disease variables).
* means $P < 0.05$.

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TABLE 5 Sensitivity analysis of the relationship between balance ability and death (original data).

Outcomes	*HR* (95% CI)		
Death	Model 1	Model 2	Model 3
Balance ability (continuous)	0.89 (0.84–0.94)*	0.90 (0.85–0.95)*	0.91 (0.86–0.96)*
Balance ability (binary)			
<10 s	1.00	1.00	1.00
≥10 s	0.53 (0.39–0.74)*	0.59 (0.42–0.81)*	0.65 (0.46–0.90)*

Model 1 was adjusted for age and gender.
Model 2 was adjusted as model 1 plus *hukou*, body mass index (BMI), education, marriage, drinking, and smoking.
All 16 items were entered simultaneously in model 3.
* means $P < 0.05$.

with obesity may be caused by larger balance motor commands' variability (22). However, this association between balance ability and eventual death risk was insignificant. The present study did not find the interaction, even though chronic kidney diseases, cardiac diseases, cancer, or some other chronic diseases may lead to premature death (23–25). After calculation, the two confounders had no significant moderating effect on the association between balance ability and death risk. The inconsistency of interactions and subgroups may be due to the relatively small sample size. It is worth mentioning that early resistance training can improve balance ability and physical function in the elderly (26).

Our study supplements further the evidence of the relationship between balance ability and death in middle-aged and older people based on the Chinese population. It is a community-based prospective study with good national representation. Stratification of factors, such as chronic disease, overweight, and obesity, was considered at the design stage, and potential confounding factors were adjusted to reinforce the existing evidence. However, the limitations of this study are that, first of all, the grouping of balance ability is uneven and does not consider the balance ability beyond 10 s may be achieved. Second, balance ability is a single body index, which needs to be combined with different measurements of body function or can improve the predictive ability of death risk. Third, all-cause deaths include deaths caused by external forces not directly related to health, such as car accidents, and there may be underreporting. Finally, overweight and death were combined in the subgroup analysis, which weakened the effect of balance ability on death in a single BMI status.

In summary, the balance ability of middle-aged and older people was associated with the risk of all-cause death, and this association did not decrease with the presence or absence of chronic diseases, overweight, and obesity. The measurement of balance ability can be included as a routine examination method. When the physical examination shows that the balance ability of middle-aged and older people is significantly weakened, the reasons that may cause the balance ability to decline should be screened. For middle-aged and older people with poor balance ability and obvious clinical symptoms, it may be appropriate to increase the balance ability training to intervene and avert a fall.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: https://charls.pku.edu.cn/en/.

Ethics statement

The studies involving human participants were reviewed and approved by Peking University (IRB 00001052-11014). The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

KHX planned the study, supervised the data analysis, and wrote the paper. XH performed all statistical analyses and contributed to revising the paper. XHH helped find the source and analysis method. All authors have read and approved the manuscript and they have no conflicts of interest.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Engaging social activities prevent stroke and myocardial infraction by raising awareness of warning symptoms: A cross-sectional survey study

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Background: Stroke and myocardial infarction (MI) are medical emergencies, and early treatment within the golden hour is crucial for good prognosis. Adequate knowledge about the warning symptoms can shorten the onset-to-door time. Various factors affect the level of awareness, including social activity. This study aimed to determine if engaging in social activity is associated with the awareness of the warning symptoms of stroke and MI.

Methods: This cross-sectional study analyzed 451,793 participants from the 2017 and 2019 Korea Community Health Survey. Based on five questions for each of stroke and MI symptoms, participants were divided into an awareness group (replied "Yes" to all five questions) and unawareness group. Engagement in social activities (i.e., religious, friendship, leisure, and volunteer activity) was evaluated through a questionnaire. Multiple logistic regression analysis was performed to evaluate the relation between social activity and awareness of warning symptoms.

Results: Overall, 52.6% participants were aware of the warning symptoms of stroke, and 45.8% of MI. Regular engagement in at least one social activity, particularly friendship or volunteer activity, was associated with better awareness of the warning symptoms, both stroke (OR: 1.21, 95% CI: 1.20–1.23) and MI (OR: 1.22, 95% CI: 1.20–1.24). Additionally, more diverse types of social activities were associated with higher levels of awareness. Relationship between social activity and awareness showed positive association with participants older than 60 years, rural residents, or with low socioeconomic status.

Conclusion: Engagement in social activity was significantly associated with better knowledge about the warning symptoms of stroke and MI. For early hospital treatment after symptom onset, participation in social activities could be beneficial.

KEYWORDS

social activity, cardiovascular disease, stroke, myocardial infarction, self-awareness, prevention

Highlights

- The golden hour care for stroke and myocardial infarction is essential that can impact its prognosis.
- Regular engagement in at least one social activity was associated with better awareness of the warning symptoms of stroke and MI.
- Engagement in social activity was significantly associated with better knowledge about stroke and MI warning symptoms that can lead to early detection and prevention.

Introduction

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels, such as stroke and myocardial infarction (MI). According to the World Health Organization (WHO), an estimated 17.9 million people died from CVDs in 2019 worldwide, accounting for 32% of the total global deaths. In particular, 85% of these deaths were due to stroke and MI, which are therefore considered major public health concerns worldwide (1). In South Korea, CVD is the second leading cause of death after cancer. In 2020, there were about 27.4 and 42.6 deaths per 100,000 people from cerebrovascular disease (i.e., stroke) and ischemic heart disease (i.e., MI), respectively (2). Given that the population is rapidly aging and the risk factors for CVDs are increasing, the socioeconomic burden of these diseases continues to remain high (3).

Ischemic stroke and MI occur when the blood supply to the brain or heart muscle is obstructed. It can rapidly cause irreversible tissue damage, which can lead to serious complications and even death (4). Therefore, stroke and MI are medical emergencies, and urgent interventions such as thrombolysis or endovascular procedure are required. In fact, it has been shown that early treatment after the onset of symptoms is crucial for a better prognosis (5–7). However, according to Korean national statistics in 2020, only 41.4% of stroke patients and 44.0% of MI patients arrived at the hospital within 3 h after the onset of symptoms. Moreover, only 18.5 and 18.6% of stroke and MI patients, respectively, arrived within 1 h, the so-called golden hour (8). This is partially due to a lack of knowledge about the warning symptoms of stroke and MI, not only among the patients themselves but also among the surrounding people. Previous studies have shown that the better a person recognizes symptoms, the faster he or she presents for emergency treatment (9–11). Accordingly, the Korean government has made efforts through health projects to raise public awareness regarding the warning symptoms of CVDs since 2018 (12).

Previous studies have reported various factors that are associated with the level of knowledge about the warning symptoms of CVDs, including sex, age, race, region, marital status, education level, income, occupation, smoking, drinking, physical activity, and comorbidities (13–21). In fact, there exist several routes for people to learn about the warning symptoms of CVDs, for example through family members, mass media, school class, workplace, and hospital visit. Considering that the population is aging and one-person households are becoming more common these days, social activities such as religious activities or volunteer work can also be useful channels to obtain such knowledge (22).

Although there have been studies on the awareness of warning symptoms of CVDs among Koreans, no study has evaluated its relationship to social activities. Public health projects promoting social activities may be effective in reducing serious complications following stroke and MI if they can help in increasing awareness of the warning symptoms of CVDs. Thus, we aimed to determine if engagement in social activities is associated with increased awareness of the warning symptoms of stroke and MI. Furthermore, we also assessed if the awareness differs by the type and number of social activities, using a representative nationwide health survey.

Methods

Study population and data

The study data were obtained from the Korea Community Health survey (KCHS) conducted in 2017 and 2019. This nationwide survey has been conducted annually by the Korea Disease Control and Prevention Agency (KCDC) since 2008. The dataset is publicly available on the KCHS's official website (https://chs.kdca.go.kr/chs/). Multistage, stratified sampling methods were used to select representative households, and trained surveyors carried out personal interviews with adults aged 19 years or older living in these households. The KCHS questionnaire consists of ∼200 items in 20 fields including demographics, health-related behaviors, morbidities, and social environments.

A total of 228,381 people participated in the 2017 KCHS and 229,099 people in 2019. Among them, we excluded individuals who refused to respond to the questions on the warning symptoms of stroke and MI or to the questions on social activities. Participants with missing data on any variables used in this study were also excluded. Finally, 451,793 participants were included in the analysis.

Variables

The dependent variable was defined as the level of awareness of the warning symptoms of stroke and MI. To evaluate awareness of the warning symptoms of stroke, participants were asked the following questions: "If you think that the following are the symptoms of stroke, answer 'Yes,' or if you do not think so, answer 'No.' Please answer 'I do not know' if you are

unsure." Warning symptoms included the following: (1) sudden numbness or weakness of the face, arm, or leg on one side of the body; (2) sudden difficulty in speaking or understanding speech; (3) sudden visual impairment of one or both eyes, or double vision; (4) sudden dizziness or loss of balance; (5) sudden severe headache never experienced before. These are the five cardinal symptoms of stroke, which are well-established for assessing stroke awareness (9). Only participants who replied "Yes" to all five questions were considered to have awareness of the warning symptoms of stroke, based on the definition by the Korean Disease Control and Prevention Agency (KDCA) (23). Participants who replied "No" or "I do not know" to at least one of the five questions were categorized as the unaware group. The questions for evaluating awareness of the warning symptoms of MI were the same as those for stroke awareness. According to the United States Centers for Disease Control and Prevention (CDC), the five symptoms included the following: (a) sudden pain or discomfort in the jaw, neck, or back; (b) sudden weakness, dizziness, nausea, or cold sweating; (c) sudden pain, pressure, or discomfort in the chest; (d) sudden pain or discomfort in the arm or shoulder (e) sudden shortness of breath (24). Participants who answered "Yes" to all five questions were assigned to the awareness group based on the KDCA definition and results of previous studies (15, 21, 23).

The main variable of interest was engagement in social activity, which was defined on the basis of the following four questions. Participants were asked "Do you regularly engage in religious activities at least once a month?" and the same question was asked also on friendship, leisure, and volunteer activities. Individuals who replied "Yes" to at least one of the four questions were assigned to the "social activity group," while those who replied "No" to all four were assigned to the "no social activity group."

This study included the potential confounding variables as covariates: sex, age, region, marital status, household type, monthly household income, level of education, occupation, smoking, drinking, and comorbidities. The year of examination was also adjusted. Household types were divided based on the number of cohabiting generations, in which individuals living alone were classified into one generation group. Monthly household income was categorized into following three groups: low ($<200 \times 10^4$ KRW), middle ($200–400 \times 10^4$ KRW), and high ($\geq 400 \times 10^4$ KRW). We classified the participants' occupations into white-collar worker (managers, professionals, clerks, and service and sale workers), blue-collar worker (agricultural, forestry and fishery workers, mechanical and manual laborers, and armed forces), and unemployed (housewives, students, and unemployed). Smoking status was categorized into never, current and ex-smoker. Those who smoked <100 cigarettes in their lifetime were classified as non-smokers. Alcohol consumption was divided based on the frequency of drinking over the past year. Comorbidities included hypertension and diabetes.

Statistical analysis

All analyses were done separately for stroke and MI. The frequencies and proportions of independent variables were compared using the chi-square test to confirm the differences between the individuals who were aware of the warning symptoms and those who are not. We performed multivariate logistic regression analysis after adjusting for demographics, socioeconomic status, comorbidities, and the examination year to identify the factors that are associated with an awareness of the warning symptoms. The results are shown as odds ratios (ORs) and 95% confidential intervals (95% CIs). In addition, each factor (i.e., type and number) of social activity was also analyzed through multiple logistic regression analysis to determine which factor was the most relevant to the awareness of the warning symptoms. Finally, we conducted subgroup analyses stratified by other covariates. All statistical analyses were conducted using SAS software (version 9.4, SAS Institute, Cary, NC, USA), and p-value < 0.05 was considered statistically significant.

Results

General characteristics of the study population are described in Table 1. Of the total 451,793 participants, 237715 (52.6%) were aware of all five warning symptoms of stroke and 206,743 (45.8%) of those of MI. A total of 319,796 (70.8%) participants regularly engaged in social activities at least once a month. Among them, 177,374 (55.5%) recognized stroke symptoms and 154,461 (48.3%) recognized MI symptoms. In the group not engaging in social activity, the number of participants who recognized stroke and MI symptoms were 60,341 (45.7%) and 52,282 (39.6%), respectively.

Table 2 shows the factors associated with the awareness of warning symptoms of stroke and MI. After adjusting for covariates, people who participated in social activities were more likely to have awareness of the warning signs than people who did not. These results were significant for both stroke (OR: 1.21, 95% CI: 1.20–1.23) and MI (OR: 1.22, 95% CI: 1.20–1.24). Moreover, women (stroke, OR: 1.19, 95% CI: 1.16–1.21; MI, OR: 1.11, 95% CI: 1.09–1.13), married individuals (stroke, OR: 1.27, 95% CI: 1.24–1.30; MI, OR: 1.22, 95% CI: 1.19–1.25), and highly educated individuals with college or above educational level (stroke, OR: 2.06, 95% CI: 2.01–2.11; MI, OR: 1.84, 95% CI: 1.80–1.89) showed a significantly positive level of awareness. On the contrary, current smoking (stroke, OR: 0.82, 95% CI: 0.81–0.84; MI, OR: 0.87, 95% CI: 0.85–0.88) and drinking more than 4 times per week (stroke, OR: 0.91, 95% CI: 0.88–0.93; MI, OR: 0.90, 95% CI: 0.88–0.93) was associated with low knowledge of stroke and MI symptoms.

The associations between social activities and awareness of warning symptoms of stroke and MI are shown in Figures 1, 2. Regarding the types of social activities, people

TABLE 1 General characteristics of study population.

	Total		Aware of warning symptoms of stroke			Aware of warning symptoms of MI		
	N	%	*n*	%	*p*-value	*n*	%	*p*-value
Total	451,793	(100.0)	237,715	(52.6)		206,743	(45.8)	
Social activity					<0.0001			<0.0001
Yes	319,796	(70.8)	177,374	(55.5)		154,461	(48.3)	
No	131,997	(29.2)	60,341	(45.7)		52,282	(39.6)	
Sex					<0.0001			<0.0001
Male	202,519	(44.8)	102,903	(50.8)		90,727	(44.8)	
Female	249,274	(55.2)	134,812	(54.1)		116,016	(46.5)	
Age					<0.0001			<0.0001
19–29	47,097	(10.4)	19,972	(42.4)		19,370	(41.1)	
30–39	56,007	(12.4)	29,434	(52.6)		26,879	(48.0)	
40–49	74,470	(16.5)	42,813	(57.5)		37,181	(49.9)	
50–59	88,030	(19.5)	52,661	(59.8)		44,899	(51.0)	
60–69	84,655	(18.7)	48,476	(57.3)		41,087	(48.5)	
≥70	101,534	(22.5)	44,359	(43.7)		37,327	(36.8)	
Region					<0.0001			<0.0001
Capital area	144,209	(31.9)	74,354	(51.6)		64,865	(45.0)	
Urban	70,506	(15.6)	37,518	(53.2)		33,285	(47.2)	
Rural	237,078	(52.5)	125,843	(53.1)		108,593	(45.8)	
Marital status					<0.0001			<0.0001
Married	302,800	(67.0)	170,735	(56.4)		146,991	(48.5)	
Divorced, widowed, or separated	79,446	(17.6)	36,054	(45.4)		30,614	(38.5)	
Never married	69,547	(15.4)	30,926	(44.5)		29,138	(41.9)	
Household type					<0.0001			<0.0001
1 generation	213,039	(47.2)	110,220	(51.7)		94,652	(44.4)	
2 generations	206,473	(45.7)	110,770	(53.7)		97,359	(47.2)	
3 or more generations	32,281	(7.2)	16,725	(51.8)		14,732	(45.6)	
Monthly household income					<0.0001			<0.0001
Low	151,814	(33.6)	71,303	(47.0)		60,930	(40.1)	
Middle	140,412	(31.1)	75,462	(53.7)		66,152	(47.1)	
High	159,567	(35.3)	90,950	(57.0)		79,661	(49.9)	
Highest level of education					<0.0001			<0.0001
Elementary school and below	107,963	(23.9)	46,668	(43.2)		39,410	(36.5)	
Middle school	51,835	(11.5)	27,717	(53.5)		23,496	(45.3)	
High school	128,515	(28.5)	71,695	(55.8)		61,581	(47.9)	
College and above	163,480	(36.2)	91,635	(56.1)		82,256	(50.3)	
Occupation					<0.0001			<0.0001
White-collar worker	145,556	(32.2)	84,167	(57.8)		74,763	(51.4)	
Blue-collar worker	137,857	(30.5)	70,141	(50.9)		60,200	(43.7)	

(Continued)

TABLE 1 (Continued)

	Total		Aware of warning symptoms of stroke			Aware of warning symptoms of MI		
	N	%	*n*	%	*p*-value	*n*	%	*p*-value
Unemployed	168,380	(37.3)	83,407	(49.5)		71,780	(42.6)	
Smoking					<0.0001			<0.0001
Never smoker	291,135	(64.4)	156,933	(53.9)		136,007	(46.7)	
Ex-smoker	84,468	(18.7)	44,478	(52.7)		38,160	(45.2)	
Current smoker	76,190	(16.9)	36,304	(47.7)		32,576	(42.8)	
Drinking					<0.0001			<0.0001
None	155,551	(34.4)	80,291	(51.6)		69,015	(44.4)	
≤1 time per month	110,123	(24.4)	59,707	(54.2)		51,694	(46.9)	
2–4 times per month	89,799	(19.9)	48,128	(53.6)		42,417	(47.2)	
2–3 times per week	62,936	(13.9)	33,090	(52.6)		29,320	(46.6)	
≥4 times per week	33,384	(7.4)	16,499	(49.4)		14,297	(42.8)	
Diagnosed with hypertension					<0.0001			<0.0001
Yes	126,624	(28.0)	65,514	(51.7)		55,259	(43.6)	
No	325,169	(72.0)	172,201	(53.0)		151,484	(46.6)	
Diagnosed with diabetes					<0.0001			<0.0001
Yes	51,071	(11.3)	25,748	(50.4)		22,133	(43.3)	
No	400,722	(88.7)	211,967	(52.9)		184,610	(46.1)	
Examination year					<0.0001			<0.0001
2017	225,383	(49.9)	110,437	(49.0)		95,651	(42.4)	
2019	226,410	(50.1)	127,278	(56.2)		111,092	(49.1)	

who were regularly involved in friendship activity (stroke, OR: 1.24, 95% CI: 1.22–1.25; MI, OR: 1.23, 95% CI: 1.22–1.25) or volunteer activity (stroke, OR: 1.23, 95% CI: 1.20–1.26; MI, OR: 1.24, 95% CI: 1.22–1.27) were the most likely to be aware of stroke and MI symptoms. In addition, the more diverse the types of social activities, the higher the odds of having awareness of stroke and MI symptoms. Especially, people who participated in all four types of social activities had a significantly better level of awareness (stroke, OR: 1.67, 95% CI: 1.60–1.75; MI, OR: 1.70, 95% CI: 1.63–1.78) compared to people who participated in none of them.

Table 3 represents the subgroup analysis stratified by other independent variables. In the oldest age group of 70 years or older, individuals who were involved in social activities were significantly more likely to be aware of the warning symptoms of stroke (OR: 1.33, 95% CI: 1.29–1.36) and MI (OR: 1.34, 95% CI: 1.30–1.38). Among participants who were divorced, widowed, or separated, engagement in social activities was significantly associated with the awareness of warning symptoms (stroke, OR: 1.28, 95% CI: 1.24–1.32; MI, OR: 1.28, 95% CI: 1.24–1.32). Furthermore, the association between social activities and awareness of warning symptoms was especially significant in the group with low household income, poor education, or unemployed status.

Discussion

Recognizing the early warning symptoms of CVD can help the patients to obtain emergency treatment within the critical period, which can significantly improve the prognosis and survival (5–7, 9–11). Therefore, raising public awareness of CVDs is an important national issue to reduce the socioeconomic burden of CVDs in the upcoming aging society of Korea. This study was designed to examine if engagement in social activities was related to the awareness of warning symptoms of stroke and MI. Our large population-based analysis revealed that the people who participated in social activities were significantly more likely to have an exact knowledge of the warning symptoms of CVDs compared to people who did not.

TABLE 2 Factors associated with awareness of warning symptoms of stroke and MI.

	Aware of warning symptoms of stroke			Aware of warning symptoms of MI		
	OR[a]	95% CI	*p*-value	OR[a]	95% CI	*p*-value
Social activity						
Yes	1.21	(1.20–1.23)	<0.0001	1.22	(1.20–1.24)	<0.0001
No	1.00	-		1.00	-	
Sex						
Male	1.00	-		1.00	-	
Female	1.19	(1.16–1.21)	<0.0001	1.11	(1.09–1.13)	<0.0001
Age						
19–29	1.00	-		1.00	-	
30–39	1.29	(1.25–1.33)	<0.0001	1.15	(1.12–1.19)	<0.0001
40–49	1.59	(1.54–1.64)	<0.0001	1.25	(1.22–1.29)	0.0157
50–59	1.92	(1.86–1.99)	<0.0001	1.42	(1.38–1.47)	<0.0001
60–69	2.10	(2.02–2.17)	<0.0001	1.51	(1.45–1.56)	<0.0001
≥70	1.50	(1.45–1.56)	0.2442	1.12	(1.08–1.17)	<0.0001
Region						
Capital area	1.00	-		1.00	-	
Urban	1.09	(1.07–1.11)	0.1886	1.11	(1.09–1.13)	0.0038
Rural	1.21	(1.19–1.23)	<0.0001	1.18	(1.17–1.20)	<0.0001
Marital status						
Married	1.27	(1.24–1.30)	<0.0001	1.22	(1.19–1.25)	<0.0001
Divorced, widowed, or separated	1.00	(0.97–1.03)	<0.0001	1.00	(0.97–1.03)	<0.0001
Never married	1.00	-		1.00	-	
Household type						
1 generation	1.02	(1.00–1.05)	0.0082	1.00	(0.97–1.02)	0.1041
2 generations	1.00	(0.97–1.02)	0.0866	0.97	(0.95–0.99)	0.0001
3 or more generations	1.00	-		1.00	-	
Monthly household income						
Low	1.00	-		1.00	-	
Middle	1.06	(1.04–1.07)	0.3704	1.04	(1.03–1.06)	0.0076
High	1.10	(1.08–1.12)	<0.0001	1.05	(1.03–1.07)	0.0002
Highest level of education						
Elementary school and below	1.00	-		1.00	-	
Middle school	1.38	(1.35–1.41)	<0.0001	1.30	(1.27–1.33)	<0.0001
High school	1.70	(1.66–1.73)	<0.0001	1.52	(1.49–1.56)	<0.0001
College and above	2.06	(2.01–2.11)	<0.0001	1.84	(1.80–1.89)	<0.0001
Occupation						
White-collar worker	1.14	(1.13–1.16)	<0.0001	1.16	(1.14–1.18)	<0.0001
Blue-collar worker	1.00	(0.98–1.02)	<0.0001	1.00	(0.98–1.01)	<0.0001
Unemployed	1.00	-		1.00	-	

(Continued)

TABLE 2 (Continued)

	Aware of warning symptoms of stroke			Aware of warning symptoms of MI		
	OR[a]	95% CI	*p*-value	OR[a]	95% CI	*p*-value
Smoking						
Never smoker	1.00	-			-	
Ex-smoker	0.95	(0.93–0.97)	<0.0001	0.94	(0.92–0.96)	0.2301
Current smoker	0.82	(0.81–0.84)	<0.0001	0.87	(0.85–0.88)	<0.0001
Drinking						
None	1.00	-			-	
≤1 time per month	0.98	(0.97–1.00)	<0.0001	0.96	(0.94–0.98)	0.2159
2–4 times per month	0.97	(0.95–0.99)	0.0866	0.95	(0.94–0.97)	0.7106
2–3 times per week	0.94	(0.92–0.96)	0.0058	0.95	(0.93–0.97)	0.3064
≥4 times per week	0.91	(0.88–0.93)	<0.0001	0.90	(0.88–0.93)	<0.0001
Diagnosed with hypertension						
Yes	1.09	(1.08–1.11)	<0.0001	1.05	(1.04–1.07)	<0.0001
No	1.00	-		1.00	-	
Diagnosed with diabetes						
Yes	0.96	(0.94–0.98)	<0.0001	1.00	(0.98–1.02)	0.7631
No	1.00	-		1.00	-	
Examination year						
2017	1.00	-		1.00	-	
2019	1.33	(1.32–1.35)	<0.0001	1.31	(1.29–1.32)	<0.0001

[a]Adjusted for social activity, sex, age, region, marital status, household type, monthly household income, highest level of education, occupation, smoking, drinking, hypertension, diabetes, and examination year.

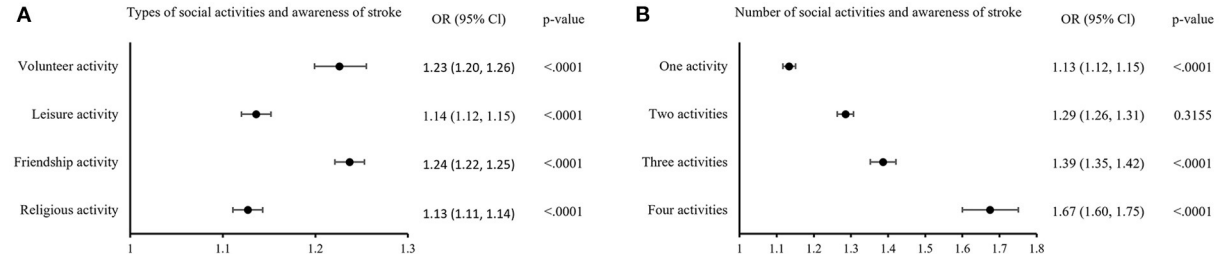

FIGURE 1
Subgroup analysis of social activities and awareness of warning symptoms of stroke. **(A)** Shows the odds of having awareness in individuals who participate in each types of social activities compared to who do not. **(B)** Shows the odds of having awareness depending on the number of social activities. Odds ratio were adjusted for sex, age, region, marital status, household type, monthly household income, highest level of education, occupation, smoking, drinking, hypertension, diabetes, and examination year.

The odds of association between them were not much different for stroke and MI.

We examined demographic, socioeconomic, and health-related factors to identify other meaningful factors that are related to the awareness of CVD warning symptoms. First, sex was found to be an influential predictor of symptom awareness. Women exhibited higher knowledge than men both for stroke and MI, which is consistent with the results of previous studies (13, 17, 18, 21, 25). Given that the incidence of stroke and MI is higher in men than in women (8), further intervention to raise awareness, especially among men is needed. Regarding the association between age and awareness of CVD symptoms, the results of previous studies varied. Some papers have reported higher awareness in old age (16, 20), while others have revealed

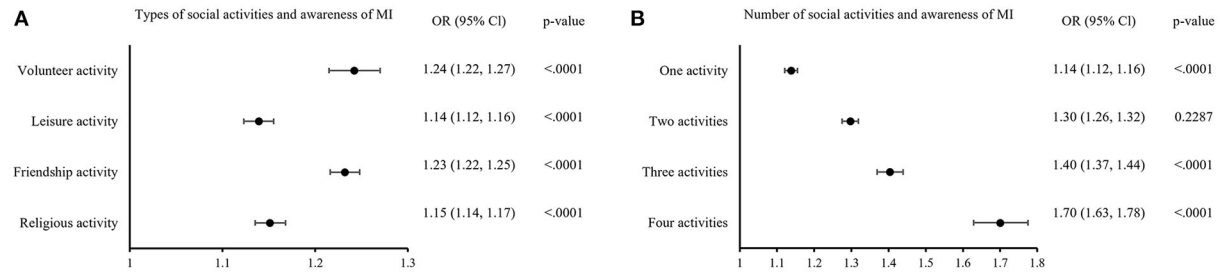

FIGURE 2
Subgroup analysis of social activities and awareness of warning symptoms of MI. **(A)** Shows the odds of having awareness in individuals who participate in each types of social activities compared to who do not. **(B)** Shows the odds of having awareness depending on the number of social activities. Odds ratio were adjusted for sex, age, region, marital status, household type, monthly household income, highest level of education, occupation, smoking, drinking, hypertension, diabetes, and examination year.

the opposite (14, 15, 25). However, most of the studies reported that middle-aged people showed the highest level of awareness. Additionally, in the present study, participants aged 50–69 years had a better knowledge of the warning symptoms compared to the younger and older age groups. This was true for both stroke and MI, but the ORs were higher for stroke compared to MI. This can be explained by the fact that since people over the age of 50 years are at high risk of CVDs (4, 8), they may hear of such experiences from the people around them, and thus tend to be exposed more often to the relevant information. In contrast, young adults lack chances to encounter such situations, and even so, they may not be much interested in health issues. The elderly aged 70 years and older seem to have difficulty in recognizing the warning symptoms due to under education or cognitive impairment (18, 21).

The region of residence was also associated with symptom awareness of stroke and MI, with individuals living in rural areas having higher awareness levels than those living in capital or urban areas. Preceding studies have explained that national projects to spread the knowledge about CVDs may have been more actively promoted in rural areas where emergency treatment is not easily accessible (16, 18). In addition, rural dwellers tend to establish closer connections with their neighbors than city dwellers, which can lead to a higher chance of sharing health knowledge (26). However, further investigations are needed since some studies have also demonstrated contradictory results in that the urban residents knew more about the CVD symptoms (13, 15, 25). Socioeconomic factors such as high household income, high level of education, and white-collar occupations are known predictors of high knowledge of warning symptoms (13–17, 19, 20, 25). This was also seen in our study, both for stroke and MI. People with low socioeconomic status are in a relatively unfavorable condition to acquire health-related information (16), which may result in poor knowledge regarding CVDs.

Smoking and heavy drinking are well-known modifiable risk factors of CVDs (1, 4). In this study, individuals who smoke or drink showed lower awareness of stroke and MI symptoms, which was consistent with previously reported results (13, 16, 20, 21). Hypertension, diabetes, and dyslipidemia also increase the risk of stroke and MI (1, 4), and past studies have revealed that patients with the above underlying diseases had stronger awareness of CVD symptoms (13, 21, 27). This may be because these patients regularly visited doctors and learned about the complications, including stroke and MI (16). In our study, the same results were obtained for hypertension, but not for diabetes.

We further analyzed the association between social activity and awareness about CVD symptoms in terms of the type and number of social activities. Among four types of social activities, friendship and volunteer activities were significantly associated with both stroke and MI awareness. Activities related to friendship and volunteer work tend to allow much time for the participants to engage in conversations with each other (28, 29). During these activities, people build a strong bond, allowing them to share personal matters. This exercise can lead to a higher chance of gaining health-related information and self-awareness on health than people who do not participate in those activities (29–31). Additionally, analysis of the number and types of social activities showed that the more the variety of activities one takes part in, the higher the level of awareness about CVD warning symptoms. In particular, individuals who engaged in all four types of social activities had significantly better knowledge than those who engaged in none of them.

Subgroup analysis revealed that the relationship between social activity and awareness of stroke and MI symptoms differed by demographic and socioeconomic factors. The association was significant in subgroups of individuals aged over 60 years, those living in rural areas, divorced, widowed, separated, or with low socioeconomic status (low household income, low level of education, unemployed). People with these characteristics seem to lack access to other extensive routes to learn about CVD

TABLE 3 Subgroup analysis of the association between social activities and awareness of warning symptoms of stroke and MI stratified by covariates.

	Aware of warning symptoms of stroke			Aware of warning symptoms of MI		
	Social activity			Social activity		
	No	Yes		No	Yes	
	OR	OR[a]	CI	OR	OR[a]	CI
Sex						
Male	1.00	1.21	(1.18–1.23)	1.00	1.24	(1.22–1.27)
Female	1.00	1.22	(1.20–1.24)	1.00	1.21	(1.19–1.23)
Age						
19–29	1.00	1.15	(1.11–1.19)	1.00	1.17	(1.12–1.21)
30–39	1.00	1.11	(1.07–1.15)	1.00	1.13	(1.09–1.17)
40–49	1.00	1.17	(1.13–1.21)	1.00	1.19	(1.15–1.23)
50–59	1.00	1.19	(1.15–1.23)	1.00	1.20	(1.16–1.24)
60–69	1.00	1.21	(1.17–1.25)	1.00	1.21	(1.17–1.25)
≥70	1.00	1.33	(1.29–1.36)	1.00	1.34	(1.30–1.38)
Region						
Capital area	1.00	1.11	(1.08–1.13)	1.00	1.12	(1.10–1.15)
Urban	1.00	1.21	(1.17–1.25)	1.00	1.21	(1.17–1.26)
Rural	1.00	1.27	(1.25–1.30)	1.00	1.28	(1.25–1.30)
Marital status						
Married	1.00	1.21	(1.18–1.23)	1.00	1.22	(1.20–1.24)
Divorced, widowed, or separated	1.00	1.28	(1.24–1.32)	1.00	1.28	(1.24–1.32)
Never married	1.00	1.16	(1.12–1.20)	1.00	1.16	(1.13–1.20)
Household type						
1 generation	1.00	1.23	(1.20–1.25)	1.00	1.24	(1.22–1.27)
2 generations	1.00	1.19	(1.16–1.21)	1.00	1.20	(1.17–1.22)
3 or more generations	1.00	1.26	(1.20–1.32)	1.00	1.27	(1.21–1.34)
Monthly household income						
Low	1.00	1.26	(1.23–1.29)	1.00	1.28	(1.25–1.31)
Middle	1.00	1.21	(1.18–1.24)	1.00	1.21	(1.18–1.24)
High	1.00	1.16	(1.13–1.19)	1.00	1.16	(1.13–1.19)
Highest level of education						
Elementary school and below	1.00	1.31	(1.27–1.34)	1.00	1.33	(1.30–1.37)
Middle school	1.00	1.24	(1.19–1.29)	1.00	1.23	(1.18–1.29)
High school	1.00	1.18	(1.15–1.21)	1.00	1.19	(1.16–1.22)
College and above	1.00	1.14	(1.11–1.17)	1.00	1.15	(1.12–1.18)
Occupation						
White-collar worker	1.00	1.17	(1.14–1.20)	1.00	1.16	(1.13–1.19)
Blue-collar worker	1.00	1.20	(1.18–1.23)	1.00	1.23	(1.20–1.26)
Unemployed	1.00	1.24	(1.21–1.26)	1.00	1.25	(1.22–1.28)
Smoking						
Never smoker	1.00	1.22	(1.20–1.24)	1.00	1.22	(1.20–1.24)
Ex-smoker	1.00	1.21	(1.17–1.25)	1.00	1.27	(1.23–1.31)

(Continued)

TABLE 3 (Continued)

	Aware of warning symptoms of stroke			Aware of warning symptoms of MI		
	Social activity			Social activity		
	No	Yes		No	Yes	
	OR	OR[a]	CI	OR	OR[a]	CI
Current smoker	1.00	1.17	(1.14–1.21)	1.00	1.20	(1.16–1.24)
Drinking						
None	1.00	1.27	(1.24–1.30)	1.00	1.28	(1.25–1.31)
≤1 time per month	1.00	1.20	(1.17–1.23)	1.00	1.21	(1.18–1.25)
2–4 times per month	1.00	1.15	(1.11–1.18)	1.00	1.15	(1.12–1.19)
2–3 times per week	1.00	1.16	(1.12–1.20)	1.00	1.17	(1.12–1.21)
≥4 times per week	1.00	1.19	(1.14–1.26)	1.00	1.23	(1.17–1.30)
Diagnosed with hypertension						
Yes	1.00	1.24	(1.21–1.27)	1.00	1.27	(1.24–1.31)
No	1.00	1.20	(1.18–1.22)	1.00	1.20	(1.18–1.22)
Diagnosed with diabetes						
Yes	1.00	1.21	(1.16–1.26)	1.00	1.26	(1.21–1.31)
No	1.00	1.21	(1.19–1.23)	1.00	1.22	(1.20–1.24)
Examination year						
2017	1.00	1.22	(1.19–1.24)	1.00	1.24	(1.21–1.26)
2019	1.00	1.21	(1.19–1.23)	1.00	1.21	(1.18–1.23)

[a]Adjusted for sex, age, region, marital status, household type, monthly household income, highest level of education, occupation, smoking, drinking, hypertension, diabetes, and examination year.

symptoms, such as the internet, family members, school, workplace, or hospital visit (16, 32). This could have resulted in the relatively high emphasis on the role of social activities.

In our study, 52.6 and 45.8% of the overall Korean population had knowledge about the warning symptoms of stroke and MI, respectively. The results show that the awareness of stroke and MI had increased in 2019 from 2017. There was a higher number of individuals who were aware of warning symptoms, and results of logistic analysis exhibited that awareness has increased significantly. From this study, we were not able to seek a specific cause yet; this could be the positive outcome of a continuous national-level health promotion campaign by the government. Since 2013, the Korean government has started health projects to raise awareness of warning symptoms and early management of CVDs. Moreover, comprehensive CVD management plans, regional cardio-cerebrovascular centers, and educational programs were established (12). However, despite such remarkable progress, perception rates are still relatively low compared to 53.0% in the United States (17) and 57.8% in Singapore (33). Together with the rapidly aging population, elderly individuals living alone are emerging as one of the priority groups in Korea (34). These people cannot easily get help from others when a stroke or MI occurs; therefore, being aware of the early warning symptoms is crucial for ensuring proper emergency treatment. Our study results suggest social activity as one of the solutions to reduce the social burden of CVDs in the upcoming aging society. According to our results, social activities are expected to play a significant role, especially among individuals with a low socioeconomic status, dwelling in rural areas, or no longer living with a spouse.

The present study has several strengths. First, this study was based on KCHS, the nationwide representative data of the Korean general population. These data are reliable in that the survey was performed by a national institution. In addition, the large sample size of over total 450,000 participants enabled more precise statistical adjustments. Third, to our knowledge, this is the first study to identify an association between social activities and awareness of warning symptoms of CVDs in Korea. Although previous studies have evaluated some factors related to the awareness of CVD warning symptoms, our research mainly focused on social activities, specifically the type and number of social

activities people regularly engage in. Our findings indicate that promoting social activities could also play significant role in shortening the door-to-treatment time in patients with stroke and MI.

However, this study also has some limitations. First, since this was a cross-sectional study, we could not confirm a causal relationship between participation in social activity and awareness of CVD warning symptoms. The possibility of reverse causality cannot be excluded. For example, more health-conscious and, therefore, healthier individuals might tend to participate in more social activities. Further longitudinal studies are needed to clarify this point. Second, variables regarding social activities were self-reported; therefore, recall bias may have been present. Third, we could not evaluate the detailed frequency of social activities because the questionnaire only asked "Do you regularly engage in the activity at least once a month?" Fourth, the knowledge of warning symptoms of stroke and MI was evaluated using closed-ended questions, which are likely to elicit more positive response than open-ended questions. Some studies have proven that closed-ended questions can provide respondents with some indication of what the correct answer could be (35). The questionnaire also did not include any negative or trap questions. This may have resulted in an overestimation of the participants' awareness of the warning symptoms of CVD. Lastly, there may be other behavioral or health-related factors contributing to the level of awareness. For example, the level of exposure to mass media or medical history of CVD may have influenced the knowledge of the warning symptoms of CVD, but these data were unavailable in KCHS. Nonetheless, we included any obtainable factors as covariates, such as a history of hypertension and diabetes which are the main risk factors of CVD (1).

Conclusion

This study found that engaging in social activity was related to a higher awareness of the Korean population's warning symptoms of stroke and MI. In particular, the association was prominent in people who participated in friendship or volunteer activities and those who were older, lived-in rural areas, or had low socioeconomic status. Stroke and MI are both major health concerns worldwide, and public awareness of the warning symptoms of these diseases is crucial for ensuring early treatment within the golden hour. Therefore, national campaigns and policies for raising awareness of stroke and MI should encourage social activities as the study discovered its association. However, further longitudinal studies are needed to clarify causality.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found at: The Korea National Health and Nutrition Examination Survey.

Ethics statement

Ethical approval was not provided for this study on human participants because, data used for the study is open source data provided by the Government agency for research purpose. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

GK, WC, and S-IJ designed the study. GK performed the statistical analysis and wrote the original manuscript. WC participated in the analysis. SK, BL, HJ, and S-YJ participated in literature reviews and conceptualization. WC and S-IJ reviewed the manuscript and revised it. All authors reviewed the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Health-related quality of life and its association with socioeconomic status and diet diversity in Chinese older adults

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Objectives: The study aimed at examining the combined association of socioeconomic status (SES) and diet diversity (DD) with health-related quality of life (HRQoL) and exploring whether DD played a mediating role in the relationship between varied SES and HRQoL among Chinese older persons.

Method: A multi-stage random sampling method was conducted in Shanxi Province of China, with 3,250 older adults participating in this cross-sectional survey. SES was divided into groups by quartiles and DD by means, and these variable groups were combined in pairs to generate a total of eight combinations. The PROCESS macro developed by Hayes was employed for the simple mediation analysis.

Results: Compared with the reference group (those with both high SES and high DD), older adults who were classified to have lower SES or DD had elevated odds of having worse HRQoL: low SES/ low DD (*OR* = 1.65, 95% CI 1.41–2.92); low SES/ high DD (*OR* = 1.45, 95% CI 1.17–1.80); middle low SES/ low DD (*OR* = 1.43, 95% CI 1.24–1.65); middle low SES/ high DD (*OR* = 1.23, 95% CI 1.03–1.47); upper high SES/ low DD (*OR* = 1.41, 95% CI 1.21–1.65); and high SES/ low DD (*OR* = 1.30, 95% CI 1.10–1.53). The mediation analysis revealed that DD mediated the relationship between SES and HRQoL (*B* = 0.011, 95% CI 0.008–0.013), with its indirect effects accounting for 39.29% of the total effects.

Conclusions: These findings highlighted the role of DD as a mediator of the relationship between SES and HRQoL. As DD could be protective, modifiable, and easy for older adults to understand and implement, village clinics and community health stations should work collaboratively to design proper DD intervention measures for better HRQoL.

KEYWORDS

health-related quality of life (HRQoL), diet diversity, socioeconomic status, older adults, health management

Introduction

With increasing average life expectancy, populations are now living longer but longevity does not necessarily mean that people have a better life quality (1). Health-related quality of life (HRQoL) is a multi-dimensional concept capturing the overall health and wellbeing of individuals or groups with various socio-economic characteristics (2). Among the many

determinants of older adults' HRQoL, the researchers have paid close attention to socioeconomic status (SES), a measure of people's combined economic and social status representing the individuals' access to culturally relevant resources needed to succeed in society (3, 4). The "health choice theory" and the "social causation theory," two theoretical explanations for the relationship between SES and HRQoL, both recognized the positive relationship between SES and health. The relationship between SES and health in our study may be more consistent with the social causation theory given the observation time point and the suggestion made by a prior Chinese cohort study that older individuals' SES had been formed before their retirement (5, 6). Low SES was associated with poor HRQoL in China (7), with a similar trend also observed in other countries such as Korea and Greek (8, 9). Although the relationship between SES and HRQoL has been well established, how the mechanism works particularly remained less apparent.

People's behaviors and observable attributes could be affected by SES, and these behaviors could also insert an impact on people's health (10). As a major component of lifestyle behaviors, dietary behavior was one of the key modifiable factors in promoting health and longevity (11). A local study found that unhealthy dietary behavior was highly prevalent and was associated with older adults' HRQoL in China (12). Therefore, we have begun to consider the role of dietary behaviors that might help to explain the relationship between SES and HRQoL. Dietary diversity (DD) is an indicator providing an overall assessment of dietary behaviors (13), reflecting people's nutrient adequacy and diet quality (14, 15). The importance and value of DD have been widely recognized by both the national and international dietary guidelines (16, 17). Previous population-based studies have clarified the relationship between SES and DD. In eight Latin American countries, Gomez et al. reported that respondents' DD increased with SES (18). Similar associations had also been observed among adults from Mexico (19), rural Mali (20), and other low and middle-income countries (21). These findings supported the hypothesis that the SES may subsequently beget people's DD.

In terms of the association between DD and HRQoL, it has also been confirmed by previous research. According to a 20-year longitudinal study of 91,993 Chinese citizens over the age of 65, poor DD was significantly associated with a poor quality of life after being adjusted for potential confounders (22). Other cross-sectional and longitudinal studies have also identified that DD could benefit older adults' physical functional capacity (23) and memory status (24), as well as suppress cognitive impairment (25) and even mortality (26). Additionally, it was shown that DD could help older Chinese populations to achieve a better aging process (27). Taken together, the pathway through DD may be one of the intermediate mechanisms between SES and HRQoL among older adults, and it is necessary to elucidate the potential mediating role of DD on the association among Chinese older adults. Meanwhile, although the former study has clarified how SES and DD were associated with HRQoL, respectively, the combined association of them with HRQoL was less known.

To contribute to a deeper understanding of the underlying mechanisms, the aim of the study was to examine the combined association of SES and DD with HRQoL. It also sought to explore whether DD played a mediating role in the relationship between different SES and HRQoL. We hypothesized that higher levels of DD could attenuate the impact of SES on HRQoL in Chinese older adults.

Materials and methods

Sample and participants

A questionnaire-based cross-sectional study was undertaken in all 11 cities of Shanxi Province (Taiyuan, Datong, Yangquan, Changzhi, Jincheng, Shuozhou, Jinzhong, Yuncheng, Xinzhou, Linfen, and Lvliang) using a multistage stratified sampling method. First, according to the order of districts (counties) on the government's website, each district (county) in every city was numbered. Second, two (districts) counties in each city were selected using the random number table, and then, two communities (administrative villages) were drawn from each district (county) in the same way. Third, considering the different scales of each community (administrative village), once again, we select 1 to 2 residential communities (natural villages) from each community (administrative village) by the random number table. Finally, we obtained older people's name lists and numbered them in each community or natural village. A random number table was also applied to select older adults who meet the inclusion criteria in this session.

The inclusion criteria for this study were as follows: (1) being aged 60 and above and (2) having clear awareness and barrier-free communication skills. Those who had difficulty communicating were excluded.

Before our formal survey, a pre-study had been conducted to ensure the accuracy, validity, and understandability of the questionnaires. The pre-study was conducted in Taiyuan, Shanxi Province, with 137 questionnaires distributed and 135 returned. The pre-study data were not included in the formal study. Additionally, the results demonstrated that the questionnaire had good reliability and validity and could be well understood by older adults.

All participants were interviewed face-to-face using a structured questionnaire by trained interviewers with medical knowledge in Shanxi Province, China. We used face-to-face interviews instead of self-complete questionnaires because some older adults were illiterate, and some of them could not read or write due to poor vision, hand tremors, or other reasons. The study involved 3,266 older adults, of whom 3,250 completed the questionnaire effectively, with an effective response rate of 99.51%.

Measurements

Socioeconomic status

In our study, occupation before retirement (unemployed, peasant, worker, technician, enterprise, and institution personnel), educational level (illiterate/semi-illiterate, primary education, secondary education, and higher education,) and personal monthly income (<1,000 RMB, 1,000–2,999 RMB, >3,000 RMB) were selected to measure the older adults' SES (6). As a general method to generate the SES index, the principal component analysis (PCA) was employed in this study (28). Then, we classified the SES index by quartiles into four levels: 0 = lowest SES, 1 = lower middle SES, 2 = upper middle SES, and 3 = highest SES.

Diet diversity

In our study, DD was accessed by diet diversity score. According to the Chinese dietary guidelines for Chinese populations (17), we investigated the frequency of consumption of ten food groups: staple foods (cereals, tubers, and beans), vegetables, fruits, eggs, aquatic products, meat and poultry, soybeans and nuts, milk and dairy products, salt, and oil. We asked the participants how often they ate one of the foods above, and the answers were recorded as "almost every day," "at least once a week," "at least once a month," "not every month," and "eschew." For each of the food groups, a score of 1 was given if they answered "almost every day" and no points were given otherwise (29). As salt and oil are essential components of the Chinese daily diet, they were excluded when assessing the DD score (27). In this way, the DD score was accessed by adding up the scores of eight food groups, and the DD score ranged from 1 to 8. A higher DD score indicated a more diverse diet.

Health-related quality of life

In this study, HRQoL was estimated by the European Quality of Life Five Dimension Five Level Scale Questionnaire (EQ-5D-5L), which was translated into Chinese in 2002 by Luo et al. (30). The EQ-5D instrument is a generic measure of health status with a descriptive system that consists of five dimensions covering mobility (MO), self-care (SC), usual activities (UA), pain/discomfort (PD), and anxiety/depression (AD). Each dimension had five levels of response: 1, no problem; 2, slight problem; 3, moderate problem; 4, severe problem; and 5, extreme problem. As a result, a total of 3,125 unique health status statements can be combined in this system. The EQ-5D utility scores were calculated based on the recently available Chinese value set (31). The score ranges from −0.391 to 1, where 1 represents full health (1,1,1,1,1), and the lowest score is −0.391, which represents a health status worse than death (5,5,5,5,5). The internal consistency measured by Cronbach's alpha was 0.894 in our sample.

Control variables

We identified potential confounders for HRQoL based on the existing studies (32, 33). Potential confounders included age, gender, residential area, marital status, family size, physical activities, body mass index (BMI), and the number of chronic diseases.

Demographic information was collected by self-report. The family size information was measured based on the question "How many people live with you now (including yourself)?" The answers were grouped as live alone; 2 people; 3–4 people; 5 people; and above. Physical activity level was measured by the International Physical Activity Questionnaire long-form (IPAQ), which consists of 27 questions reflecting on the last 7 days' activities (34). Based on the Chinese guidelines for data processing and analysis concerning the IPAQ (35), participants' physical activity was divided into three levels, including 1 = low, 2 = moderate, and 3 = high. BMI was calculated by weight (kg) divided by squared height (m^2). According to the Chinese criteria, participants' BMI was classified as underweight (<18.50 kg/m^2), normal (18.50–23.99 kg/m^2), overweight (24.00–27.99 kg/m^2), and obese (≥28.00 kg/m^2) (36). Information on chronic diseases was collected through self-reporting and supported by diagnostic evidence from the medical records or physicians' prescriptions.

Statistical analysis

Data were analyzed using SPSS version 24.0 (IBM, Armonk, NY, USA). Categorical variables are presented as the number of participants and compared across SES quartiles by the chi-square tests. Continuous variables are presented as means and standard deviations, compared across SES quartiles by Kruskal–Wallis test because of the non-normal distribution of both the DD score and EQ-5D utility score. The association between the continuous variables was examined using Pearson's correlation.

To examine the combined association of SES and DD on HRQoL, DD scores were grouped into two groups by the mean score of 5 (high: >5, low: ≤5). DD groups were combined in pairs with SES divided by quartiles and generated a total of eight combinations as follows: low SES/ low DD; low SES/ high DD; middle low SES/ low DD; middle low SES/ high DD; upper high SES/ low DD; upper high SES/ high DD; high SES/ low DD; and high SES/ high DD. A generalized linear model (GLM) with a Gamma distribution and a log link was applied to investigate the combined association of SES and DD on HRQoL. As the GLM required none-negative values, EQ-5D disutility score (disutility score = 1-utility score) was generated and entered as the dependent variable in this study (37).

A common method bias test was performed using Harman's single factor test to control for common method bias effects. If there is a problem with the common method variance, the first unrotated factor extracted from the factor analysis would account for a large proportion of the total variance. The threshold was 40% according to the former study (38).

The mediation analysis was conducted to establish a mediating model of three variables with adjustment for the above-mentioned control variables by the PROCESS macro developed by Hayes. In the mediation model, SES was determined to be the independent variable (IV), and HRQoL was the dependent variable (DV). DD (MV) was used as the pathway from SES to HRQoL. The total, direct, and indirect effects were estimated by the SPSS PROCESS macro (model 4). A total effect (c) refers to the relationship between the IV and DV without controlling for the MV. A direct effect (c') refers to the relationship between the IV and DV after controlling for the MV (DD) and other control variables. The indirect effects of the mediation analysis were the effects of the IV on the DV through the MV. To test the mediation role of DD between SES and HRQoL, a bootstrap estimation procedure was conducted with 5,000 bootstrap samples. According to the bootstrap test, the effect was significant when the path coefficient of a 95% CI did not overlap 0 (39). All the analyses were performed with SPSS 23.0 at a significance level of 0.05.

Results

Table 1 shows the sample characteristics by SES quartiles. There were 3,250 participants in total, with an average age of 69.65 ± 6.77 years. Different SES groups showed a statistically significant

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TABLE 1 Characteristics of the participants across socioeconomic status quartiles ($N = 3,250$).

Variables	Socioeconomic status quartiles[a]				*P*
	Lowest	Lower middle	Upper middle	Highest	
Number of participants	562	1,063	752	873	
Age group					
60–70	218	571	473	507	<0.001
71–80	239	412	223	290	
>80	105	80	56	76	
Gender					
Male	133	426	443	513	<0.001
Female	429	637	309	360	
Residential area					<0.001
Urban	158	214	409	672	
Rural	404	849	343	201	
Marriage status					
Married	344	770	625	743	<0.001
Others	218	293	127	130	
Body mass index (BMI)					0.019
Underweight	79	147	100	126	
Normal	312	639	459	560	
Overweight	114	196	145	137	
Obesity	57	81	48	50	
Family size					
Live alone	15	21	14	14	<0.001
2 people	18	43	68	126	
3–4 people	435	806	536	599	
5 people and above	94	193	134	134	
Physical activities					<0.001
Low	164	244	169	146	
Moderate	234	396	305	386	
High	164	423	278	341	
Number of chronic diseases					<0.001
0	190	418	351	390	
1	159	316	201	240	
2 and above	213	329	200	243	
Diet diversity score	4.26 ± 1.79	4.68 ± 1.68	5.30 ± 1.74	5.90 ± 1.61	<0.001
EQ-5D utility score	0.80± 0.27	0.85± 0.23	0.89± 0.20	0.92± 0.18	<0.001

[a]Socioeconomic status (SES) was grouped by quartiles from low to high.

difference in both the EQ-5D utility and DD scores, as well as other variables including age, gender, residential area, marital status, family size, physical activities, BMI, and the number of chronic diseases ($p < 0.05$).

Table 2 presents the odds ratios (ORs) for the prevalence of HRQoL across combined categories. The adjusted results showed that in comparison with older adults categorized as high SES/ high DD, most other combinations have significantly higher EQ-5D disutility scores (higher EQ-5D disutility score means better HRQoL): low SES/ low DD ($OR = 1.65$, [95% CI 1.41 to 2.92], $p < 0.001$); low SES/ high DD ($OR = 1.45$, [95% CI 1.17–1.80], $p = 0.001$); middle low SES/ low DD ($OR = 1.43$, [95% CI 1.24–1.65], $p < 0.001$); middle low SES/ high DD ($OR = 1.23$, [95% CI 1.03–1.47], $p = 0.021$); upper high SES/ low DD ($OR = 1.41$, [95% CI 1.21–1.65], $p < 0.001$); and high SES/ low DD ($OR = 1.30$, [95% CI 1.10–1.53], $p = 0.002$), except for the dyad of upper high SES/ high DD ($p > 0.05$).

TABLE 2 Combined association of SES and DD on HRQoL according to the EQ-5D disutility score[a] ($N = 3,250$).

	OR	95% CI	[b]P
Low SES/ Low DD	1.65	1.41, 1.92	<0.001
Low SES/ High DD	1.45	1.17, 1.80	0.001
Middle low SES/ Low DD	1.43	1.24, 1.65	<0.001
Middle low SES/ High DD	1.23	1.03, 1.47	0.021
Upper high SES/ Low DD	1.41	1.21, 1.65	<0.001
Upper high SES/ High DD	0.95	0.81, 1.13	0.575
High SES/ Low DD	1.30	1.10, 1.53	0.002
High SES/ High DD	1.00		

SES, Socioeconomic Status; HRQoL, Health Related Quality of Life; DD, Diet Diversity.
[a]EQ-5D disutility score: converted from EQ-5D utility score (disutility score = 1-utility score), higher EQ-5D disutility score represents lower HRQoL; DD scores were grouped into two groups by the mean score of 5 (high: >5, low: ≤5).
[b]The analysis was adjusted by age, gender, residential area, marital status, family size, physical activities, body mass index, and the number of chronic diseases.

In terms of the correlation between key variables, prominently, DD score and HRQoL were positively correlated with SES, respectively (for DD, $r = 0.333$, $p < 0.01$; for HRQoL, $r = 0.182$, $p < 0.01$). HRQoL was also significantly and positively correlated with DD ($r = 0.239$, $p < 0.01$). In addition, the results of the common method biases showed that the eigenvalues of seven factors were greater than one in the unrotated factors, implying that the data are explained by more than one factor. In addition, the first factor explained 28.14% of the variance, less than the threshold of 40%. As a result, the problem of common method bias in this study is not serious.

This mediation analysis provided the estimates of path coefficients and significance tests for specified mediational models, as well as the estimates of indirect effects. All paths for the adjusted model are presented in Figure 1. The total effect of SES on HRQoL was path c = 0.028 ($p < 0.001$). The significance of the direct effect of SES on HRQoL (path c' = 0.017, $p < 0.001$) remained significant when the mediator of DD was included in the model, indicating that the mediating effect was partial. Moreover, the total indirect effects through the pathway of SES→ DD→ HRQoL were 0.011, which accounted for 39.29% of the total effect.

The regression coefficients in the mediation analysis between SES on HRQoL with DD as a mediator are presented in Table 3. The effects of SES on HRQoL were partly mediated by DD. After controlling covaries, the direct effect of SES on HRQoL ($B = 0.028$, $p < 0.001$) remained significant when the mediator of DD was included in the model. In addition, SES was significantly associated with DD ($B = 0.468$, $p < 0.001$), with DD also significantly associated with HRQoL ($B = 0.022$, $p < 0.001$).

Discussion

In the present cross-sectional study, we explored the combined association of SES and DD with HRQoL among older adults, finding people who have lower SES and DD have higher odds of lower HRQoL. Through the bootstrapping analysis, the current study also confirmed that DD mediated the association between SES and HRQoL, which is in accordance with our theoretical assumption. As DD explained more than one-third of this relationship, the results may further suggest the value and importance of promoting DD for attenuating the negative impact of SES and HRQoL.

The positive association of SES with HRQoL in the current study was consistent with the social causation theory and earlier studies (8, 9, 40). The impact of SES highlighted the importance of graded socioeconomic differences in HRQoL. A recent study in China regarded SES as the main contributor to health inequality measured by the EQ-5D (41). Previous studies also discovered that the indicators of SES including education level, monthly income, and occupation were independently associated with HRQoL. In older Brazilian community-dwelling adults, participants with 5 or more years of education tended to report better HRQoL (42). Household income was identified as a risk factor exacerbating the disparities in the prevalence of poor quality of life in a Chinese longitude study from 1998 to 2018 (22). The findings from Chen et al. show that older adults' previous occupations played a role in affecting their HRQoL in mainland China (43). Low SES older adults have dual vulnerabilities and their HRQoL demands more government and academic attention, given the current pro-rich inequality in health status among Chinese older adults (44).

Our findings suggest that SES had a major influence on participants' DD echoed with a recent study in China that higher SES, including more education, family income, and perceived income status, was associated with higher DD (45). Another study emphasized the role of material resources, showing that income has an impact on diet: the higher the income, the more diverse the diet (46). Income reflects a person's purchasing power and is a good indicator of a person's economic resources. When people are making their dietary-related consumption decisions, income levels could limit their budgets. The tighter the budget is, the more limited choices they face, which would hinder the DD practice. However, money is not everything. Fraval et al. found that increasing income did not necessarily lead to improved DD in a study in Sub-Sahara Africa (47). Other social resources such as educational level were also found to be associated with DD (48). Education is a form of human capital, and people with high levels of education are more likely to have stable careers and income, which enable them to support investments in health including having a diverse diet. Nutrition awareness may be another issue as a previous study pointed out that among older adults, less educated people have lower nutrition awareness (49), and poor nutrition awareness was found to be associated with lower HRQoL (50). Put together, stronger purchasing power, higher willingness to stay healthy, and better nutrition awareness that came with more advanced SES may further help to explain people's tendency to consume a diverse diet.

According to our findings, maintaining a diverse diet was positively associated with better HRQoL, which was in line with the former study in China that a higher DD score was associated with better health, such as being less likely to experience higher-level psychological stress (51), having reduced risk of bladder cancer (52) and a lower risk of frailty (53). DD had the potential to promote HRQoL through the pathway of nutrition intakes (54, 55). Increased DD was associated with better multi-nutrient intake such as calories, protein, nucleic acid, vitamin C, and zinc, as compared to the individuals with lower DD (56). A diverse diet with adequate protein intake could boost the anabolic activity of skeletal muscle and stimulate muscle protein synthesis (57), preventing the negative impact of age-related degradation in skeletal muscle mass and

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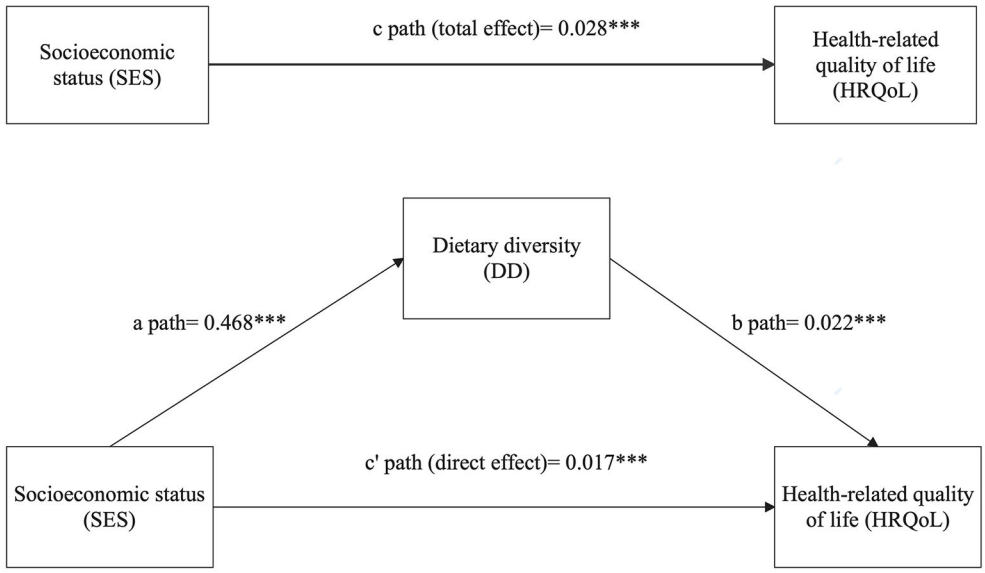

FIGURE 1
The mediation model of the association between SES and HRQoL through dietary diversity, adjusted for age, gender, residential area, marital status, family size, physical activities, body mass index, and the number of chronic diseases. Path coefficients are shown. ***$p < 0.001$.

TABLE 3 Regression coefficients in the mediation analysis between SES on HRQoL with DD as mediator ($N = 3,250$).

Criterion	Predictors	R^2	F	B	SE	t	95% CI	P
HRQoL	SES	0.178	77.726	0.028	0.004	6.994	(0.020, 0.035)	<0.001
DD	SES	0.140	58.650	0.468	0.032	14.444	(0.404, 0.532)	<0.001
HRQoL	SES	0.204	83.165	0.017	0.004	4.325	(0.009, 0.025)	<0.001
	DD			0.022	0.002	10.432	(0.017, 0.026)	<0.001

HRQoL, Health Related Quality of Life; SES, Socioeconomic Status; DD, Diet Diversity; age, gender, residential area, marital status, family size, physical activities, body mass index (BMI), and the number of chronic diseases were analyzed as control variables.

function on older adults' HRQoL (58). Additionally, as shown in a local study among Chinese centenarians, higher DD was also a protective factor against mental disorders (29).

The findings of the present study suggest that in comparison with the individuals with both high SES and high DD, another relatively low SES either in combination with high or low DD was found to be associated with decreased HRQoL except for the combination of upper high SES and high DD. Although sub-average SES was significantly associated with higher odds of lower HRQoL, the protective role of high DD was still evident in ameliorating the negative impact of relatively low SES. It is worth noting that even for older adults with more advanced SES, lower DD was also associated with decreased HRQoL. Considering the fact that when people get older, they are more likely to consume a monotonous diet (59), and it was valuable to pay attention to older adults' DD for ensuring their quality of late life. In terms of the exception for older adults who have high DD, no significant difference in HRQoL between those from upper high and high SES groups was observed in our study. The finding suggested that the HRQoL could be more secure for older adults having both above-average SES and DD. The study revealed that DD could play a mediating role in bridging the HRQoL inequity caused by the SES gap, slightly weakening this relationship and providing a new perspective explaining the relationship between SES and HRQoL. Our findings further indicated the priority targets for future DD interventions, as the research had suggested that the cumulative health disadvantage caused by SES could be ameliorated by lifelong health-related behavior (60). DD screening and assessment have the practical merit of being fast, widely applicable, and easy to understand for older people (13, 29), and increasing DD could be one promising intervention strategy to promote HRQoL in later life.

Limitations

There are some limitations to this study that should be addressed. First, given the cross-sectional design of the present study, it is not possible to make causal inferences. Second, participants' consumption of food groups was collected through only self-reported, which may exist recall bias as well as social desirability bias. There was also unintentional bias as the participants who have difficulties in communication were excluded from our research without having proxy interviews. Third, the study participants were recruited locally from Shanxi Province, which does not represent other areas in China.

Conclusion

Based on the study of 3,250 older adults in Shanxi province, China, the results not only presented the combined association of SES and DD on HRQoL but also suggested that the association between SES and HRQoL was partly mediated by DD. The findings had some implications for HRQoL enhancement as it is crucial to ensure that older populations from various socioeconomic backgrounds could equally enjoy their quality twilight years. Given the findings that higher DD could attenuate the negative impact of SES and HRQoL in Chinese older adults, village clinics and community health stations should work together on intervention programs encouraging older adults to adopt a diverse diet for improving or maintaining HRQoL.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Shanxi Medical University. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

CZ designed this study and served as the lead writer. JZ did the data interpretation and drafted the manuscript. SX and LS were involved in the study design and gave many valuable comments on the draft. YX and XZ participated in data analysis and critically revised the article. YK and XB helped with the language and format editing of this manuscript. XL, YC, YL, and GZ participated in data collection and post-works. All authors have read and approved the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Falls and associated risk factors in a sample of old age population in Egyptian community

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Introduction: Falling is a major health problem among old age persons and are the sixth cause of mortality and morbidity among them. Assessing the prevalence of falls among elderly in an Egyptian community and investigating its associated risk factors using the Arabic translation of the SHARE-Questionnaire.

Subjects and methods: This cross-sectional analytic study was a part of the pilot for AL-SEHA project. It included 289 old age people (50+ years age) residing in the study areas. The main project data were collected using the Arabic translation of the SHARE (Survey of Health, Aging, and Retirement in Europe) questionnaire. The original project data were collected by investigators from five universities, then uploaded to the internet server domain of the American University in Cairo (AUC) Social Research Center.

Results: The prevalence of falls was 11.07% (95% CI: 7.95–15.21). Falls were significantly more among 70 years or older ($p < 0.001$), unemployed or housewives ($p = 0.026$), have a family caregiver ($p = 0.022$), and home facilities for disability ($p = 0.015$). They had significantly higher rates of ischemic heart disease, hypertension, dyslipidemia, stroke, and diabetes mellitus. The most frequently reported problems were the fear of fall and dizziness (62.5%). The multivariate analysis identified the history of stroke and diabetes mellitus, the fear of fall and dizziness, and the total number of health problems and the score of difficulty in performing physical activities as significant independent predictors of fall occurrence. The history of stroke was the strongest risk factor (OR 33.49, CI: 3.45–325.40).

Discussion and recommendations: The prevalence of falls among old age persons in the studied community is not alarmingly high. It is highest among stroke patients. Community interventions and rehabilitation programs are recommended to train and educate old age people, especially those at risk such as stroke and diabetic patients, and those with dizziness to improve their physical fitness and reduce the fear of fall among them.

KEYWORDS

risk factors, old age, Egyptian aging study, falls, AL-SEHA

Introduction

Falling is a common incident and a major health problem among old age persons. The World Health Organization (WHO) reports indicate that worldwide more than half-million falls with fatality occur yearly, mostly among persons 65 years age or older (1). Falls and consequent injuries and associated complications are the sixth cause of mortality and morbidity among elderly. They account for more than one-third of all deaths due to injuries and are a leading cause of related mortality among those 65 years or older in the United States. Moreover, approximately one-third of the old age persons 65 years or older and living in community dwellings experience one fall incident per year (2). The problem has deleterious consequences on fallers, their families, and the community at large (3).

Research addressing falls in old age attributes its high incidence to a combination of several intrinsic as well as extrinsic factors (4). Among the intrinsic risk factors identified are those related to old age persons' health status often associated with chronic diseases and polypharmacy, in addition to visual, auditory, and equilibrium problems, as well as the psychological disorders as the symptoms of depression. The extrinsic factors are mostly related to environmental hazards (5, 6).

Several environmental factors have been identified as risk factors underlying falls in the old age population (7). Among these are the slippery floors whether ceramic or old rugs, tripping obstacles, and poor lighting. Other factors include disordered furniture, ill-designed footsteps, broken stairs, and lack of handrails (8). Added to these are the lack of safety measures like grab rails, as well as first-aid and other indoor and outdoor environmental factors (9).

The fear of falling (FOF) has also been identified as an intrinsic factor of considerable importance in the incidence of falling among the elderly. Thus, it has been demonstrated that the prevalence of FOF is significantly higher among those old age persons who experienced falling in comparison with those with no history of falls. Moreover, those who fear falling tend to limit their physical activities and this in turn leads to reduction in their quality of life (10). Furthermore, research showed that the old persons 65 years or older with history of falls have a higher probability of falling again (2).

Falling and consequent injuries and complications among old age people constitute a major burden for them, their caregivers, the society, as well as the system of healthcare. The problem gains more importance with the demographic changes in Egypt with increasing numbers and proportion of elderly in the population. Thus, measuring the magnitude of the problem and identifying its underlying risk factors is of importance in mitigating such burden.

This study is a part of the pilot of the Egyptian aging study (AL-SEHA) which is the first of its type in Egypt. The current study aimed at assessing the prevalence of falls among elderly in an Egyptian community and investigating its associated risk factors using the SHARE-Questionnaire. The SHARE survey and its updated questionnaires can be accessed from this link: http://www.share-project.org/home0.html. The research questions are: (1) What is the prevalence of falls among Egyptian old age persons? and (2) What are the significant risk factors associated with these falls? The outcomes of this work should be advising policies to decrease the rate of falling among seniors through understanding of the current situation and risk factors in Egypt.

Subjects and methods

Research design

A cross-sectional analytic study was used where all dependent and independent variables are assessed at one and the same point in time.

Setting

The study is a part of a DAAD funded project (Aging in the East Mediteranean Region: Emage) which is piloting the Egyptian Longitudinal Aging Study (AL-SEHA).

Participants

Old age people (50+ years age) residing in the study areas constituted the sampling population for the study. The inclusion criteria were being able to communicate, and living independently at home, in rented accommodation, in a hostel, or in a retirement home. Those having a gross psychiatric disturbance were excluded. The sample consisted of 289 old age persons. This sample size was large enough to estimate an expected fall prevalence rate of 11% or higher with 4% absolute precision at 95% level of confidence and 80% power. A non-probability convenience sampling technique was used in recruiting participants according to the eligibility criteria.

Data collection tool

The main project data were collected using the Arabic translated version of the SHARE (Survey of Health, Aging, and Retirement in Europe) questionnaire. It was validated by expertise from five Egyptian universities and the Social Research Center (SRC) American university Egypt. This is an extensive interview questionnaire developed by Mehrbrodt et al. (11). It consists of 16 sections covering respondent's personal and family information, health status and physical activity, mental abilities, mental health, health care, work and retirement, physical testing, relations with children, social support, finances, living conditions, family income, family assets, social activities, in addition to two sections for the data collector's views and information.

Fieldwork

The original project data were collected by investigators from five universities who were trained in interviewing using the prepared SHARE form translated into Arabic. The sample of eligible old age persons was selected. The investigators in each governorate contacted the potential participants in their area, explained to them the aim of the study and the procedure of data collection. They were invited to participate after being informed about their rights. Those who gave their consent to participate were asked for the suitable time to conduct the interview. At the set time, the investigators visited participants at their homes. They were interviewed using the data collection form. The procedure of data collection lasted for about 1 month. Each investigator was assigned 15 old age person for

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TABLE 1 Comparison of the demographics of old age persons with and without fall history.

	Fall group				Chi-squared test	*p*-value
	No ($n = 257$)		Yes ($n = 32$)			
	No.	%	No.	%		
Age						
<60	136	52.9	9	28.1		
60–	78	30.4	9	28.1		
70+	43	16.7	14	43.8	14.066	<0/001*
Mean ± SD	60.6 ± 8.0	67.6 ± 10.6				
Gender						
Male	113	44.0	10	31.3		
Female	144	56.0	22	68.8	1.883	0.170
Residence						
Urban	157	61.1	20	62.5		
Rural	100	38.9	12	37.5	0.024	0.877
Education						
None	36	14.0	8	25.0		
Basic/intermediate	98	38.1	13	40.6		
University	123	47.9	11	34.4	3.420	0.181
Job						
Working	111	43.2	6	18.8		
Retired	57	22.2	9	28.1		
Unemployed/housewife	89	34.6	17	53.1	7.293	0.026*
Family caregiver	29	11.3	9	28.1	Fisher	0.022*
Live alone	39	15.2	7	21.9	0.954	0.329
Crowding index						
<2	240	93.4	31	96.9		
2+	17	6.6	1	3.1	Fisher	0.704
Mean ± SD	0.94 ± 0.55		0.82 ± 0.56		1.177	0.246
Water closet						
Private	256	99.6	32	100.0		
Shared	1	0.4	0	0.0	Fisher	1.000
Home facilities for disability	19	7.4	7	21.9	Fisher	0.015*
Building						
1–2 floors	196	76.3	25	78.1		
3+ floors	61	23.7	7	21.9	0.055	0.815
Family financial ability						
Very low	28	10.9	3	9.4		
Low	58	22.6	10	31.3		
Moderate	145	56.4	15	46.9		
High	26	10.1	4	12.5	1.597	0.660

*Statistically significant at $p < 0.05$.

interviewing. The collected data were then uploaded to the internet server domain of the American University in Cairo (AUC) Social Research Center.

In the present study, data pertaining to the old age persons residing in Beni Suef were extracted from the main project dataset. These data included parts of the personal and family information

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TABLE 2 Comparison of health status of old age persons with and without fall history.

	Fall group				Chi-squared test	*p*-value
	No ($n = 257$)		Yes ($n = 32$)			
	No.	%	No.	%		
BMI[#]						
Normal (18.5–<25.0)	40	20.4	7	31.8		
Overweight (25.0–<30.0)	58	29.6	4	18.2		
Obese (30.0+)	98	50.0	11	50.0	2.802	0.423
Mean ± SD	30.95 ± 6.9		30.08 ± 6.2		0.608	0.548
Use eyeglasses	94	36.6	16	50.0	2.175	0.140
Visual acuity						
Excellent	38	14.8	3	9.4		
Very good	86	33.5	5	15.6		
Good	91	35.4	10	31.3		
Poor	32	12.5	10	31.3		
Very poor	10	3.9	4	12.5	14.877	0.005*
Use hearing aid	7	2.7	0	0.0	Fisher	1.000
Hearing						
Excellent	61	23.7	6	18.8		
Very good	95	37.0	11	34.4		
Good	77	30.0	10	31.3		
Poor	22	8.6	2	6.3		
Very poor	2	0.8	3	9.4	12.712	0.013*
Ever smoker	50	19.5	10	31.3	2.406	0.121
Current smoker	26	10.1	5	15.6	Fisher	0.361
Physical exertion frequency						
>1/week	139	54.1	10	31.3		
1/week	60	23.3	3	9.4		
1–3/month	18	7.0	4	12.5		
Rare	40	15.6	15	46.9	21.215	<0.001*
Recall of words (mean ± SD: max = 10)	4.33 ± 1.96		3.38 ± 2.27		2.280	0.028*
Felt depressed	111	43.2	23	71.9	9.415	0.002*
Used antidepressants	24	9.3	8	25.0	Fisher	0.015*
Have sleep problems	124	48.2	25	78.1	10.170	0.001*
Hospital admission	28	10.9	8	25.0	Fisher	0.041*
Have difficulty getting aids	4	1.6	0	0.0	Fisher	1.000
Good grip	235	91.4	29	90.6	Fisher	0.747
Walking ability						
High	221	86.0	23	71.9		
Moderate	10	3.9	4	12.5		
Low	26	10.1	5	15.6	5.830	0.054
Score of difficulty with						
Physical activities (max = 10)	3.11 ± 3.08		6.53 ± 2.26		7.718	<0.001*
Daily life activities (max = 13)	1.38 ± 2.23		4.59 ± 3.91		4.557	<0.001*

*Statistically significant at $p < 0.05$.
[#]Missing data.

section such as age, gender, residence, education, etc.; parts of the health status and physical activity section as the history of chronic diseases, health problems, medication administration, vision, and hearing, etc.; mental abilities as recall; mental health as sleep problems; health care utilization; job; physical testing as grip; relations with children as caregiving; as well as the living conditions and facilities.

Statistical analysis

The data were extracted from the SPSS (Version 25) dataset. Bivariate analyses included chi-squared or Fisher exact tests for the comparison of categorical risk factors between faller and non-faller groups. Numeric data were compared using independent *t*-tests or Mann-Whitney tests as suitable. Multiple logistic linear regression with backward Wald method and ROC (Receiver Operator Curve) analysis were used to identify the independent risk factors of falling and model its risk. Statistical significance was considered at $p < 0.05$.

Results

In a sample of 289 seniors, 32 reported fall incidents indicating a prevalence rate of 11.07% (95% CI: 7.95–15.21). Table 1 indicates that the old age people who experienced falls were significantly more among those aged 70 years or older ($p < 0.001$), unemployed or housewives ($p = 0.026$), have a family caregiver ($p = 0.022$), and home facilities for disability ($p = 0.015$). Their percentages also tended to be higher among females although the difference was not statistically significant ($p = 0.170$).

As illustrated in Table 2, one-half of the old age persons in both groups were obese. Those in the fall group had significantly poorer visual acuity ($p = 0.005$) and hearing ($p = 0.013$), and less exercise frequency ($p < 0.001$). They also had lower recall rates for words ($p = 0.028$) with more depression ($p = 0.002$), use of antidepressants ($p = 0.015$), more sleep problems ($p = 0.001$), and hospital admission ($p = 0.041$). Their scores of difficulty in performing physical and daily life activities were higher ($p < 0.001$).

Table 3 demonstrates that the old age persons in the fall group reported significantly higher rates of ischemic heart disease ($p < 0.001$), hypertension ($p = 0.015$), dyslipidemia ($p = 0.042$), stroke ($p = 0.008$), and diabetes mellitus ($p < 0.001$). They also had higher rates of osteoporosis ($p = 0.031$), cataract ($p < 0.001$), and arthritis ($p < 0.001$), in addition to more history of fracture hip ($p = 0.016$). Overall, the mean number of chronic diseases was higher among them (3.38 ± 1.77) compared with those in the no-fall group (1.74 ± 1.63), and the difference was statistically significant ($p < 0.001$).

Concerning the health problems reported by old age persons. Table 4 indicates statistically significantly higher percentages among those in the fall group in all types of problems. The only exception was that of recurrent cough ($p = 0.080$). The most frequently reported problems among them were the fear of fall and dizziness (62.5%), while the lowest were recurrent cough (15.6%) and incontinence of urine (21.9%). The table shows that all those in the fall group had at least one reported problem compared to 62.3% of those in the no-fall group ($p < 0.001$). Overall, the mean number of health problems was higher among those in the fall group (5.34 ± 1.81) compared with those in the no-fall group (1.39 ± 1.53), and the difference was statistically significant ($p < 0.001$).

Similarly, the old age persons in the fall group had higher percentages of administration of almost all types of medications,

TABLE 3 Comparison of the prevalence of chronic diseases reported by old age persons with and without fall history.

Diseases	Fall group				Chi-squared test	*p*-value
	No ($n = 257$)		Yes ($n = 32$)			
	No.	%	No.	%		
Ischemic heart	35	13.6	13	40.6	14.985	<0.001*
Hypertension	118	45.9	22	68.8	5.941	0.015*
Dyslipidemia	55	21.4	12	37.5	4.142	0.042*
Stroke	8	3.1	5	15.6	Fisher	0.008*
Diabetes mellitus	68	26.5	19	59.4	14.653	<0.001*
Bronchial asthma	15	5.8	0	0.0	Fisher	0.388
Pulmonary disease	8	3.1	0	0.0	Fisher	0.604
Neoplasm	7	2.7	0	0.0	Fisher	1.000
Osteoporosis	33	12.8	9	28.1	Fisher	0.031*
Genitourinary	16	6.2	3	9.4	Fisher	0.452
Parkinsonism	2	0.8	0	0.0	Fisher	1.000
Cataract	21	8.2	11	34.4	Fisher	<0.001*
Arthritis	62	24.1	14	43.8	5.655	0.017*
Total number (mean ± SD)	1.74 ± 1.63		3.38 ± 1.77		4.951	<0.001*
History of fracture hip	6	2.3	4	12.5	Fisher	0.016*

*Statistically significant at $p < 0.05$.

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TABLE 4 Comparison of health problems reported by old age persons with and without fall history.

Health problems	Fall group				Chi-squared test	*p*-value
	No ($n = 257$)		Yes ($n = 32$)			
	No.	%	No.	%		
Back pain	128	49.8	26	81.3	11.304	0.001*
Angina	32	12.5	12	37.5	Fisher	0.001*
Dyspnea	34	13.2	11	34.4	Fisher	0.004*
Recurrent cough	17	6.6	5	15.6	Fisher	0.080
Edema lower limbs	38	14.8	17	53.1	27.145	<0.001*
Sleep disorders	44	17.1	21	65.6	38.404	<0.001*
Fear of fall	14	5.4	20	62.5	Fisher	<0.001*
Dizziness	27	10.5	20	62.5	56.491	<0.001*
Incontinence of urine	22	8.6	7	21.9	Fisher	0.028*
Have at least 1 problem	160	62.3	32	100.0	18.180	<0.001*
Mean ± SD	1.39 ± 1.53		5.34± 1.81		−11.873	<0.001*

*Statistically significant at $p < 0.05$.

TABLE 5 Comparison of the administration of medications as reported by old age persons with and without fall history.

Medications for	Fall group				Chi-squared test	*p*-value
	No ($n = 257$)		Yes ($n = 32$)			
	No.	%	No.	%		
Dyslipidemia	48	18.7	9	28.1	1.604	0.205
Hypertension	117	45.5	20	62.5	3.289	0.070
IHD	28	10.9	11	34.4	Fisher	0.001*
Other cardiac	14	5.4	8	25.0	Fisher	0.001*
Bronchial asthma	13	5.1	0	0.0	Fisher	0.374
Diabetes mellitus	63	24.5	18	56.3	14.208	<0.001*
Arthritis	65	25.3	15	46.9	6.622	0.010*
Analgesics	87	33.9	19	59.4	7.981	0.005*
Sleep pills	14	5.4	4	12.5	Fisher	0.124
Antidepressants	4	1.6	2	6.3	Fisher	0.134
Osteoporosis (hormonal)	25	9.7	6	18.8	Fisher	0.130
Osteoporosis (other)	6	2.3	1	3.1	Fisher	0.564
Antacids	44	17.1	7	21.9	0.443	0.506
Bronchitis	26	10.1	8	25.0	Fisher	0.035*
Take at least 1 medication	201	78.2	32	100.0	8.649	0.003*
Mean ± SD	2.16 ± 1.96		4.00 ± 2.09		−4.730	<0.001*

*Statistically significant at $p < 0.05$.

reaching statistical significance regarding medications for IHD and other cardiac diseases ($p = 0.001$), diabetes ($p < 0.001$), arthritis ($p = 0.010$), analgesia ($p = 0.005$), and bronchitis ($p = 0.035$) as presented in Table 5. The table also indicates that all those in the fall group had at least one medication administered compared to 78.2% of those in the no-fall group ($p = 0.003$). Overall, the mean number of medications was higher among those in the fall group (4.00 ± 2.09) compared with those in the no-fall group (2.16 ± 1.96), and the difference was statistically significant ($p < 0.001$).

The multivariate analysis (Table 6) demonstrates that the statistically significant independent predictors of fall occurrence are the history of stroke and diabetes mellitus, the fear of fall and dizziness, in addition to the total number of health problems and the score of difficulty in performing physical activities. It is evident that

TABLE 6 Best fitting multiple logistic regression model for the occurrence of fall.

	Wald	Df	*p*-value	OR	95.0% CI for OR	
					Upper	Lower
Constant	31.334	1	0.000	0.00		
Stroke	9.160	1	0.002	33.49	3.45	325.40
DM	7.032	1	0.008	7.42	1.69	32.61
Fear of fall	6.656	1	0.010	7.14	1.60	31.78
Dizziness	4.653	1	0.031	5.08	1.16	22.23
No. of health problems	16.113	1	0.000	2.72	1.67	4.42
Score of difficulty in physical activities	5.124	1	0.024	1.33	1.04	1.71

Nagelkerke *R* Square: 0.74.
Hosmer and Lemeshow Test: $p = 0.181$.
Omnibus Tests of Model Coefficients: $p < 0.001$.
Variables entered on step 1: Age, gender, sleep problems, IHD, dyslipidemia, hypertension, stroke, diabetes, fracture hip, fear of fall, dizziness, urine incontinence, No. of problems, score of difficulty with physical activities and ADL, exercise frequency, recall of words, depression.

the history of stroke is the strongest risk factor for falling, increasing its risk more than 33 folds (OR 33.49, CI: 3.45–325.40).

Discussion

This study was aimed at assessing the prevalence of falls among elderly in an Egyptian community and investigating its associated risk factors using the SHARE-Questionnaire. The findings indicate a relatively high prevalence, with stroke being the most important risk factor underlying falls in this population.

According to the current study results, slightly more than one-tenth of the old age persons in the sample gave a positive history of previous fall incidents. This is quite a high rate that needs to be addressed carefully given its untoward consequences on the elderly person and his/her family, as well as the whole community and health care system. Nonetheless, the rate is still lower than that reported by Geetha et al. (12) in a study of fall risk in India who reported a rate 27.6%. This discrepancy might be due to that the Indian study was in a rural area, and the age of their participants was older in comparison with our study. Similarly, a study in China reported a prevalence rate of 20.65 among elderly persons living in rural and urban community dwellings (13). Their age group was also more than one decade older in comparison with the present study.

The bivariate analyses of the current study identified significant associations between certain old age persons' age, and being unemployed, retired, or housewife. Additionally, there was a trend of higher prevalence among women. In agreement with this, a study in New Zealand found significant associations with older age and female gender (14). On the same line, Guerreiro et al. (15) in a study in Spain demonstrated that female gender was a significant predictor of falls among old age people. However, the multivariate analysis could not confirm a significant independent role in the risk of falling.

Meanwhile, factors related to old age persons' health status and identified in bivariate analyses as having significant associations with the occurrence of falls were poor vision and hearing, lack of physical activity, sleep problems, inadequate recall, depression symptoms, and previous hospital admission. In addition, the difficulty in performing physical and daily life activities was a significant risk factor. These are all indicative of poorer health status that may lead to higher risk for accidents and injuries. They also reflect a low physical fitness leading to inability to prevent falling in case of stumbling or losing equilibrium. Similar associations between old age persons' falls and poor vision or hearing impairment (16, 17), sleep disorders (18), depression (19), and impaired recall and mental abilities (20) were previously reported.

Nevertheless, only the score of difficulty in performing physical activity was identified in the present study multivariate model as a significant independent risk factor of falling among old age persons. This would undoubtedly be due to that this score is the summative outcome of poor physical health. In congruence with this, several systematic reviews with meta-analyses provided a strong evidence of the positive effect of exercise training interventions in decreasing the risk of falling among old age people (21–23). Moreover, exercise interventions associated with lifestyle changes proved to have a high effectiveness in reducing the risk of falling in the elderly (24).

Concerning the health problems related to the occurrence of fall incidents among old age persons, the current study bivariate analyses demonstrated significant associations with their affection by certain chronic ailments such as ischemic heart disease, hypertension, dyslipidemia, stroke, and diabetes mellitus, as well as osteoporosis, cataract, arthritis, and history of fracture hip. These chronic conditions certainly have negative impacts on the elderly' physical and mental abilities, thereby increasing their risk of falling. In fact, the number of health problems was identified in the multivariate analyses as an independent significant positive predictor of the risk of falling. The findings are in agreement with a recent study in China that examined the relation between the number of chronic diseases and falling in the elderly population (25).

The multivariate analysis also identified stroke and diabetes mellitus as significant independent predictors of falling among old age persons. The influence of stroke is quite understandable given its negative impacts on the affected person's physical as well as mental abilities. In congruence with this, a study in Japan identified stroke as an independent predictor of the risk of falling among elderly (26). As for diabetes mellitus, it might increase the risk of falling due to associated neuropathy that may make the diabetic person more vulnerable to accidents and injuries. Moreover, diabetic patients may have impaired reactive balance to disequilibrium as demonstrated in a study in the United States, thus increasing their risk of falling (27).

The present study bivariate analyses also showed that the old age persons in the fall group reported significantly higher rates of almost all symptoms related to various chronic diseases. This again reflects their poor health status. However, the only symptom confirmed in the multivariate analysis was that of dizziness. This is quite conceivable given that it can lead to disequilibrium and the old age person is often unable to rapidly regain his/her equilibrium and his/her physical fitness and abilities cannot help in preventing falling. Similar significant relations between dizziness and the risk of falling among elderly were reported in studies in Sweden (28) and Greece (29).

The fear of fall (FOF) was also identified as a major factor affecting the occurrence of falls among the old age persons in the present study. Its role was evident both in bivariate and multivariate analyses. It may act through limiting the old person's physical activities, thus leading to low physical fitness and weak muscles, and may lead to frailty and even sarcopenia. In line with this, a study of elderly in Iran clarified that the fear of fall among them is associated with disturbance of their activities of daily living, with consequent negative impact on their quality of life (30). Furthermore, Qin et al. (31) in a study in China demonstrated a significant association between FOF and frailty among old age people.

The current study results revealed that the old age persons who experienced falling had higher rates of medication use compared with the non-fallers in the bivariate analyses. They also had higher rates of administration of polypharmacy. The influence of polypharmacy as a risk factor predicting falls in the old age people has been previously documented in the literature (32, 33). Yet, the effect of polypharmacy on the occurrence of fall was not confirmed in the current study multivariate analysis. This might be explained by that the effect of the disease itself as stroke or diabetes mellitus was more important than that of related medications.

The present study multivariate regression analysis produced a model that depends on the history of stroke and diabetes mellitus, the fear of fall and dizziness, the total number of health problems and the score of difficulty in performing physical activities. A similar model was developed by Gade et al. (28) in Denmark. The risk factors included in their model were old age person's level of education, feeling dizzy, alcohol intake, history of previous falls, perceived risk of falling, disabilities, and symptoms of depression. The differences with the present study model might be attributed to the differences in the study designs, where the Denmark study was a cohort one, in addition to the socio-demographic differences between the two studies such as the level of education and alcohol consumption. However, as highlighted by Seaman et al. (34), the development of predictive fall models for the elderly is still in "its infancy." Thus, more research is needed.

Our study has some limitations that could jeopardize its generalizability to the whole Egyptian population. Firstly, the inclusion of participants in the fifth decade of age could make the study results not comparable to many old age studies. Secondly, the convenience sampling could have led to bias in the level of education, which might not reflect the true population figures. Lastly, the sample size was calculated using a relatively large margin of error, which might have led to a small sample size for a prevalence study; however, the sample size was large enough for the multivariate analysis.

Conclusion and recommendations

The prevalence of falls among old age persons in the studied community is not alarmingly high, yet it could be reduced since the target should be "no-falls." The risk is highest among stroke patients. The study recommends rehabilitation & community interventions to train and educate old age people, especially those at risk such as stroke and diabetic patients, and those with dizziness to improve their physical fitness and reduce the fear of fall among them. The developed prediction model needs to be validated through longitudinal studies.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by IRB of the American University in Cairo (IRB-AUC). The patients/participants provided their written informed consent to participate in this study.

Author contributions

AE, MS, OM, and AA: drafted the first version, conceptualized the idea, conducted data collection, and analysis. MS: funding, conceptualization, and final revision. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Factors influencing seniors' willingness to pay intention for exercise in the civil sports and recreation centers

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Background: The increasing trend for an older population is a phenomenon that is well recognized around the world. The percentage of senior citizens participating in sports, recreation, and leisure activities is also increasing in order to sustain a healthier society. As long as seniors recognize the importance and benefits of keeping healthy, they would prefer to be active in various sports and fitness activities. The seniors could engage in making decisions about their own health by exercising regularly and by encouraging their similar-age peers. The civil sports and recreation centers (CSRCs) in Taiwan have adopted operating transfer (OT) and are located mainly in metropolitan areas, with programs consisting of indoor sports offering people daily exercise. The major aims of the CSRC are to keep the citizens in good health and not to be the city government's financial burden. The extant literature examines the determinants of general consumer behavior, neglecting studies on older adults. This study aims to explore the factors influencing seniors' willingness to pay (WTP) more for exercise in CSRCs outside of free hours.

Methods: This mixed-method study consists of quantitative and qualitative analyses. For the quantitative component, we invited five experts in the sports industry from the industry and academia to evaluate the validity of the questionnaire. A questionnaire consisting of motivation, exercise involvement, and constraint constructs in the quantitative method was administered to 193 older adults in CSRCs. The collected data were analyzed through descriptive statistics, *t*-test, one-way analysis of variance (ANOVA), and structural equation model (SEM).

Results: Empirical results indicate that WTP in groups of people aged 75–79, 70–74, and 65–69 years is higher than in the group of people aged 85 years and above. Exercise involvement and motivation had more of a positive impact on seniors' WTP.

Discussions: Developing a regular exercise habits and having social interaction in exercise courses drive female seniors to pay more for body health. The results of this study provide managers of CSRCs with decision-making recommendations: (1) initiate entry-level sports courses, such as quick chair exercise, to cultivate among seniors the habit of exercise; (2) motivate seniors to participate in sports with other seniors in order to enhance their social activity and raise their WTP more for sports consumption outside of free scheduled periods; and (3) recruit seniors as exercise coaches or personal trainers to pass their experiences with other people of their age. In addition to expanding seniors' social connections, it encourages peers to exercise. Managerial implications and future research are also discussed.

Conclusion: This study contributes to exploring the determinants of seniors' WTP intention. Motivation and exercise involvement had a significantly positive impact on seniors' WTP intention.

KEYWORDS

civil sports and recreation centers (CSRC), WTP more, exercise involvement, motivation, constraint

Introduction

The World Health Organization (1) indicated that the number of people aged 60 years and above was 1 billion in 2019 and this number will increase to 1.4 billion by 2030 and 2.1 billion by 2050. The increasing trend for an older population is a phenomenon that is well recognized around the world. Senior adults are the most inactive sector of the U.S. population (2). The research claimed that senior adults may possibly face more constraints on physical activity (PA), such as lack of time, interest, fear of falling, and injuries (3). This is mainly due to the chronic diseases associated with age, most particularly, physical disability and discomfort leading to health constraints. Senior adults of low socioeconomic status (4), women (3), and those with less disposable income (5) are at greater risk of physical inactivity. Senior adults also report constraints that are more perceptual in nature, including lack of time, lack of motivation, misconceptions about PA, fear of injury, and lack of skill (6). As of 2017, an estimated 962 million people aged 60 years or above comprise 13% of the global population. The population of people aged 60 years and above is growing at a rate of about 3% per year. According to definitions from the World Health Organization, when the proportion of society that is elderly (over 65 years old) reaches 7%, it is called an "aged society," while 14% is an "old-age society." If this figure is 20% or more, it is a "super-aged society" (7). According to the Ministry of the Interior, the ratio of the elderly population in Taiwan exceeded 14% in 2018, and it became an aged society. The elderly population in Taiwan has accelerated. As of January 2021, Taiwan's elderly population (over 65 years old) accounted for 16.2% of the total population, officially making it an old-age society (8).

The percentage of senior citizens participating in sports, recreation, and leisure activities is increasing (9, 10). Consumers aged 60 years and over actively participate in a variety of sports and fitness activities because they acknowledge the importance and benefits of keeping fit and healthy (11). Shank (12) revealed that participation in sports for people in sports facilities, in particular, is closely associated with the lifestyle preferences and personalities of consumers. It is, therefore, important and necessary to understand senior adult consumers' exercise consumption habits. Currently, there are several exercise activities and courses offered at the civil sports and recreation centers (CSRCs) in Taiwan. Taiwan's CSRCs were built using the city government's funding and then were operated and transferred (OT) to private firms within the contracted years in order to make their operating performance better and generate revenue for the local authority. Taiwan's CSRCs have two major objectives of revenue generation and exercise participation increase because of the OT management type (13). Hence, the major aims of the CSRC are to keep the citizens in good health and not to be a local authority's financial burden. Meanwhile, to increase the percentage of senior citizens participating in PA, the CSRCs in Taiwan have been regulated to offer the following free welfare hour zone for people aged 65 years and above (hereafter, seniors): (1) 8:00–10:00 a.m. for the major sports facilities (excluding basketball, squash, and roller blades) during the whole week; and (2) 2:00–4:00 p.m. from Monday to Friday (only for swimming pool and gym). All free welfare hour zones exclude public holidays and summer and winter breaks. Outside these free welfare hour zones, seniors can buy a discounted ticket—NT$50 (US$1 = NT$28) for the swimming pool (normal ticket price is NT$110) and NT$25/h for the gym (normal ticket price is NT$50/h). However, there were limited senior participants to purchase these discounted tickets leading to the fact that the CSRCs could not generate revenue from the seniors and the seniors would not be interested in extending their exercise time.

There are limited studies on the physical and psychological needs of senior customers. However, ticket sales outside of these free welfare hours are not as good as the other operating periods. Even though the CSRCs are required to offer free welfare hour zones for people aged 65 years or above, few seniors experience PA in the CSRCs in Taiwan. In contrast, the CSRCs also observed that some seniors prefer to enjoy non-crowded PA during non-free welfare hours rather than experiencing PA during free welfare hours. In particular, some seniors do not like the feeling of being looked down upon during free welfare hours. Some CSRCs have attempted to initiate marketing campaigns, such as offering promotional packages that extend discounted periods for seniors and launching a PA course only for seniors.

Willingness to pay (WTP) is consumers' perceived value of products or services, usually expressed in their local currency (14). WTP usually consists of whether or not and how much a consumer is willing to pay for something (15). In economics, WTP is regarded as a contingent valuation that represents the maximum cost that a consumer is willing to pay for an item and shows the value of that item to the consumer (15, 16). However, Pulido-Fernández and López-Sánchez (17) asserted that there is still no appropriate statistical model to estimate WTP. Wertenbroch and Skiera (18) pointed out that consumers' WTP assesses the demand for public and private goods to plan an optimal price model. Previous studies have found that many research methods can assess the price of a consumer's different conditions. Lee and Heo (16) suggested that the value of products or services can be used to assess the benefits or costs of environmental resources. Namkung and Jang (19) used one item ("How much more are you willing to pay for green practices at the restaurant?") to measure consumers' WTP more for green practices in restaurants. Yooyen and Leerattanakorn (20) asked the respondents to choose the amount or percentage that they were willing to pay from a list of possible payments. Table 1 shows the most important literature on WTP.

There is no consensus among researchers about the best measurement for WTP (17). According to the results of Table 1, the survey questionnaire to estimate WTP more might be appropriate based on the previous studies (17, 19).

Exercise has been linked to improved physical health (24, 25). For senior adults, especially, exercise has been linked to better breathing, muscle strength, flexibility, and balance, less susceptibility to falls, and improved executive control processes (26–31). Motivation is defined as promoting and continuing activity programs in both the intensity and direction of the effort (32). People are motivated to exercise for personal goals and social interaction (33–35). Beaton et al. (36) claimed that sports involvement is present when individuals evaluate their participation in a sports activity that brings hedonic and symbolic value to their life. Studies conducted in recreational settings have shown that individuals who are more involved in an activity are more likely to remain customers (37, 38). Kyle et al. (39) noticed that the patterns of leisure involvement also depend on the nature of the activity and the participant's characteristics. Among senior people with a broad range of body mass indices, poor health and lack of interest are usually mentioned as constraints on PA (40–44). Many senior people also have a fear of falling

TABLE 1 Major related extant research on WTP.

References	Issue	Field	Measure method, unit
Lee and Heo (15)	WTP for renewable energy	Renewable energy sources	CVM, WTP, KRW$
Wertenbroch and Skiera (16)	WTP for retailed products	Retailed product	BDM method, choice bracketing procedure ($0.00–$10.00 in increments of $0.25)
Hu et al. (21)	Green restaurant	Green restaurant	SEM, green restaurant patronage (Survey)
	Patronage		
Namkung and Jang (19)	WTP more for green practices at restaurants	Green products	WTP more, $
Yooyen and Leerattanakorn (20)	WTP for organic pork	Agricultural products	Pay extra price, $
Ha-Brookshire and Norum (22)	WTP for socially responsible products—Cotton apparel	Agricultural products	Pay extra price, $
Pulido-Fernández and López-Sánchez (17)	WTP for sustainable destination in Spain.	Economic implications for sustainable tourists.	WTP more, $

CVM, contingent valuation method; BDM, Becker et al. (23) method.

and injury and feel insecure when exercising outdoors (45–48). Less is known about the perceived constraints on PA among obese senior people. No studies have examined whether or not perceived constraints can explain the increased risk of physical inactivity among obese senior people. Constraint captures the explanations for physical inactivity, which can be internal or external, intrapersonal or interpersonal, intervening or antecedent, blocking or inhibiting, and permanent or temporary (49). Based on the literature, this article has established three hypotheses, namely, (1) motivation for exercise positively affected WTP; (2) exercise involvement positively affected WTP; and (3) constraints negatively affected WTP. Our aim of this article is to examine the relationships among motivations, exercise involvement, constraints, and WTP in order to gain insights that will result in effective services to senior adult consumers in a sports and fitness center. This article is the first to discuss the factors influencing senior citizens' exercise consumption habits using WTP.

Materials and methods

Research method

This study is based on the concept of WTP, aiming to explore the factors influencing senior citizens' WTP more for exercise in the CSRCs outside of free hours. Pulido-Fernández and López-Sánchez (17) claimed that parametric methods are most used, but non-parametric approaches have some advantages with respect to the parametric analysis since the WTP estimators are easily assessed and are more robust to misspecifications of the probability distribution function. The structural equation model (SEM) has a few advantages over multiple regression and path analysis (50). Wertenbroch and Skiera (18) argued that the external validity of contingent valuation and related approaches may be limited. They provide less incentive to consumers to truthfully reveal their WTP because responses are hypothetical. Pulido-Fernández and López-Sánchez (17) asserted that there is still no standard about which is the appropriate statistical model to estimate the WTP. Hence, this article adopted the survey questionnaire to estimate WTP more from the study of Namkung and Jang (19).

Sample design and data collection

In order to ensure the respondents who have visited a CSRC in Taiwan and whose age is above 65 years, this article adopted purposive sampling and the researchers waited for visitors beside the entrances of CSRCs during the free welfare time zones for seniors (8:00–10:00 a.m. during the whole week, and 2:00–4:00 p.m. from Monday to Friday). We provided both paper-based and mobile-based (with a QR code) questionnaires for participants. We collected 193 valid on-site questionnaires from the CSRCs. The last part of the demographic section of the questionnaire screened out invalid respondents. The valid collected data were analyzed using SEM.

Measurement

This study adopted the mixed-method study including quantitative and qualitative analyses. After developing the questions from the well-established literature and then translating them into Mandarin Chinese to ensure participants' full comprehension, the first stage of this study invited five experts from the industry and academic fields in the sports industry to examine the validity of the questionnaire. The quantitative method in the second stage gathered data through the questionnaire. The questionnaire survey consisted of six sections: the first section introduced the purpose of this scale and informed participants that individual responses would be kept highly confidential and anonymous. The first section asked respondents to fill in their real feeling. The second section assessed a motivation construct made up of 15 items (Cronbach's $\alpha = 0.944$). Examples of items include "Maintain physical health and physiological functions." and "Keep pace with social trends;" an exercise involvement construct made up of 13 items (Cronbach's $\alpha = 0.950$). Examples of items include "PA is very important to me;" and constraints made up of 13 items (Cronbach's $\alpha = 0.894$). Examples of items include "I am more introverted" and "I never did PA before." The participants were asked to provide their level of agreement to disagreement with the related statements, adopting a 5-point Likert scale from 1 for "highly disagree" to

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TABLE 2 Major related extant research on WTP.

Constructs	Items	Factor loading	CR	AVE
Motivation	Q1 Maintain physical health and physiological functions	0.503	0.944	0.537
(The reasons to join PA)	Q2 Relax your mind and regulate your body and mind	0.519		
	Q3 Maintain physical strength and good spirits	0.492		
	Q4 keep a regular lifestyle	0.685		
	Q5 Make friends	0.774		
	Q6 Keep social contacts with peers	0.815		
	Q7 Become a member of the sport group and have a sense of belonging	0.864		
	Q8 Invite friends to join PA	0.662		
	Q9 Keep pace with social trends	0.812		
	Q10 Stay in touch with society and maintain social identity	0.862		
	Q11 Guide others	0.817		
	Q12 Challenge yourself	0.767		
	Q13 Unleash creativity	0.782		
	Q14 Learn new knowledge to enrich the quality of life	0.760		
	Q15 For self-realization	0.732		
Exercise Involvement (EI)	Q16 PA is very important to me	0.540	0.958	0.641
	Q17 Participating in PA is very satisfying	0.908		
	Q18 I am happy to join PA.	0.869		
	Q19 I am interested in joining PA.	0.936		
	Q20 Join PA is a pleasure	0.896		
	Q21 I love to join PA	0.822		
	Q22 PA accounts for a large portion in my life.	0.842		
	Q23 PA accounts for a central position in my life.	0.839		
	Q24 PA accounts for an important position in my life.	0.870		
	Q25 I love to discuss PA with my friends.	0.773		
	Q26 I can perform PA well.	0.690		
	Q27 I can explain a lot when other people play PA.	0.739		
	Q28 I like acting PA.	0.564		
Constraint(The reasons why I don't want to join PA)	Q29 I am more introverted	0.693	0.857	0.44
	Q30 PA requires special skills	0.580		
	Q31 I never did PA before	0.665		
	Q32 I feel uncomfortable doing PA	0.592		
	Q33 People who are important to me believe that I am not suitable to do PA.	0.636		
	Q34 People who are important to me can't accompany me to Join PA	0.672		
	Q35 I need to take care of grandchildren	0.594		
	Q36 I can't find the right person to go exercise with me	0.573		
	Q37 Bad weather	0.484		
	Q38 Insufficient safety of sports facilities	0.704		
	Q39 Too crowded	0.530		
	Q40 Poor sanitation	0.623		
	Q41 No relevant PA information	0.801		

5 for "highly agree." This article puts all questionnaire items in Table 2.

Namkung and Jang (19) examined customers' WTP more for green practices in restaurants using hypothetical scenarios. Namkung and Jang (19) used one item ("How much more are you willing to pay for green practices at the restaurant?") to measure consumers' WTP. This study adopts this previously validated questionnaire item from the study of Namkung and Jang (19). The third section addressed demographic variables and measured WTP using a Likert instrument (How much will you pay for exercise outside of the free welfare hours? 1: NT$0; 2: NT$1–5; 3: NT$6–10; 4: NT$11–15; 5: NT$16–20; 6: NT$21–25; 7: NT$26–30; 8: NT$31–35; 9: NT$36–40; 10: NT$41–45; 11: NT$46–50; 12: NT$51 and above; (US$1 = NT$28).

Measurement model

This article used the purposive sampling method to collect on-site data from participants in 12 CSRCs over an 8-week period during the free welfare time zones for seniors (8:00–10:00 a.m. and 2:00–4:00 p.m.) in Taipei City.

One of the demographic questionnaire items asked respondents about their age range. If the respondent's answer was below 65 years old, their questionnaire would not be included in the further analysis. A total of 210 questionnaires were distributed, and a total of 193 valid samples were collected for analysis.

We examined the insignificant difference in WTP more between women and men using the *t*-test. We further examined the relationship between age group and WTP more using one-way analysis of variance (ANOVA) and the *post-hoc* Dunnett T3 test. This study further assessed the reliability, validity, and Spearman's correlation through SPSS version 26.0. Confirmatory factor analysis (CFA) and path analysis were undertaken with the IBM AMOS 26 Graphics.

Results

Descriptive statistics

Table 3 lists the descriptive statistics of the participant data. Of the 193 valid samples, 104 (53.9%) are men; 89 (46.1%) are women. A total of 56 (29%) respondents are aged 65–69 years; 52 (27%) respondents are aged 70–74 years; 28 (14.5%) respondents are aged 75–79 years; 43 (22.3%) respondents are aged 80–84 years; and there are 14 (7.3%) respondents above 85 years old.

We examined the insignificant difference in WTP more between women and men using the t-test. We further examined the relationship between age group and WTP more using one-way ANOVA. The Levene homogenous variance test value is 9.71 (p-value < 0.0001), indicating that the hypothesis of homogenous variance of WTP more is rejected. The *post-hoc* Dunnett T3 test with heterogeneous variance (Table 4) shows that WTP more in the groups of people aged 75–79, 70–74, and 65–69 years is higher than in the group of people aged 85 years and above. However, the WTP more of the group of people aged 80–84 years is only insignificantly higher than that of people in the group aged 85 years and above.

Since WTP more in the groups of participants aged 75–79, 70–74, and 65–69 years is higher than in the group of participants aged 85 years and above, the CSRC could motivate seniors aged 65–79 years, particularly for the 75–79 years age group, who are most willing to pay more, to experience sports with marketing promotions in order to raise their WTP for sports consumption outside of free welfare hours.

TABLE 3 Demographics of the selected participants.

Characteristics	Frequency (percentage %)
Gender	
Male	104 (53.9%)
Female	89 (46.1%)
Age	
65–69	56 (29.0%)
70–74	52 (26.9%)
75–79	28 (14.5%)
80–84	43 (22.3%)
85 above	14 (7.3%)

The average WTP more among people aged 65–69, 70–74, 75–79, 80–84, and 85 years and above is 8.52 (NT$31–40), 9.23 (NT$36–45), 10.36 (NT$41–50), 7.65 (NT$26–35), and 4.14 (NT$11–20), respectively. These empirical results indicated that the maximum average WTP more among different age groups is <NT$50.

Reliability and validity

This study further assessed convergent validity and discriminant validity of all constructs through factor loadings, composite reliability (CR), and average variance extracted (AVE) in Table 2. All CR values show a greater degree of reliability than the recommended cutoff value of 0.70 and AVEs are >0.40, respectively (51).

Bivariate correlations

Existing research has used the Spearman correlation analysis to indicate the associations between variables before SEM (50, 52). This article also used the Spearman correlation analysis to indicate significant links between research variables. This is illustrated in Table 5, which shows that motivation and exercise involvement are significantly positively related to WTP more. Constraints for exercise are insignificantly negatively related to WTP more.

Confirmatory factor analysis and structural equation modeling

CFA validation

Confirmatory factor analysis is the first stage of the SEM that validates the goodness-of-fit of our model. The examination of the measurement model of the scales and the assessment of the path analysis were undertaken with the IBM AMOS 26 Graphics. The main criteria used to judge model fit, such as Bentler's (53) Comparative Fit Index (CFI) and Normal Fit Index (NFI), for which

TABLE 4 WTP more comparison among five age groups.

Age group	*N*	%	WTP more Mean	SD	*F*-value	*Post-hoc* Dunnett T3 test
1. 65–69	56	29%	8.52	4.15	5.834**	1 > 5*, 2 > 5**, 3 > 5***
2. 70–74	52	27%	9.23	3.45		
3. 75–79	28	15%	10.36	3.58		
4. 80–84	43	22%	7.65	5.22		
5. 85 and above	14	7%	4.14	5.16		
Total	193	100%	0.60	0.28		

WTP more: 1: NT$0; 2: NT$1–5; 3: NT$6–10; 4: NT$11–15; 5: NT$16–20; 6: NT$21–25; 7: NT$26–30; 8: NT$31–35; 9: NT$36–40; 10: NT$41–45; 11: NT$46–50; 12: NT$51 and above (US$1 = NT$28).
*p-value < 0.1; **p-value < 0.05; ***p-value < 0.01.

TABLE 5 Bivariate correlations between research variables and descriptive statistics.

Variables	Mean	SD	Motivation	Exercise involvement	Constraints
WTP more	8.47	4.46	0.271**	0.217**	−0.074
Motivation	4.23	0.71	–	0.748**	−0.014
Exercise involvement	4.16	0.80	–	–	−0.013
Constraints	3.12	0.76			–

**Correlation is significant at 0.05 level.

TABLE 6 CFA for each construct and the research model.

Construct	No of items	NFI	CFI	RMSEA
Motivation	16–>5	0.96	0.98	0.09
Exercise involvement	12–>3	0.98	0.99	0.07
Constraint	15–>8	0.88	0.92	0.09
Overall model	21–>16	0.82	0.88	0.09

NFI, normal fit index; CFI, comparative fit index; RMSEA, root mean square error of approximation.

values >0.85 validate a good model fit (54), and the root mean square error of approximation (RMSEA), with a value of <0.1 considered acceptable (55), are shown in Table 6. If the model does not fit well, modification indices (MIs) for the lambda matrix might be used to improve it (56).

Table 6 shows that both each construct and the whole model achieve goodness-of-fit by eliminating unfit items through MI improvement (56). However, Shook et al. (57) advise that the Bollen–Stine bootstrapping approach can be used to adjust the model fit if the data cannot fulfill normal distribution. In particular, Thode (58) recommends the Shapiro–Wilk test as the best choice for normality testing of the dependent variable. This article used the Kolmogorov–Smirnov test with the Lilliefors correction and Shapiro–Wilk statistics for a normality test (57, 59). The *p*-values for these two normality tests are <0.001, indicating that the data do not seem to fit a normal distribution. Hence, this article further used the Bollen–Stine bootstrapping method to modify the fitness indices.

Path analysis from the SEM model

The results of the SEM [$\chi^2(115) = 315.85$, $p < 0.0001$; NFI = 0.824; CFI = 0.879; RMSEA = 0.095] are shown in Table 7. However, due to the non-normal data in SEM, Shook et al. (57) suggest using the Bollen–Stine bootstrapping approach to adjust the model fit. The model fit indices in this study achieved a reasonable fit (51, 60) after Bollen–Stine bootstrapping, as shown in Table 7.

Table 8 indicates that motivation ($\beta = 0.11^{**}$) has a significantly positive impact on WTP, supporting Hypothesis 1. Exercise involvement ($\beta = 0.20^{***}$) has a significantly positive impact on WTP, supporting Hypothesis 2. In contrast, constraints have an insignificant effect on WTP, which does not support Hypothesis 3. Meanwhile, the coefficient of exercise involvement is larger than the coefficient of motivation, indicating that exercise involvement has a more positive impact on WTP.

Discussion

The findings of this article shed light on seniors' WTP processes in order to help develop effective marketing and exercise involvement strategies that drive future economic valuation decisions. Examining the relationship between age and WTP in Table 4, the *post-hoc* Dunnett T3 test shows that WTP among people aged 75–79, 70–74, and 65–69 years is higher than among people aged 85 years and older. However, the WTP of people aged 80–84 years is insignificantly higher than that of people aged 85 years and older. Hence, CSRCs could offer exercise courses for seniors aged 65–79 years, particularly for those aged 75–79 years, who are most willing to pay more, to create a win–win situation: one for the healthier seniors and the other for the wealthier CSRC.

The first aim of this study was to identify the determinants that could drive senior adults to participate in PA in the CSRC outside of the free welfare time zone. According to the empirical results, exercise involvement and motivation could drive seniors' WTP to do so. As for the second objective, this article examined whether motivation, exercise involvement, or constraints could inspire, or

TABLE 7 Suggested goodness-of-fit statistics and acceptable cutoff criteria.

Goodness-of-fit statistic	Goodness-of-fit statistics	After Bollen–Stine bootstrapping was employed	Suggested cut-off criteria
NFI	0.82	0.99	>0.85
CFI	0.88	0.99	>0.85
RMSEA	0.09	0.03	<0.08

NFI, normal fit index; CFI, comparative fit index; RMSEA, root mean square error of approximation.

TABLE 8 The result of SEM and hypothesis.

Path	Standard estimate	S.E.	C ratio	p-value
H1: WTP <– Motivation	0.11	0.657	2.139	0.032**
H2: WTP <– Exercise_Involvement	0.20	0.406	2.686	0.007***
H3: WTP <– Constraint	–0.07	0.396	−0.915	0.360

S.E., standard error; C ratio, critical ratio; **Significant at level 0.05, ***Significant level at level 0.01.

discourage senior adults to join PA in the CSRC. The empirical results suggest that both exercise involvement and motivation could have a positive impact on seniors' WTP; meanwhile, exercise involvement has a more significant effect on WTP. As long as the seniors recognized the importance and benefits of keeping healthy, they preferred to be active in various sports and fitness activities. This result is consistent with work from previous studies (61). Important preventative exercise has been linked to improved physical health (24, 25). Once a senior has regular exercise habit, they intend to pay more in order to maintain their health.

Meanwhile, seniors like to chat with their peers. One interesting topic is exercise. Buman et al. (61) indicated that social interaction is a crucial element in driving senior consumers to exercise involvement. The CSRC is a public area where everyone can not only perform some exercise but also connect with one another. If they are already used to doing regular exercise, they would spend more time on exercise or socializing outside of the free welfare hours, and will, therefore, pay more. According to our empirical findings, seniors would prefer to link with cutting-edge technology in modern society, such as social media chatting and wearable devices, while pursuing PA in the CSRC. Hence, launching advanced technology integrated with the exercise course would be a specific marketing strategy for the CSRC.

High body mass indices, poor health, and lack of interest are usually mentioned as constraints on PA (42, 45). However, this empirical result proves that as long as senior adults can develop their regular exercises, they are willing to pay more and exercise more often.

This article has several limitations. The first is the sample size. Due to the exploratory nature of this empirical work, our sample size was small because the participants had to be at least 65 years old. A second limitation is a generalizability. This article investigated only an empirical study in the CSRC in Taipei City. Thus, it may not be possible to generalize the findings to other private gyms and other sports and fitness facilities. The third limitation is convenience sampling, which excluded seniors who would not go to the CSRCs.

Wilson et al. (62) indicated that exercise could offer benefits in combating disease and improving the quality of life. Deci and Ryan (63) proposed the self-determination theory (SDT) and indicated that exercise can fulfill people's psychological needs, including competence (effectively facing and conquering challenging goals), autonomy (having a sense of ownership), and relatedness (keeping a close social connection with others). Our empirical study validates that exercise involvement (autonomy) and motivation (competence and relatedness) have a positive effect on WTP intention. These findings are also consistent with the theoretical perspective of SDT.

In this context, one of the strongest agreements in the motivation construct is "*I* could guide others." This finding means that the seniors thought that they could pass their experiences onto similar-age or younger generations and by doing so, they help them strengthen their capacities and would obtain recognition from others (64). Hence, CSRCs in Taiwan could benchmark the practice of private gyms in other countries to recruit seniors as exercise coaches. Besides cultivating a patient, older coach, seniors would gain the peer learning effect that would provide more intention to experience exercise. The main policy implication of this study would be the promotion of regular exercise activities for seniors and the launching of exercise marketing campaigns in the community, linked to the local CSRC. Programs that promote social participation among seniors claim welfare in participants' happiness and a decrease in anxiety as well as depression levels (65, 66). The results of this study provide managers of CSRCs with the following decision-making recommendations: (1) initiate entry-level sports courses to cultivate in seniors the habit of exercise; (2) motivate seniors to participate in sports with marketing promotions in order to raise their WTP for sports consumption outside of free welfare hours; and (3) recruit seniors as exercise coaches or personal trainers to pass their experiences onto similar-age generations. In addition, the CSRCs could initiate resistance training, Tai Chi, and Eight Brocades exercise classes for seniors because these exercises have improved the pressure swing center and the stability limit for seniors (67–69).

Conclusion

Willingness to pay in people aged 75–79, 70–74, and 65–69 years is higher than in those 85 years and above. CSRCs could offer exercise courses for seniors whose age is 65–79 years, particularly for those aged 75–79 years, who have the highest mean WTP more. Taking this paid course creates a win–win situation for healthier seniors and wealthier CSRC. The empirical

results revealed that motivation and exercise involvement had a significantly positive impact on WTP intention, supporting hypotheses 1 and 2 through SEM. Future researchers could collaborate with colleagues in other countries to expand the sample size and sampling method and proceed with a cross-country study.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study is extended from the project of sports centers (MOST 105-2410-H-003-048). This project was approved by the Research Ethics Committee, National Taiwan Normal University (REC Number: 201603HS010).

Author contributions

C-YF contributed to conceptualization, literature review, methodology, software, and writing. P-YC contributed to literature review and data collection. YL contributed to writing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Effect of basal metabolic rate on osteoporosis: A Mendelian randomization study

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Purpose: Basal metabolic rate may play a key role in the pathogenesis and progression of osteoporosis. We performed Mendelian random analysis to evaluate the causal relationship between basal metabolic rate and osteoporosis.

Methods: Instrumental variables for the basal metabolic rate were selected. We used the inverse variance weighting approach as the main Mendelian random analysis method to estimate causal effects based on the summary-level data for osteoporosis from genome-wide association studies.

Results: A potential causal association was observed between basal metabolic rate and risks of osteoporosis (odds ratio = 0.9923, 95% confidence interval: 0.9898–0.9949; $P = 4.005^{e-09}$). The secondary MR also revealed that BMR was causally associated with osteoporosis (odds ratio = 0.9939, 95% confidence interval: 0.9911–0.9966; $P = 1.038^{e-05}$). The accuracy and robustness of the findings were confirmed using sensitivity tests.

Conclusion: Basal metabolic rate may play a causal role in the development of osteoporosis, although the underlying mechanisms require further investigation.

KEYWORDS

basal metabolic rate, osteoporosis, genome-wide association study, Mendelian randomization, aging

1. Introduction

Osteoporosis (OP) is a systemic disease, which is based on low bone mass and microstructural destruction of bone tissue. The disease has become increasingly common worldwide with the growth of the elderly population (1). According to the European Demographic Report, the population aged 65 years and older accounts for approximately 20% of the total population, and it is estimated that by 2050, this proportion will reach 30% (2). In 2015, there were an estimated 20 million patients with OP in the European Union and Sweden (EU6). Among them, the prevalence rates of OP among men and women aged 50 or above is 6.8 and 22.5%, respectively (3). OP can lead to many complications such as chronic pain, decreased activities of daily living, and fractures, which can greatly reduce the quality of life of patients and increase mortality and medical care costs (3, 4). Fracture-related costs for the EU6 in 2017 were estimated to total €37.5 billion (an increase of 27% from 2010), and are projected to increase to €47.4 billion in 2030 (3).

Many risk factors are associated with osteoporotic fractures, including low peak bone mass, hormonal disturbances, certain medications (e.g., glucocorticoids), smoking, low physical activity levels, low calcium and vitamin D intake, ethnicity, smaller body size, and personal or family history of fractures (5). Aging is associated with an increased rate of bone remodeling in both cancellous and cortical bone, combined with a negative remodeling balance, resulting in bone loss and disruption of bone microarchitecture (6, 7). This plays a critical role in the progression of OP. The most striking feature of aging is the reduction in metabolism and basal metabolic rate (BMR) (8). OP is considered an inevitable consequence of aging (9) and a retrospective study suggested that a decrease in BMR in women with type 2 diabetes mellitus was associated with postmenopausal OP (10). Similar to this case, a previous study revealed that BMR was strongly associated with bone density in elderly individuals (11). However, these conclusions were limited to postmenopausal women and their studies could not further to invest the causal relationship between BMR and OP. BMR can reflect the body's overall metabolism, which is very important for maintaining normal physiological function (12). During the processing of aging, the decline in function is inescapable. This process also could be happened to the bone. We notice that BMR decline and high incidence of OP in elderly is strikingly consistent. BMR may be a modifiable factor in reducing the incidence of osteoporosis.

Thus, to further identify the effect and causality between basal metabolic rate and OP, we conducted Mendelian randomization (MR) (13) to explain the relationship from a genetic perspective. MR is a new method for assessing the causal relationship between risk factors and outcomes, based on genetic variables. Unlike traditional statistical methods, it can significantly decrease potential confounding factors and provide a complex interpretation of results (14, 15).

2. Materials and methods

2.1. Study design

Assumption 1 is that there is a strong correlation between the instrumental variable and the exposure factor; Assumption 2 is that the instrumental variable was not associated with any exposure-outcome confounding factor, and Assumption 3 is that the instrumental variable does not affect the outcome unless it is possible to do so through association with exposure. In this study, BMR was used as the exposure factor, single nucleotide polymorphisms (SNPs) significantly related to BMR were used as instrumental variables (IVs), and OP was the outcome variable. Here, we conducted a bidirectional two-sample MR analysis to estimate the causal effects in both directions of BMR and OP. A stratified analysis was performed to examine the causal effect of BMR on OP risk (Figure 1).

2.2. Genetic associations with outcomes

BMR and genome-wide association study (GWAS) data of OP were obtained from GWAS databases (http://gwas-api.mrcieu.ac.uk/, accessed on September 6, 2022). Therefore, additional ethical approval was not required. The OP data were divided into primary and secondary outcome data. The outcome data were obtained from the main result data of the public GWAS dataset (GWAS ID: ukb-b-12141). The dataset was constructed by the MRC Integrated Epidemiology Unit consortium using Biobank UK and included 462,933 Europeans (7,547 cases and 455,386 controls) with 9,851,867 SNPs. The secondary outcome data were obtained from a publicly available GWAS dataset (GWAS ID: ukb-a-87). This dataset was derived from the Neale Lab Consortium's summary data from the UK Biobank (UKB) and consisted of 337,159 Europeans (5,266 cases and 331,893 controls) with 10,894,596 SNPs. The details of the included GWAS are shown in Table 1.

2.3. Selection of instrumental variables

All selected SNPs were calculated as r^2 values to evaluate linkage disequilibrium (LD). We first applied 546 SNPs associated with BMR at genome-wide significance ($P < 5e^{-8}$). For any pair of SNPs with $r^2 > 0.001$ (LD) in the range of 10,000 kb and with a minor allele frequency (MAF) > 5%, we retained those with the strongest associations on the exposure and obtained 521 independent SNPs. The potential confounders associated with the selected SNPs were analyzed using the PhenoScanner database (http://www.phenoscanner.medschl.cam.ac.uk/ accessed on September 14, 2022), and SNPs that were significantly associated with any known risk factors (age, inflammation, smoking, diabetes, renal function, vitamin D deficiency, and cancer, for example) for OP were removed. A total of 46 SNPs were excluded (Supplementary Table 1). Finally, the remaining SNPs and the related GWAS database measured the intersection point and obtained a significant correlation with the OP of the effective SNPs as instrumental variables. We conducted secondary analyzes on the data because the UKB individuals participated in both BMR and OP GWASs, which could cause weak instrumental bias due to sample overlap. We also examined possible pleiotropy of the selected SNPs using the outlier (MR-PRESSO) test, and abnormal SNPs were eliminated (16). Finally, the remaining SNPs were used for MR analysis.

We obtained the value of R^2 from the MR Steiger directionality test. where N is the number of samples from the exposure GWAS, K is the number of SNPs in IV (when calculating a single SNP, the K value is 1), and R^2 is the percentage of iron status variability explained by each SNP. R^2 was calculated using Equation 1:

$$R^2 = 2 \times EAF \times (1 - EAF) \times \beta^2$$

In addition, we used the F-statistic to evaluate whether there was a weak IV bias (F-statistic < 10 was considered a weak IV) (17). The F-statistic was calculated using Equation 2:

$$F = \frac{N - K - 1}{K} \times \frac{R^2}{1 - R^2}$$

2.4. Statistical analysis

To determine whether there is a causal relationship between the genetic risk of exposure and outcome, we used inverse-variance weighting (IVW), MR-Egger, weighted median (WM), and weighted mode techniques to account for the likelihood of pleiotropy bias. The IVW method uses a meta-analysis approach to combine

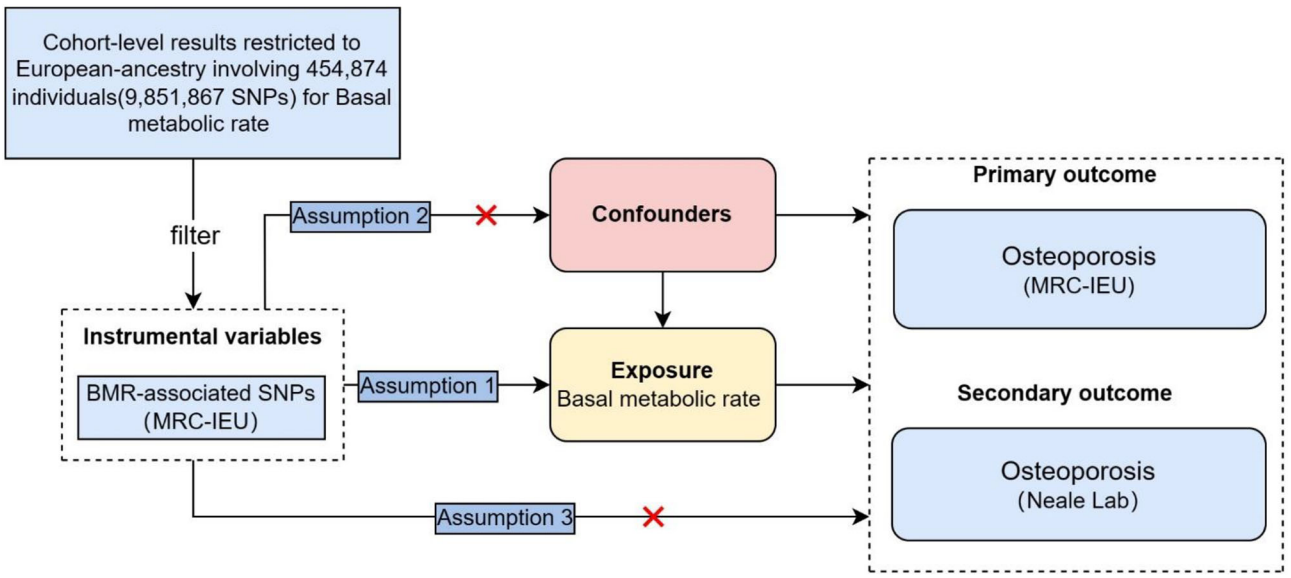

FIGURE 1
Schematic representation of the study.

TABLE 1 Summary of the GWAS included in this two-sample MR study.

Exposure/ outcomes	Dataset	Sample size	Number of SNPs	Population	Consortium	Sex	Year
BMR	ukb-b-16446	454,874	9,851,867	European	MRC-IEU	Males and females	2018
OP	ukb-b-12141	462,933	9,851,867	European	MRC-IEU	Males and females	2018
OP	ukb-a-87	337,159	10,894,596	European	Neale Lab	Males and females	2017

Wald estimates of each SNP to obtain an overall estimate of the effect of BMR on OP (18). Meanwhile, the fixed effects model or random effects model was selected according to heterogeneity (19). If significant heterogeneity ($P < 0.05$) was observed, a random-effects IVW model was applied. The MR-Egger method adds an intercept term to the IVW to express the average pleiotropy of instrumental variables, but the effective estimation of the EG method may be strongly influenced by external genetic variation, so the effective estimation is not accurate enough. The weighted-median method was supplemented to provide a robust and consistent estimate of the effect, even though nearly 50% of genetic variants were invalid instruments (20). The weighted mode method can only evaluate the causal validity according to the cluster with the largest number of SNPs, but cannot estimate the bandwidth parameter. After Bonferroni correction, the corrected P value was 0.0125 ($P = 0.05/N$, $N =$ testing method number), which was statistically significant.

2.5. Sensitivity analysis

We used a sensitivity analysis to test and correct the robustness of the MR estimation. First, MR-Egger interceptions were used to evaluate the multiplicity of the SNPs. A lower multiplicity was considered when the intercept was closer to zero. Cochran's Q test was used to assess heterogeneity. Finally, to ensure the robustness of the results, we used the leave-one-out test to judge the stability of the MR results by excluding the IVs one by one.

3. Results

3.1. Genetic variables for BMR

In the primary group, IV (rs4974072 Rssobs = 1.176^{e-06}, $P = 0.044$) was identified as an outlier in the MR-PRESSO test and was excluded from subsequent analyzes. In the secondary group, no IVs were excluded using the MR-PRESSO test. Finally, we applied 439 valid SNPs as IVs in the secondary group and obtained 462 SNPs in the secondary group (Supplementary Tables 2, 3). Individual SNPs of iron status had F-statistics of more than 10, indicating that bias from weak instruments was unlikely. The details of IV are listed in Table 2.

3.2. Primary MR analysis of BMR and OP

R^2 was 2.7527%, and the F-statistic of a single SNP ranged from 11.56 to 256.80, indicating that causal association was less likely to be affected by weak instrumental variable bias. Cochran's Q test identified heterogeneity across the included IVs (Q = 598.4290, $P = 4.9487^{e-07}$), and a multiplicative random-effects model was used in this MR analysis. A significant causal association was observed in the IVW analysis between BMR and OP (MRC-IEU) (odds

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TABLE 2 Sensitivity analysis of primary and secondary MR analyses.

Outcome	Number of IVs	R^2	F	Heterogeneity test		MR-Egger pleiotropy test		MR-PRESSO global pleiotropy test		MR-PRESSO Distortion Test
				Q	*p*-value	Intercept	*p*-value	RSSobs	*p*-value	*p*-Value
Primary outcome	439	2.7527%	27.7101	598.4290	4.9487; e-07	−7.8420; e-05	0.0929	618.5921	<5e-05	0.87425
Secondary outcome	462	2.8955%	29.3289	574.6058	2.3845; e-3	−5.7447; e-05	0.2339	577.3748	7e-04	*NA*

ratio [OR] = 0.9923, 95% confidence interval [95% CI]: 0.9898–0.9949; $P = 4.005^{e-09}$), and was replicated using WME (OR = 0.9926, 95% CI: 0.9888–0.9964; $P = 1.176^{e-04}$), MR Egger (OR = 0.9980, 95% CI: 0.9909–1.0051; $P = 5.740^{e-01}$), and weighted mode (OR = 1.0020, 95% CI: 0.9904–1.0136; $P = 7.393^{e-01}$). The robustness of the results was confirmed using a leave-one-out sensitivity test. No directional pleiotropy was found in the MR-Egger regression (intercept = -7.8420^{e-05}, se = 4.6563^{e-}05, $P = 0.0929$).

3.3. Secondary MR analysis of BMR and OP

R^2 was 2.8955%, and the F-statistic of a single SNP ranged from 11.56 to 257.10, indicating that causal association was less likely to be affected by weak instrumental variable bias. Cochran's Q test identified heterogeneity across the included IVs (Q = 574.6058, $P = 2.3845^{e-4}$), and a multiplicative random-effects model was used in this MR analysis. The IVW analysis reported a significant causal relationship between BMR and OP (OR = 0.9939, 95% CI: 0.9911–0.9966; $P = 1.038^{e-05}$), which was consistent with the findings of the WME (OR = 0.9932, 95% CI: 0.9893–0.9972; $P = 7.765^{e-04}$), MR-Egger analysis (OR = 0.9979, 95% CI: 0.9907–1.0051; $P = 5.620^{e-01}$), and weighted mode (OR = 0.9946, 95% CI: 0.9843–1.0049; $P = 3.046^{e-01}$). The robustness of the results was confirmed using a leave-one-out sensitivity test. No directional pleiotropy was found in the MR-Egger regression (intercept = -5.7447^{e-05}, se = 4.8194^{e-05}, $P = 0.2339$).

The scatter and forest plots of the causal relationships between BMR and the risk of OP are shown in Figure 2 and Supplementary Figures 1, 2. The funnel plot (Figure 3) shows that when a single SNP is used as an IV, the points representing causal effects are symmetrically distributed, which indicates that causal effects are less likely to be affected by potential bias. In the leave-one-out analysis (Supplementary Figures 3, 4), the removal of each SNP in turn has little effect on the results, indicating that there is no single SNP which has a significant influence on the overall causal effect estimation. The details of the sensitivity analysis are presented in Table 2. Detailed causal effect estimates for the associations between exposure and outcomes in different models are illustrated in Figure 4.

4. Discussion

Few studies have reported a relationship between BMR and OP. In our study, we used two-sample MR analysis to assess the causal association between BMR and OP. We found a significant causal association between the genetic risk of BMR and OP, showing an average of 0.8% decreased risk of OP per 1-SD increment in BMR and this conclusion was also applicable to the secondary group (OR = 0.9939, 95% CI: 0.9911–0.9966).

Osteoporosis is an enormous and growing public health problem. As a common disease in the elderly, especially postmenopausal women (21) OP is considered to be an important factor for fractures and strategies to prevent OP could decrease half of all hip fractures (22). Interestingly, an observational study of osteoporosis in postmenopausal women showed that BMR was related to BMD independent of age and patients with OP had

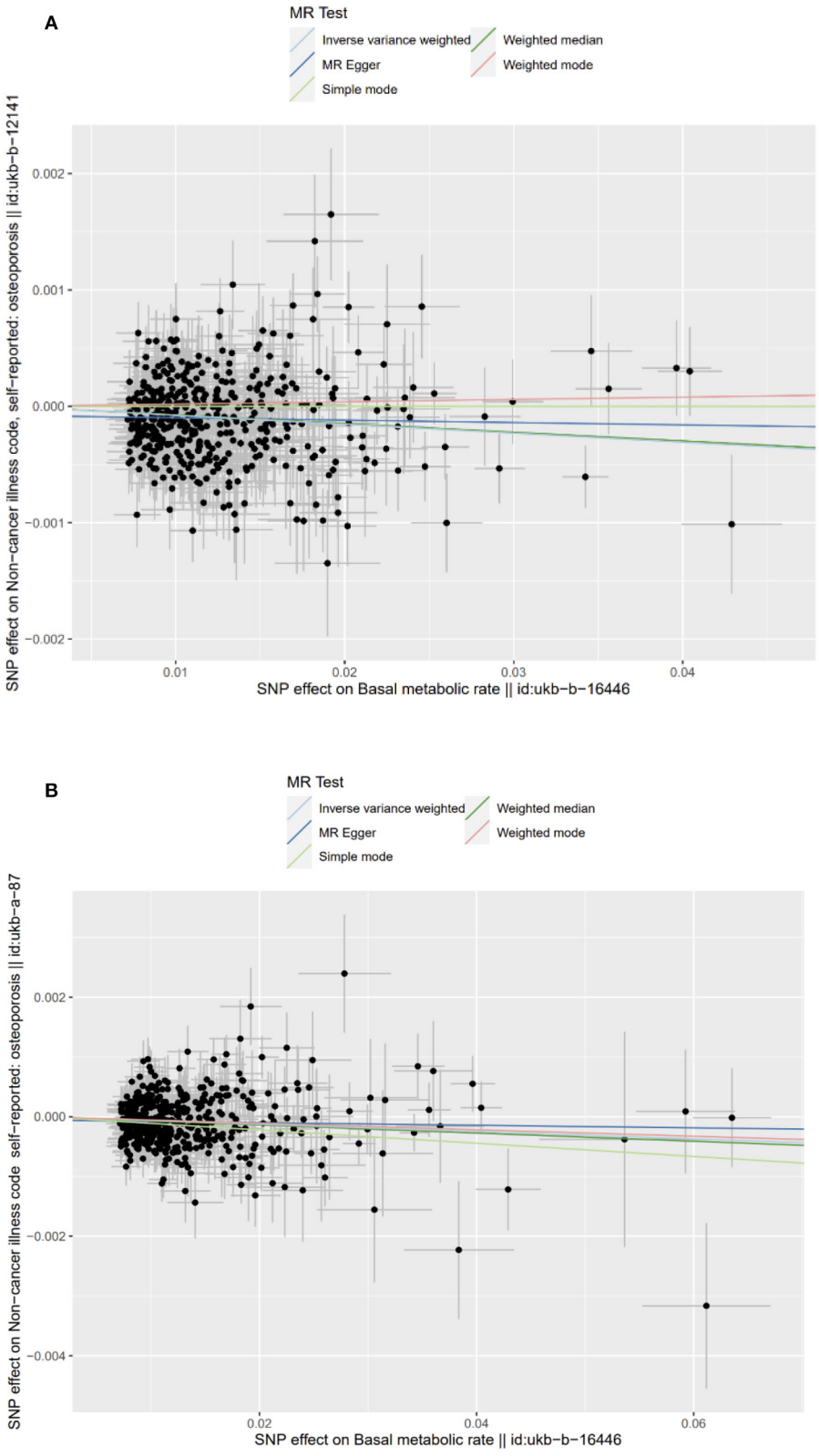

FIGURE 2
Scatter plots of causality. The slope of each line corresponding to the estimated MR effect in different models. **(A)** Primary outcome (ukb-b-12141); **(B)** Secondary outcome (ukb-a-87).

a significantly lower BMR compared to those non-OP. Similarly, in the process of human aging, there is an inevitable decline in BMR, and this alteration is strikingly similar to the high incidence of osteoporosis in the elderly. We calculate that there is a causal relationship between BMR and OP and that the increase in BMR can reduce the incidence of osteoporosis. Thus,

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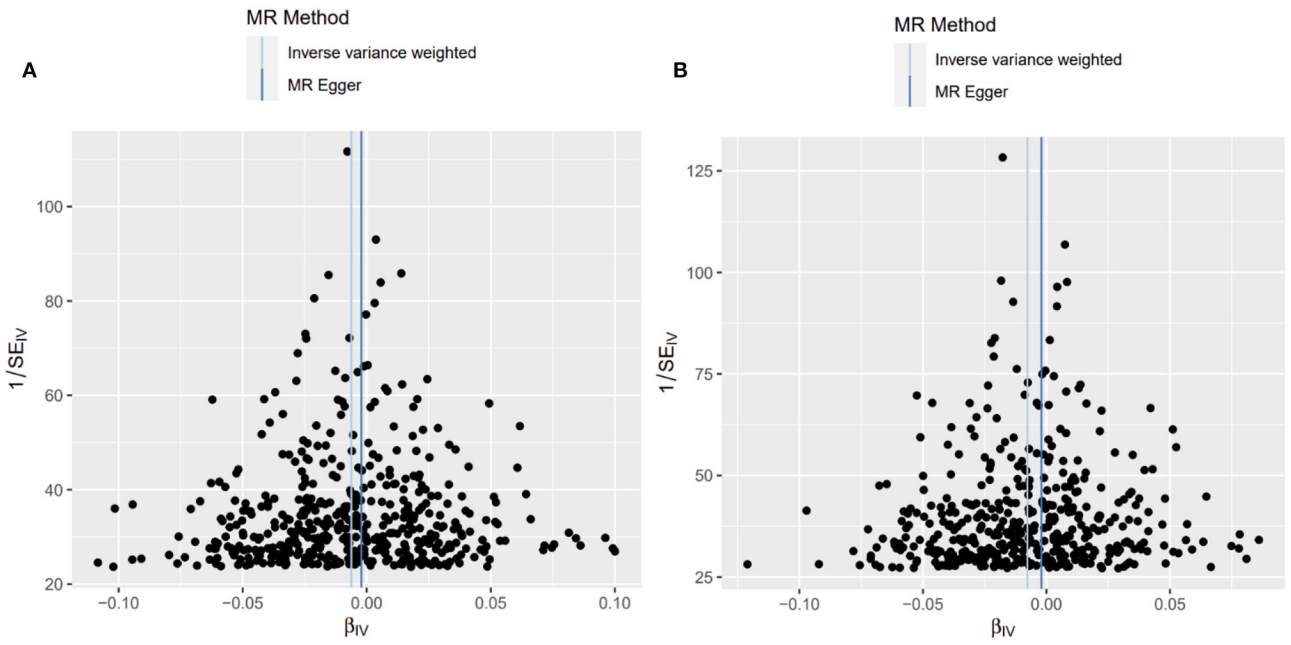

FIGURE 3
Funnel plot of causality. **(A)** Primary outcome (ukb-b-12141); **(B)** Secondary outcome (ukb-a-87).

Exposure	Outcomes	Number of IVs	Method	Forest polts	OR	OR(95% CI)	*P* value
BMR	Osteoporosis (MRC-IEU)	439	Weighted mode		1.0020	(0.9904, 1.0136)	7.393e-01
			Weighted median		0.9926	(0.9888, 0.9964)	1.176e-04
			MR Egger		0.9980	(0.9909, 1.0051)	5.740e-01
			IVW		0.9923	(0.9898, 0.9949)	4.005e-09
	Osteoporosis (Neale Lab)	462	Weighted mode		0.9946	(0.9843, 1.0049)	3.046e-01
			Weighted median		0.9932	(0.9893, 0.9972)	7.765e-04
			MR Egger		0.9979	(0.9907, 1.0051)	5.620e-01
			IVW		0.9939	(0.9911, 0.9966)	1.038e-05

FIGURE 4
Causal estimates given as odds ratios (ORs) and 95% confidence intervals for the effect of basal metabolic rate on osteoporosis by different consortium.

we conducted a two-sample Mendelian randomized study, and our study provided evidence supporting a potential causal relationship between low BMR levels and an increased risk of osteoporosis. MR-Egger's causal estimate and weighted median analysis are consistent with IVW analysis, indicating that the causal effect is reliable. Our study confirmed that an increased BMR could promote the reduction of OP from a genetic perspective and provide a positive causality of BMR in reducing OP and this conclusion is not limited to postmenopausal women. This provides a new insight for preventing and treating OP at a reversible stage, which may significantly reduce the risk of fracture and related burdens in patients.

Over the past decades, research on BMR has mainly focused on obesity and metabolic-related diseases (23), and it has been well applied in the treatment of diabetes. BMR plays a key role in maintaining normal structure and function, and an imbalance in metabolic demands and BMR may be closely related to clinical diseases. The decrease in physical activity with the onset of the aging process masks the lifestyle of the entire elderly population, resulting in a substantial increase in sedentary time (24, 25). Maybe it is an important reason for the decline in BMR in the elderly and leads to an increased OP. Guidelines (26, 27) endorse lifelong physical activity (both weight-bearing exercise and muscle-strengthening exercise) for osteoporosis prevention. This may be achieved by improving BMR. Although frequency and intensity of activity are not specified in guidelines, a common clinical practice is to recommend both 30 min of walking per day and gentle resistance exercises (4). And we also noticed that counter-resistance exercises are effective in maintaining bone mineral mass and bone mineral density since mechanical stimulation promotes the formation of new bone tissue (28). But high-intensity physical activity is limited to the elderly.

Once humans enter the aging stage, subsequently a decrease in total energy consumption and energy availability follows (29, 30). More importantly, energy metabolism is highly correlated with body composition. Once energy metabolism changes, functional changes will inevitably be affected. According to our results, we speculate that the decrease of BMR may affect bone metabolism and lead to the occurrence of osteoporosis, but how to realize this process needs more basic and clinical research to further clarify.

Drugs used to treat OP, such as antiresorptive drugs, inhibit the recruitment and activity of osteoclasts, thereby rebalancing bone resorption and synthesis (31). In patients with OP, the normal balance is compromised, leading to an abundance of missing reconstructed osteons and a decrease in bone quality. At present, the recommended first-line drugs for treating osteoporosis include bisphosphonate and teriparatide, which have been confirmed effective in clinical practice, but there are the following concerns. Teriparatide can improve osteoporosis by increasing bone density, but it needs to be taken for a long time. Once stopped, the curative effect drops rapidly and even accelerates bone loss. Bisphosphate is one of the most common drugs for OP in clinical practice. Bisphosphonate treatment is associated with 40–70% reductions in vertebral fractures and 40–50% reductions in hip fractures. However, it is limited in patients with severe renal damage. bisphosphonate may also lead to gastrointestinal irritation and musculoskeletal abnormalities. Supplementation of bone anabolic elements (such as calcium and vitamin D), may help to ameliorate this, but the benefit of supplementation is only observed in individuals with low intake and impaired absorption (7). These routine measures can slow OP in the elderly, but they do not restore BMD and are not adequate treatments for patients with an elevated risk of fracture. Our study further confirmed the causal relationship between BMR and OP in terms of genetic risk, enhancing the importance of BMR in bone development, bone metabolism, and related bone diseases and provides new targets for the treatment and research of OP in the future.

5. Conclusion

In conclusion, our results suggest that higher BMR may reduce the risk of OP. Interventions with modifiable goals to improve BMR may help reduce the burden of this chronic disease.

6. Limitation

This study has several limitations. First, the OP cases in this study were from self-reported osteoporosis patients in the UKB. Self-reported disease status may miss cases of OP and mistakenly include other bone diseases. Second, our results apply only to European lineages, and the effect of BMR on OP in other lineages has not yet been studied. Second, it is the only publicly available GWAS on OP. We did not report on the subtypes of OP. These include postmenopausal OP, senile OP, and drug-induced OP. Third, it is impossible to further classify OP and conduct a stratified MR analysis based on the subtypes of OP. This would be helpful in drawing more accurate causal inferences, with more control over potential confounders. In addition, since limited to the database, we failed to assess the health status of the sample population, which may lead to potential confounding bias. Finally, in this study, BMR genes were selected as instrumental variables to calculate the causal relationship between BMR and OP. No study has explored the mechanism underlying the relationship between BMR and OP. Assessing the role of BMR in OP from a genetic perspective may only partially explain the role of BMR in OP.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study. Written informed consent was not obtained from the individual(s), nor the minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

Author contributions

JZ and ZY finished the original manuscript. LX and QP designed the study and supervised the study. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1096519/full#supplementary-material

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Effects of a cognitive-based intervention program using social robot PIO on cognitive function, depression, loneliness, and quality of life of older adults living alone

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Objective: Social robot interventions are being implemented to reduce cognitive decline, depression, and loneliness among older adults. However, the types, functions, and programs of effective social robots have not yet been confirmed. This study investigated whether a social robot intervention is effective in improving cognitive function, depression, loneliness, and quality of life in older adults living alone.

Methods: This study used a non-equivalent control group pre-test–post-test design. It was conducted twice a week, with each session lasting 50 mi; twelve sessions were conducted over 6 weeks. This study was conducted at three senior welfare centers in Korea. In each group, 10 or fewer participants used the PIO social robot. The total participants included 64 people in the experimental ($n = 31$) and control groups ($n = 33$), and consisted of older people over 65 years of age living alone.

Results: There was a statistically significant difference in the pre-post values for cognitive function ($z = 5.21$, $p < 0.001$), depression ($z = -2.99$, $p = 0.003$), and loneliness ($t = -4.27$, $p < 0.001$) in the experimental and control groups. However, there was no statistically significant difference for quality of life ($z = 1.84$, $p = 0.066$).

Conclusions: It was confirmed that a cognitive intervention program using the social robot PIO can improve cognitive function and reduce depression and loneliness in older adults living alone.

KEYWORDS

social robot, cognitive function, depression, loneliness, quality of life, older adults

1. Introduction

The global population aged over 65 years is expected to increase from 9.3% in 2020 to approximately 16% in 2050 (1). The population of those aged 65 years and above in Korea was 15.7% in 2020; this population of older adults belongs to an aging society, among which the proportion of those living alone is 19.6% (2). Older adults who live alone experience deterioration in their health owing to aging, economic poverty, dependence due to reduced income, loneliness due to social and psychological conflicts, severance of human relationships, and helplessness due to loss of social roles (3). In addition, older people living alone are more vulnerable compared to those living together concerning physical health, mental health, and quality of life (QoL) due to a lack of social cohesion through family relationships (4), social isolation, and reduced social support (5).

The decline in cognitive function due to aging reduces an individual's ability to adapt and causes emotional problems such as depression and anxiety, making it difficult to form interpersonal relationships that lead to poor QoL (6). Depression affects QoL in the older adults (7, 8), and living alone is a contributing factor to depression (5). Loneliness not only

causes suffering in older adults by itself, but also indicates mental disorders such as depression, dementia, suicide, and physical diseases such as hypertension, heart disease, and diabetes (9, 10). Various non-pharmacological interventions are being tried in various ways to prevent cognitive decline and increase cognitive function in the older people. A cognition-based intervention is a comprehensive and complex approach aimed at improving cognitive function, cognitive stimulation, cognitive training, and cognitive rehabilitation (11). Computer-assisted cognitive rehabilitation (CACR) research has been increasing recently. In CACR, the group that received cognitive training using only a computer program saw a significant effect on cognitive function and memory but no effect on emotions or emotional variables (12). Various intervention studies using social robots are being attempted worldwide to alleviate the burden of care for older people amid changes in the family structure. The PARO robot is an emotional support robot that responds to touch, light, sound, and temperature through bodily sensors (13). A meta-analysis of the PARO robot showed that the effects were inconsistent on variables, such as cognitive function, problematic behavior, depression, and loneliness (14, 15). As a result of a cognitive intervention using Sil-Bot, the social robot, thinning of the anterior cingulate cortex was reduced, and age-related structural brain changes could be alleviated (16). Social robot programs for older people are mostly applied by substituting animal-assisted therapy (AAT) programs (17) with them or by placing social robots in centers and through facilitating interaction with them. As per past research, traditional cognitive training, such as stimulating the senses, was performed (18–20), and the study variables were mainly emotional. However, it was difficult to find studies that applied a CACR program to social robots to improve participants' cognitive functions and confirm emotional variables through interactions between social robots and participants.

Therefore, this study aimed to improve the cognitive function of older adults living alone by using the social robot PIO, to which the CACR program was applied. In addition, this study aimed to confirm the effect of reducing depression and loneliness and improving QoL through the interaction of the social robot PIO.

2. Methods

2.1. Study design

This was a non-equivalent control group pre-test–post-test design.

2.2. Participants

Participants were recruited from November 22, 2021 to January 5, 2022, at three senior welfare centers in Seoul, Korea. Forty-one people in the experimental group and 39 in the control group expressed their intentions to participate. Among them, five from the experimental group and three from the control group were excluded because they did not meet the selection criteria; 36 individuals each from the experimental and control groups finally participated in the study. During the study, three of 36 experimental group subjects dropped out due to health problems, two in the program refused to participate, and three out of 36 in the control group did not participate in the investigation due to COVID-19 infections. All participants adhered to the program schedule and attended all the sessions. There were no dropouts during the course of the intervention. The recruitment criteria for participants were as follows: (1) 65 years of age or older, (2) older adults living alone, (3) able to communicate in Korean, and (4) no history of severe mental illness, such as schizophrenia or delusional disorder. Exclusion criteria were: (1) older adults who were in the new cognitive intervention program at the time of the study, (2) history of psychiatric drug use within the last 4 weeks, and (3) having difficulty using their hands. Participants who wished to take part in the program were assigned to the experimental group first, and the control group was selected using convenience sampling by matching participants with those in the experimental group in terms of age, gender, education, and basic livelihood security recipient status. The final data were collected from 64 participants, who were divided into the experimental ($n = 31$) and control groups ($n = 33$). The sample size was calculated using G*power (3.1.9.6), with a significance level of 0.05, a large effect size (0.80), and a power of 0.85. According to the preliminary analysis, at least 30 people were required for each group, and an additional 20% were recruited considering the dropout rate.

2.3. Intervention

The intervention in this study was conducted from January 10 to March 2, 2022. During the study period, participants continued to participate in usual care (music, art programs, etc.) that they had previously enrolled in at the senior welfare center, and did not stop or participate in other programs. The experimental group participated in this study's program, and the control group did not. This program was conducted twice a week, 50 min per session, for 6 weeks. Each group of 10 or fewer participants underwent PIO. For smooth progress, two research assistants were used. The program, which consisted of 12 sessions, was structured by a storytelling of the process behind the parrot-shaped robot PIO hatching from an egg and growing into an adult robot. Each session started with the themes of "meeting with the social robot PIO" and "recalling the previous program." In addition, gymnastics was performed with the social robot PIO to relieve tension and improve intimacy with the robot. Before the 6th session, "Teaching movements and gymnastics," gymnastics was performed while watching a video, and after the 6th session, gymnastics was performed while watching the movements of the social robot PIO. The program lasted about 30 min according to the contents of each session. The ending involved "Expressing your impression about the program" and "Saying goodbye to social robot PIO" (Table 1). Participants were configured to naturally stimulate cognition and emotion in the process of PIO programs (Figure 1).

2.4. Social robot PIO

The social robot PIO is a parrot-shaped robot developed by Why Dots for cognitive-emotional programs with older people and older adults with dementia. The social robot PIO expresses various emotions through the eyes of an LCD display, and it is possible to implement structured conversations and various movements according to the program composition when performing a program with subjects. The size of the social robot was 200 ×170 ×325 mm, and its weight was approximately 2 kg (Figure 2).

TABLE 1 Contents of PIO program.

	Contents	Activities	Therapeutic factors
1	Hatching an egg	Program introduction	Emotion
		Stretching exercise	Cognition, exercise
		Shake eggs to hatch	Cognition, exercise
2	Making up baby PIO	Stretching exercise	Cognition, exercise
		Making up baby Social Robot	Cognition, art, emotion
		Nest decoration for baby Social Robot	Cognition, art, emotion
3	Feeding and putting baby PIO to sleep	Stretching exercise	Cognition, exercise
		Feeding milk with formula	Cognition, emotion
		Put a crying baby Social Robot to sleep	Cognition, emotion
4	Making clothes for PIO	Stretching exercise	Cognition, exercise
		Make clothes	Cognition, art, emotion
5	Teaching baby PIO to speak	Stretching exercises	Cognition, exercise
		Words for the situations	Cognition, emotion
		Searching words	Cognition, emotion
6	Teaching movements and gymnastics	Stretching exercises	Cognition, exercise
		Teach movements	Cognition, exercise
		Doing gymnastics with Social Robot	Cognition, exercise
7	Catching caterpillars	Doing gymnastics with Social Robot	Cognition, exercise
		Catching caterpillars	Cognition, exercise
8	Catching giant caterpillars	Doing gymnastics with Social Robot	Cognition, exercise
		Catching a moving giant caterpillar	Cognition, emotion
9	Teaching colors	Doing gymnastics with Social Robot	Cognition, exercise
		Teaching color words	Cognition, emotion
		Coloring caterpillars	Cognition
		Catching caterpillars	Cognition
10	Shopping with PIO	Doing gymnastics with Social Robot	Cognition, exercise
		Shopping at the supermarket	Cognition
		Order the scenes	Cognition
		Remember locations	Cognition
11	Shopping with PIO	Doing gymnastics with Social Robot	Cognition, exercise
		Clapping with Social Robot	Cognition, music
		Drawing portrait	Cognition, art, emotion
12	Farewell	Doing gymnastics with Social Robot	Cognition, exercise
		Recall the entire programs	Cognition, emotion
		Sharing your feelings	Emotion

FIGURE 1
Participants conducting PIO program.

2.5. Instruments

2.5.1. K-MMSE∼2:SV

The Korean-Mini Mental State Examination, 2nd Edition (K-MMSE∼ 2): SV (Standard Version) by Kang et al. (21), which translated the 2010 revised Mini-Mental State Examination (MMSE) developed by Folstein et al. (22) into Korean, was used. The K-MMSE∼2:SV comprises seven subscales in the following order: registration, orientation to time, orientation to place, recall, attention and calculation, language, and drawing. At the time of instrument development, Cronbach's α was 0.69 (21). In this study, Cronbach's α was 0.73.

2.5.2. Depression

The Geriatric Depression Scale Short Form: Korean Version (GDSSF-K), a tool developed by Sheikh and Yesavage (23),

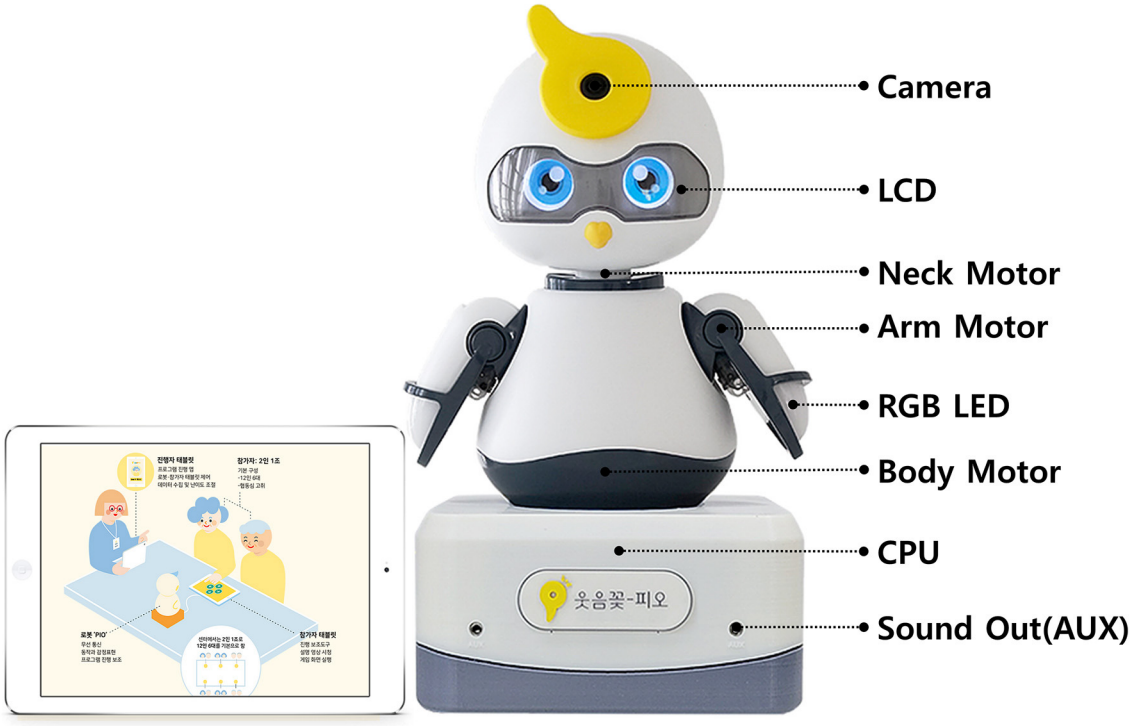

FIGURE 2
Social robot PIO (Version 2.0).

which was translated and modified by Kee (24), was used to measure depression. The GDSSF-K consists of 15 items and "yes" or "no" answers to each question. The higher the score, the greater the depression. At the time of development, the Cronbach's α was 0.88. In this study, the Cronbach's α was 0.79.

2.5.3. Loneliness

The Revised UCLA Loneliness Scale (RULS), developed by Russel et al. (25), was used to measure loneliness; the scale was translated into Korean by Kim (26). It consists of 20 items on a four-point Likert scale, and the higher the score, the greater the degree of loneliness. At the time of tool development, Cronbach's α was 0.93. In this study, Cronbach's α was 0.87.

2.5.4. QoL

QoL was measured using the EQ-5D-3L (Euro Quality of life-5Dimension-3Level) tool developed by the EuroQol group. The EQ-5D-3L consists of five domains: mobility, self-care, usual activities, pain/discomfort, anxiety/depression. In this study, the QoL tariff by Lee et al. (27) was used for calculation. In the sub-domain, the raw score was reverse-coded, with a higher score indicating a higher QoL. At the time of instrument development, Cronbach's α was 0.64 (28). In this study, the Cronbach's α was 0.61.

2.6. Statistical analysis

The data collected were analyzed using STATA 17. Descriptive statistics were used to demonstrate the demographic characteristics. The homogeneity between groups was analyzed using the *t*-test, $\chi 2$ test, and Fisher's exact test. Tests of major variables to confirm the effectiveness of the program were analyzed with an independent *t*-test for normal distribution and Mann-Whitney U test for alternative distribution. The level of significance was set at $P < 0.05$.

3. Results

3.1. General characteristics

Demographic characteristics and health information of the participants are summarized in Table 2. In the experimental group, there were 29 (93.5%) females and 2 (6.5%) males; the control group comprised 28 (84.8%) females and 5 (15.2%) males. Concerning age, 11 (35.5%) were 70–74 years old in the experimental group; 11 (33.3%) were 75–79 years old in the control group. Regarding level of education, the majority of elementary school graduates were 9 (29.0%) in the experimental group and 17 (51.5%) in the control group. Regarding marital status, bereavement was common in 18 (58.1%) and 24 (72.7 %) patients in the experimental and control groups, respectively. Regarding the presence or absence of children, there were 29 (93.5%) in the experimental group and 28 (84.8%) in the control group. Regarding the presence or absence of companion animals, 28 (90.3%) participants in the experimental group and 31 (93.9%) in the control group did not

TABLE 2 Homogeneity test of general characteristics ($N = 64$).

Characteristics	Categories	Exp. ($n = 31$)	Con. ($n = 33$)	χ^2	p
		n (%)	n (%)		
Gender	Male	2 (6.5)	5 (15.2)	1.24†	0.428
	Female	29 (93.5)	28 (84.8)		
Age	65~69	5 (16.1)	1 (3.0)	6.17†	0.206
	70~74	11 (35.5)	7 (21.2)		
	75~79	6 (19.4)	11 (33.3)		
	80~84	7 (22.6)	10 (30.3)		
	85~89	2 (6.5)	4 (12.1)		
Education level	No education	4 (12.9)	4 (12.1)	8.54†	0.074
	Elementary	9 (29.0)	17 (51.5)		
	Middle	7 (22.6)	4 (12.1)		
	High	4 (12.9)	7 (21.2)		
	College	7 (22.6)	1 (3.0)		
Married	Single	0 (0.0)	1 (3.0)	3.08†	0.358
	Separation	9 (29.0)	5 (15.2)		
	Divorce	4 (12.9)	3 (9.1)		
	Bereavement	18 (58.1)	24 (72.7)		
Children	Yes	29 (93.5)	28 (84.8)	1.24†	0.428
	No	2 (6.5)	5 (15.2)		
Pet	Yes	3 (9.7)	2 (6.1)	0.29†	0.667
	No	28 (90.3)	31 (93.9)		
Religion	Buddhism	14 (45.2)	7 (21.2)	4.65	0.199
	Christian	6 (19.4)	12 (36.4)		
	Catholic	5 (16.1)	6 (18.2)		
	None	6 (19.4)	8 (24.2)		
Number of chronic diseases	0	1 (3.2)	1 (3.0)	3.29†	0.14
	1	20 (64.5)	14 (42.4)		
	≥2	10 (32.3)	18 (54.6)		
Physical disability	Yes	6 (19.4)	7 (21.2)	0.03	0.854
	No	25 (80.6)	26 (78.8)		
Basic livelihood security recipient	None	24 (77.4)	23 (69.7)	0.65†	0.821
	Recipient	5 (16.1)	8 (24.2)		
	The secondary lower income family	2 (6.5)	2 (6.1)		

Con., Control group; Exp., Experimental group; †Fisher's exact test.

have companion animals. Regarding religion, Buddhism was the most common, with 14 (45.2%) participants in the experimental group, and Christianity was the most common, with 12 (36.4%) in the control group. Regarding religion, Buddhism was the most common, with 14 (45.2%) participants in the experimental group, and Christianity was the most common, with 12 (36.4%) in the control group. There were 10 (32.3%) and 18 (54.6%) patients in the experimental and control groups, respectively. Twenty-five (80.6%) patients in the experimental group and 26 (78.8%) in the control group had no physical disabilities. Twenty-four (77.4%) patients in the experimental group and 23 (69.7%) in the control group did not have a basic livelihood.

3.2. Effects of PIO interventions on cognition function

For the cognition function variable, the difference between the pre-post scores of the experimental and control groups were statistically significant ($z = 5.21$, $p = 0.001$). The experimental group

TABLE 3 Comparison of cognition function ($N = 64$).

Variables	Group	Pre		Post		Post-Pre		z	p
Cognition function		M ± SD	Median (IQR)	M ± SD	Median (IQR)	M ± SD	Median (IQR)		
Total	Exp. ($n = 31$)	25.87 ± 3.37	27 (5)	28.87 ± 1.52	29 (2)	3.00 ± 2.73	2 (3)	5.21	<0.001
	Con. ($n = 33$)	25.91 ± 3.21	26 (5)	25.30 ± 3.36	26 (6)	−0.61 ± 1.78	−1 (3)		
Registration	Exp.	2.97 ± 0.18	3 (0)	3.00 ± 0.00	3 (0)	0.03 ± 0.18	0 (0)	−0.53	0.595
	Con.	2.85 ± 0.44	3 (0)	2.91 ± 0.38	3 (0)	0.06 ± 0.24	0 (0)		
Orientation to Time	Exp.	4.74 ± 0.63	5 (0)	5.00 ± 0.00	5 (0)	0.26 ± 0.63	0 (0)	1.7	0.089
	Con.	4.64 ± 0.60	5 (1)	4.52 ± 0.87	5 (1)	−0.12 ± 0.74	0 (0)		
Orientation to place	Exp.	4.42 ± 0.81	5 (1)	5.00 ± 0.00	5 (0)	0.58 ± 0.81	0 (1)	3.41	<0.001
	Con.	4.88 ± 0.33	5 (0)	4.94 ± 0.24	5 (0)	0.06 ± 0.24	0 (0)		
Recall	Exp.	1.90 ± 1.01	2 (2)	2.48 ± 0.81	3 (1)	0.58 ± 1.06	0 (1)	1.66	0.097
	Con.	2.06 ± 0.97	2 (2)	2.18 ± 0.95	2 (1)	0.12 ± 0.89	0 (1)		
Attention and calculation	Exp.	3.71 ± 1.55	4 (2)	4.58 ± 0.85	5 (1)	0.87 ± 1.52	0 (2)	3.71	<0.001
	Con.	3.42 ± 1.68	2 (3)	2.67 ± 1.69	2 (3)	−0.76 ± 1.42	0 (1)		
Language	Exp.	7.35 ± 0.84	8 (1)	7.97 ± 0.18	8 (0)	0.61 ± 0.80	0 (1)	2.62	0.009
	Con.	7.27 ± 0.76	7 (1)	7.33 ± 0.85	8 (1)	0.06 ± 0.66	0 (0)		
Drawing	Exp.	0.77 ± 0.43	1 (0)	0.84 ± 0.37	1 (0)	0.06 ± 0.51	0 (0)	0.2	0.357
	Con.	0.79 ± 0.42	1 (0)	0.76 ± 0.44	1 (0)	−0.03 ± 0.31	0 (0)		

Con., Control group; Exp., Experimental group.

increased by 3.00 ± 2.73, and the median (IQR) increased to 2 (3), the control group decreased by −0.61 ± 1.78, and the median value (IQR) decreased to −1 (3). On the subscale, location orientation ($z = 3.41$, $p < 0.001$), attention and counting ($z = 3.71$, $p < 0.001$), and language ($z = 2.62$, $p = 0.009$) increased significantly, but registration ($z = -0.53$, $p = 0.595$), temporal orientation ($z = 1.70$, $p = 0.089$), memory recall ($z = 1.66$, $p = 0.097$), and drawing ($z = 0.92$, $p = 0.357$) did not show statistically significant differences (Table 3).

3.3. Effects of PIO interventions on depression, loneliness, and QoL

For the depressive variable, the difference between the pre-post scores of the experimental and control groups were statistically significant ($z = -2.99$, $p = 0.003$). The experimental group decreased by −2.42 ± 3.36, and the median (IQR) decreased to −2 (3), the control group increased by 0.03 ± 2.82, and the median (IQR) was 0 (3). For the loneliness variable, the difference between the pre-post scores of the experimental and control groups was statistically significant ($t = -4.27$, $p < 0.001$). The experimental group decreased by −11.26 ± 9.34, and the median (IQR) decreased to −12 (14), the control group decreased by −0.55 ± 10.64, and the median (IQR) was 1 (16). Regarding QoL variables, the difference between the pre-post scores of the experimental and control groups was not statistically significant ($z = 1.84$, $p = 0.066$). The experimental group increased by 0.07 ± 0.12, and the median (IQR) increased to 0.09 (0.14); the control group increased by 0.03 ± 0.10, and the median (IQR) was 0 (0.96). On the subscale, mobility ($z = 3.21$, $p < 0.001$) increased significantly, but self-care ($z = 1.03$, $p = 0.302$), usual activities ($z = 1.02$, $p = 0.310$), and anxiety/depression ($z = 1.85$, $p = 0.064$) did not show any statistically significant difference. Pain/discomfort ($z = -0.63$, $p = 0.530$) decreased, but the difference was not statistically significant (see Table 4).

4. Discussion

The results showed that the cognitive function scores improved, depression and loneliness scores decreased, and the difference between groups in the pre-post change was statistically significant. In contrast, the QoL score improved, but the between-group difference was not statistically significant.

In this study, the cognitive function score of the experimental group increased compared to that before the intervention, while that of the control group decreased. Regarding the MMSE tool, a decrease of 1–3 points can be judged as a clinically meaningful result (29). Therefore, it can be concluded that the program using the PIO robot improved the cognitive function of older adults living alone. There have been few studies on cognitive intervention programs using social robots for older people, and most of them have shown an improvement in cognitive function scores, but without any statistically significant difference (16, 30–33). In particular, the Sil-Bot robot was not able to derive statistically significant results from cognitive function variables even though it was composed of a program including the elements of CACR; however, this program was distinct as it derived statistically significant results. In a study that evaluated cognitive function using the harp-seal PARO robot for older people with dementia, the cognitive function score decreased after the intervention (18, 20, 34). This seems to be because the robot intervention consisting of an AAT program is

TABLE 4 Comparison of depression, loneliness and QoL ($N = 64$).

Variables	Group	Pre		Post		Post-Pre		$t^{\dagger}$ or z	p
		M ± SD	Median (IQR)	M ± SD	Median (IQR)	M ± SD	Median (IQR)		
Depression	Exp. ($n = 31$)	20.35 ± 3.45	20 (7)	17.94 ± 3.40	17 (5)	−2.42 ± 3.36	−2 (3)	−2.99	0.003
	Con. ($n = 33$)	21.30 ± 3.63	21 (5)	21.33 ± 3.80	22 (5)	0.03 ± 2.82	0 (3)		
Loneliness[†]	Exp. ($n = 31$)	42.45 ± 11.69	42 (18)	31.19 ± 11.05	28 (20)	−11.26 ± 9.34	−12 (14)	−4.27	<0.001
	Con. ($n = 33$)	42.03 ± 10.26	43 (16)	41.48 ± 10.65	42 (12)	−0.55 ± 10.64	1 (16)		
QoL	Exp. ($n = 31$)	0.82 ± 0.13	0.82 (0.15)	0.89 ± 0.12	0.91 (0.13)	0.07 ± 0.12	0.09 (0.14)	1.84	0.066
	Con. ($n = 33$)	0.78 ± 0.15	0.77 (0.25)	0.81 ± 0.11	0.77 (0.13)	0.03 ± 0.10	0 (0.96)		
Mobility	Exp.	2.48 ± 0.51	2 (1)	2.84 ± 0.37	3 (0)	0.35 ± 0.49	0 (1)	3.21	<0.001
	Con.	2.52 ± 0.51	3 (1)	2.48 ± 0.51	2 (1)	−0.03 ± 0.39	0 (0)		
Self–Care	Exp.	2.87 ± 0.43	3 (0)	2.94 ± 0.25	3 (0)	0.06 ± 0.36	0 (0)	1.03	0.302
	Con.	2.91 ± 0.29	3 (0)	2.91 ± 0.29	3 (0)	0.00 ± 0.00	0 (0)		
Usual activities	Exp.	2.81 ± 0.40	3 (0)	3.00 ± 0.00	3 (0)	0.19 ± 0.40	0 (0)	1.02	0.31
	Con.	2.61 ± 0.50	3 (1)	2.70 ± 0.47	3 (1)	0.09 ± 0.38	0 (0)		
Pain/discomfort	Exp.	2.16 ± 0.58	2 (1)	2.29 ± 0.59	2 (1)	0.13 ± 0.67	0 (1)	−0.63	0.53
	Con.	1.88 ± 0.65	2 (1)	2.12 ± 0.55	2 (0)	0.24 ± 0.50	0 (1)		
Anxiety/depression	Exp.	2.52 ± 0.57	3 (1)	2.74 ± 0.58	3 (0)	0.23 ± 0.56	0 (1)	1.5	0.064
	Con.	2.45 ± 0.56	2 (1)	2.42 ± 0.61	2 (1)	−0.03 ± 0.53	0 (0)		

Con., Control group; Exp., Experimental group; QoL, Quality of life; M, mean; SD, Standard deviation.

hard to operate among older adults who have not been diagnosed with dementia; it is difficult to proceed because the program is monotonous, and its effectiveness is difficult to verify in older people with dementia. Multitasking ability demands, such as allocating and shifting attention, may induce additional brain activity in older adults (16). This program required a lot of multitasking between the PIO and participants, and the session was configured to increase emotional interaction with the PIO. A study showed that a multi-domain cognitive training program is more suitable for increasing brain neuroplasticity than monotherapy such as occupational therapy, exercise therapy, or art therapy (35); moreover, repetition was shown to enhance cognitive function in older adults, which is consistent with previous studies showing that it is effective to apply a program that integrates emotional and physical stimulation as well as cognitive stimulation (36).

The experimental group participating in the program had a more significant decrease in depression scores than the control group. This is also consistent with the results of a previous study that simultaneously confirmed the subject's cognitive function and depression, using the Sil-Bot robot (31). However, Oh et al. (37) configured a complex program with play content including recreational functions preferred by older people as a Silver-Care-Robot so that the robot and participants could interact, but both cognitive function and depressive variables decreased after the intervention. Petersen et al. (18) and Liang et al. (34), who performed interventions with the PARO robot for older adults with dementia, reported a statistically significant decrease in depression, but Robinson et al. (38) and Júranson et al. (39) found that depression scores in the experimental group increased after the intervention. As such, depending on the type of social robot and characteristics of the intervention method, the effect on the depressive variable is inconsistent. Social robots are useful for their attachment to humans, simple communication, and responsiveness to learning and training, such as the relationship between humans and dogs (40). Based on the storytelling method for participants to grow their PIO, this program was designed to increase attachment through interactions between participants and the PIO. By giving the PIO a name, making clothes, and so on, it was possible to nurture the PIO and encourage the participants to perform the program well, and by performing various actions, emotional communion with the participant was increased. Therefore, it is judged that this program increased the attachment between participants and the PIO and lowered depression. This study was conducted during the COVID-19 pandemic, and conversations between participants were prohibited during the program to ensure their safety. Therefore, the study results can be seen as the interaction effect between the participant and the PIO, rather than the interaction effect between the participants during the program.

In this study, the experimental group had a more statistically significant decrease in loneliness than the control. It was judged as effective to have an emotional bond through attachment in the process of hatching and growing from an egg, just like raising a real pet to promote an emotional bond between the participant and PIO. In a previous study that used the dog-shaped social robot AIBO, Kanamori et al. (41) reported that loneliness in older people decreased, but this was not statistically significant; Banks et al. (42) reported that loneliness decreased statistically significantly. It was reported that loneliness decreased in the intervention using the PARO robot, but the difference was not statistically

significant (38). Loneliness variables were inconsistent in the social robot interventions.

Loneliness is a subjective emotion that appears by recognizing a lack of close social contact or emotional bonding (43); depression and loneliness closely interact with each other (44). This study was conducted during the COVID-19 pandemic by minimizing interaction and social contact between participants to confirm the significant effect of depressive variables. Therefore, to reduce depression or loneliness, it is necessary to construct a program for social contact and emotional bonds between subjects through social robots, or to develop a program for creating emotional bonds between social robots and participants. Older people who regularly participate in exercise programs for physical activity have improved self-esteem and reduced loneliness (40, 45). This program consisted of "Gymnastics with PIO" and participants continued stretching before and during each session. Participants observed that they paid more attention to the movement of the PIO than to the movie clip on the tablet PC.

The quality of the QoL score improved in the experimental group, but the difference was not statistically significant. Similarly, Júranson et al. (46) reported that the PARO robot improved the QoL score for older people with moderate dementia, but it was not statistically significant; however, the score was statistically significant for those with severe dementia. Valentï Soler et al. (20) reported that QoL was significantly improved by using the PARO robot. The QoL measurement tool used in this study was EQ-5D-3L. According to a study on the validity and reliability of the EQ-5D tool targeting Koreans, Koreans do not actively express their social and cultural health problems, showing a relatively high ceiling effect (47). Therefore, the participants answered their health-related questions positively in the pre-measurement; however, in the post-measurement, they may have answered their health status more exaggeratedly, so it was judged that the QoL score decreased after the intervention. Therefore, after assessing the items in the instrument and the composition of this program, it is recommended that subsequent researchers use the EQ-VAS (Euro Quality of life-Visual Analog Scale) rather than the EQ-5D-3L.

5. Limitations

This study was conducted during the COVID-19 pandemic. Although it was implemented as a group program, social interactions between participants were controlled for their safety. Therefore, it was possible to control for confounding variables through interactions between participants. Randomized controlled trials could not be conducted because of restrictions on gatherings due to COVID-19 and the anxiety of older adults living alone or within group programs. In addition, pre-and follow-up measurements are required to confirm whether the effect of the program continues; however, follow-up measurements were not performed.

6. Conclusions

The PIO robot program was confirmed to be effective in cognitive function, depression, and loneliness for the older adults living alone. If this program is applied to older adults living alone in the community, cognitive decline and progression to dementia may be prevented. This reduce the nation's social burden. When nurses directly implement the PIO program intervention, they can provide customized nursing care by identifying the actual function of the patient, which can be utilized effectively in nursing practice.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study was approved by the Institutional Review Board (IRB) of Seoul National University. The approval number is IRB No. 2108/002-012. The patients/participants provided their written informed consent to participate in this study.

Author contributions

The author confirms being the sole contributor of this work and has approved it for publication.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Unmet healthcare needs predict frailty onset in the middle-aged and older population in China: A prospective cohort analysis

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Objectives: Older populations have a relatively high prevalence of unmet healthcare needs, which can result in poor health status. Moreover, in the coming century, frailty is expected to become one of the most serious global public health challenges. However, there is a lack of clear evidence proving an association between unmet healthcare needs and frailty. This study aimed to assess whether unmet healthcare needs predict the onset of frailty in China.

Methods: The association between frailty and unmet healthcare needs was explored by analyzing data from the China Health and Retirement Longitudinal Study (CHARLS) using random-effects logistic regression and Cox regression with time-varying exposure.

Results: At baseline, 7,719 respondents were included in the analysis. Random-effects logistic regression shows that unmet outpatient healthcare needs were associated with increased risk of both contemporaneous (adjusted OR [aOR], 1.17; 95% CI, 1.02–1.35) and lagged (aOR, 1.24; 95% CI, 1.05–1.45) frailty, as were unmet inpatient needs (contemporaneous: aOR, 1.28; 95% CI, 1.00–1.64; lagged: aOR, 1.55; 95% CI, 1.17–2.06). For respondents not classified as frail at baseline (n = 5,392), Cox regression with time-varying exposure shows significant associations of both unmet outpatient needs (adjusted HR, 1.23; 95% CI, 1.05–1.44) and unmet inpatient needs (adjusted HR, 1.48; 95% CI, 1.11–1.99) with increased risk of developing frailty.

Conclusions: Reducing unmet healthcare needs would be a valuable intervention to decrease frailty risk and promote healthy aging in middle-aged and older populations. It is urgent and essential that the equity and accessibility of the medical insurance and health delivery systems be strengthened.

KEYWORDS

healthy aging, unmet healthcare needs, frailty, China, middle-aged and older

1. Introduction

Unmet healthcare needs (UHN) is defined as the subjective perception of not receiving appropriate medical help when required. It captures misalignment between needs and provision and is commonly used as an indicator of access to healthcare and to precisely evaluate health system performance (1). Equitable access to healthcare according to need, regardless of demographic characteristics, ability to pay or social background is the core aim of universal health coverage (UHC) and thus UHC is undermined where there are UHN, as these can result in poorer health status, consequent risk of catastrophic health expenditures and increasing health inequalities (2, 3). China has moved

to reduce UHN and promote health equity through introducing a series of reforms, such as the New Medical Reform in 2009 and increasing the level of health insurance compensation. However, UHN remain, potentially because some residents experience greater economic burden and traveling inconvenience in accessing healthcare and have less health literacy and trust in medical institutions or healthcare providers than others (3–5).

There is a higher prevalence of UHN in older populations. Population aging is leading to a growth in the number of older adults who are functionally or cognitively impaired, increasing their need for healthcare resources (3). However, they may also be at higher risk of being left unattended, economically unsupported or immobile. In China in particular, the current infrastructure and health system are not well-designed to meet the needs of the older population. This mismatch between need and resource access inevitably increases the number of older people with UHN. China has become an aging society and as this continues, the burden borne by family and public healthcare systems will still increase (6). Thus, the UHN of older populations are a major challenge for China's healthy aging strategy.

The core components of the healthy aging strategy in China are to establish a nationwide, affordable, annual health check system to facilitate early diagnosis and provide access to affordable treatments and to enable the elderly to live healthier, happier, longer and more productive lives (7). Thus, it positions strengthening equity in healthcare and improving health-related quality of life for older populations as the two main measures of healthy aging. UHN reduce health equity and quality of life, which has been linked to frailty. Frailty, a state of overall decline in physical, mental or cognitive functions ranging from mild to severe (8, 9), is an important cause of decreased quality of life and is associated with disease prevalence and severity (10). As numerous studies have shown a relationship between frailty and health, frailty management is seen as an important component of the healthy aging strategy.

Previous studies have shown that UHN may worsen health status and quality of life (11), leading to an increased risk of mortality (12), multimorbidity (13), depression (14, 15), dementia and mild cognitive impairment (16), which can interfere with the person's ability to perform instrumental activities of daily living (IADLs) (17). Therefore, it is possible that UHN are associated with the onset of frailty. However, clear evidence of such an association is so far lacking. In view of this, we conducted a longitudinal study to analyse whether UHN predict the onset of frailty in China with the aim of generating recommendations for the promotion of healthy aging and health equity in older populations.

2. Methods

2.1. Sample and data

Data for this study were obtained from the four waves of the China Health and Retirement Longitudinal Study (CHARLS) conducted in 2011, 2013, 2015, and 2018. Owing to its high quality and national representativeness, this micro-level database on middle-aged and older adults has been widely used for geriatrics-focused clinical, public health and sociological research in China. The 17,708 individual respondents included in the baseline 2011 survey were followed up once every 2 or 3 years; detailed descriptions of the sampling and variables measured are reported elsewhere (18). The sample inclusion criteria for the current study were: (1) responding and at least 45 years old in the 2011 wave; (2) investigated in at least one follow-up wave; (3) not missing values for the dependent (frailty) and independent (UHN) variables. The final sample comprised 7,719 respondents at baseline, 1,787 suffering from frailty and 5,392 not frail.

2.2. Variables

2.2.1. Exposure: UHN

UHN were assessed by whether participants reported that either outpatient services or inpatient services did not meet their needs. Outpatient healthcare needs were considered unmet if respondents had been ill in the last month (at review) but had not visited a provider (including public hospitals, private hospitals, public health centers, clinics, or health worker's or doctor's practices) or been visited by a health worker or doctor for outpatient care. Inpatient healthcare needs were considered unmet if a doctor had indicated a need for inpatient care in the past year but the respondent had not been hospitalized.

2.2.2. Outcome: Frailty

Frailty, the outcome variable of this study, was measured based on Rookwood's Cumulative Deficit Frailty Index (FI). The deficits used to calculate FI were selected according to the following inclusion criteria: (1) a minimum of 30 deficits; (2) associated with adverse health outcomes; (3) increase in prevalence with age at least into the tenth decade; (4) at last 1% prevalence in the population; (5) does not saturate (19). FI was calculated using 48 deficits, with binary variables coded as 0 or 1 and some ordered categorical variables coded as 0, 0.5 and 1. The details are presented in Supplementary material Page 1–2. Because chronic conditions are irreversible, a score of 1 in one wave was extended to all subsequent waves. FI was calculated by summing the number of deficits reported by the participant and dividing it by the total number of deficits they had responded on, generating an FI ranging from 0 to 1, with higher FI indicating more severe frailty. FI was then categorized using a defined cut-off point of 0.25 (i.e., robust or prefrail: <0.25; frail: ≥ 0.25–1.00) (20, 21).

2.2.3. Covariates

Respondents' demographic and economic characteristics were used as controlling covariates in the analysis. These comprised age, gender, marital status, Hukou status, education level, rural or urban residence, public health insurance coverage, current work status and household per capita consumption. The grouping details are presented in Table 1.

2.3. Statistical analysis

First, the baseline characteristics of the sample were evaluated by calculating the mean and standard deviation for continuous variables (age) and frequency and percentage for categorical variables. Statistical differences for age were tested by Kruskal-Wallis one-way analysis as it was not normally distributed, and differences for categorical variables were tested using and Chi-square tests.

TABLE 1 Baseline characteristics.

	Outpatient needs			Inpatient needs		
	Met	Unmet	*P*-value	Met	Unmet	*P*-value
Number of participants	6,466	713		6,319	157	
Age	58.43 ± 10.50	58.73 ± 10.19	0.496	58.43 ± 10.53	57.78 ± 9.33	0.466
Gender			0.215			0.145
Male	3,088 (47.76%)	358 (50.21%)		3,009 (47.63%)	84 (53.50%)	
Female	3,377 (52.24%)	355 (49.79%)		3,309 (52.37%)	73 (46.50%)	
Marital status			0.011			0.677
Divorced or widowed	742 (13.34%)	60 (9.71%)		725 (13.36%)	17 (12.14%)	
Married	4,819 (86.66%)	558 (90.29%)		4,703 (86.64%)	123 (87.86%)	
Education levels[a]			0.107			0.003
Less than lower secondary	5,644 (87.33%)	642 (90.04%)		5,530 (87.56%)	123 (78.34%)	
Upper secondary and vocational training	678 (10.49%)	60 (8.42%)		651 (10.31%)	28 (17.83%)	
Tertiary	141 (2.18%)	11 (1.54%)		135 (2.14%)	6 (3.82%)	
Hukou status[b]			0.047			0.438
Agricultural	4,269 (76.81%)	480 (77.67%)		4,170 (76.87%)	103 (73.57%)	
Non-agricultural	1,265 (22.76%)	131 (21.20%)		1,231 (22.69%)	37 (26.43%)	
Other	24 (0.43%)	7 (1.13%)		24 (0.44%)	0 (0.00%)	
Rural/urban residence			0.052			0.023
Rural	3,755 (58.07%)	441 (61.85%)		3,654 (57.83%)	105 (66.88%)	
Urban	2,711 (41.93%)	272 (38.15%)		2,665 (42.17%)	52 (33.12%)	
Current work status			0.516			0.366
Not working	2,241 (35.23%)	239 (34.00%)		2,188 (35.20%)	60 (38.71%)	
Working	4,120 (64.77%)	464 (66.00%)		4,028 (64.80%)	95 (61.29%)	
Household per capita consumption[c]			0.072			0.710
Low	1,792 (32.95%)	188 (32.41%)		1,751 (32.96%)	46 (33.82%)	
Low to middle	1,508 (27.73%)	189 (32.59%)		1,468 (27.63%)	42 (30.88%)	
Middle	1,241 (22.82%)	116 (20.00%)		1,217 (22.91%)	26 (19.12%)	
High	898 (16.51%)	87 (15.00%)		877 (16.51%)	22 (16.18%)	
Public health insurance coverage[d]			0.686			0.878
Not covered	458 (8.28%)	48 (7.80%)		447 (8.28%)	11 (7.91%)	
Covered	5,075 (91.72%)	567 (92.20%)		4,954 (91.72%)	128 (92.09%)	

[a]Education levels were classified by a simplified version of the 1997 International Standard Classification of Education codes.
[b]Hukou status indicates the respondent's hukou place and is a special identifier in China. Hukou status affects many aspects of life in China such as buying a house, buying a car, children's school enrollment and other welfare.
[c]Household per capita consumption was calculated by dividing total household consumption by the number of people in the household, where total household consumption was an aggregate of food consumption in the last week, non-food consumption in the past 30 days and other non-food consumption in the past year. The household per capita consumption values for the different survey waves were adjusted using the Consumer Price Index and then divided into quartiles.
[d]Public health insurance includes Urban Employee Medical Insurance, Urban Resident Medical Insurance, New Cooperative Medical Insurance, Urban and Rural Resident Medical Insurance, Government Medical Insurance, Medical Aid or other government insurance plan.

Second, random-effects logistic regression was employed using a panel data approach to examine the association between UHN and frailty. Only data from 2011 to 2015 were used because UHN were not measured in the 2018 wave. Both contemporaneous (2011–2015) and lagging (2013–2018) frailty status were set as dependent variables due to the potential for a time-lagged impact of UHN on frailty. Odds ratios (OR) were calculated with a 95% confidence interval.

Third, the relative risk of frailty was calculated by including respondents who were non-frail at baseline and employing Cox regression to assess the predictive effect, with survey waves as the timescale and those who remained non-frail treated as censored data. UHN were identified based on 2011–2015 data and frailty status on 2013–2018 data. In addition, as economic status, health-seeking behavior and medical insurance compensation level may change over time, affecting whether healthcare needs are met, UHN were treated

as a time-varying exposure to avoid immortal time bias (22). Hazard ratios (HR) were calculated with a 95% confidence interval.

Multiple imputation using all the covariates was performed before conducting the above regressions to avoid reductions in statistical test performance and bias caused by the direct exclusion of missing values. Five replications and chained equations were used to generate five sets of databases and calculate a pooled regression coefficient (23, 24). The details of missing values were shown in Supplementary Table S1.

The validity of the results was assessed using three sensitivity analyses. First, Cox regression with time-varying exposure was performed on data without imputation. Second, respondents without any loss-up (2011–2018) were included in the Cox analysis. Third, the methodology developed by VanderWeele and Ding was used to calculate E-values, an alternative approach for detecting unmeasured confounding (25).

In addition, as China's rural and urban areas differ significantly in terms of economic level, health insurance compensation level, proportion of older people, family structures and healthcare resources, we explored the impact of UHN on frailty for rural and urban participants separately.

3. Results

Table 1 describes the baseline characteristics of participants with and without unmet outpatient and inpatient needs. The met and unmet groups generally have similar characteristics, except for marital status and Hukou status in the outpatient analysis and education levels and residence in the inpatient analysis. The ratio of inpatient needs is significantly higher for rural residents. The prevalence of UHN is shown in Figure 1. For unmet outpatient needs, it was 9.93% in 2011 and increased to 14% in 2013 then decreased to 13.37% in 2015. The prevalence of unmet inpatient needs was 2.19% in 2011, increasing to 3.34% in 2013 and then 4.86% in 2015.

Random-effects logistic regression shows that unmet outpatient healthcare needs were associated with increased risk of both contemporaneous (adjusted OR, 1.17; 95% CI, 1.02–1.35) and lagged (adjusted OR, 1.24; 95% CI, 1.05–1.45) frailty, as were unmet inpatient needs (contemporaneous: adjusted OR, 1.28; 95% CI, 1.00–1.64; lagged: adjusted OR, 1.55; 95% CI, 1.17–2.06) (Table 2).

For respondents not classified as frail at baseline (baseline characteristics shown in Supplementary Table S2), Cox regression with time-varying exposure (Table 3) shows significant associations of both unmet outpatient needs (adjusted HR, 1.23; 95% CI, 1.05–1.44) and unmet inpatient needs (adjusted HR, 1.48; 95% CI, 1.11–1.99) with increased risk of developing frailty.

The results of the three sensitivity analyses are presented in Table 4, Supplementary Tables S3, S4. First, the results of using non-imputed data to repeat the Cox regression were consistent with the main analysis. Second, results similar to the main analysis were obtained when using data of respondents without loss-up, except that the effect of unmet outpatient needs was not significant at the 95% level ($P = 0.087$). Third, the E-values were greater than the estimated confounders for frailty, which indicates that a potential unmeasured confounder is unlikely to have a considerably greater effect on frailty than the known risk factors.

We compared how UHN affect frailty for those in urban and rural areas (Table 5). Notably, a significant increase in frailty risk in those with both unmet outpatient and inpatient needs (vs. those with met needs) was seen only in respondents in rural areas (outpatient: adjusted HR, 1.23; 95% CI, 1.01–1.50; inpatient: adjusted HR, 1.47; 95% CI, 1.04–2.08), not those in urban areas.

We further analyzed reasons for UHN. For unmet outpatient needs (Supplementary Figure S1), "illness is not serious" was the main cause (2011, 48.93; 2013, 57.97, 2015, 51.18%). For unmet

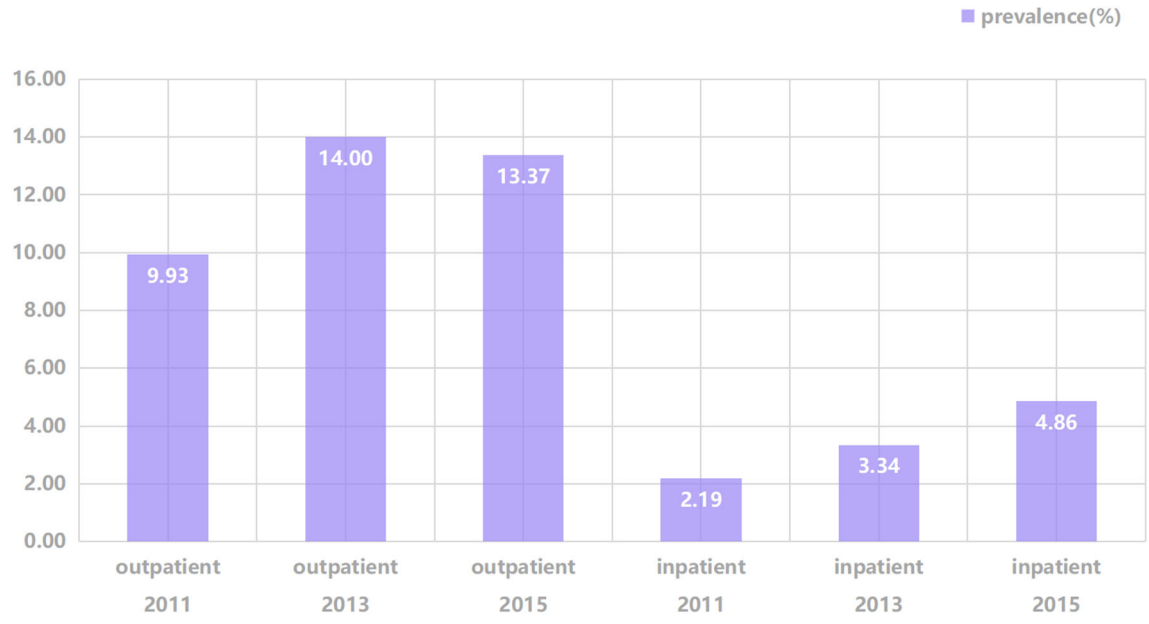

FIGURE 1
Prevalence of unmet healthcare needs across survey waves.

TABLE 2 Association between UHN and frailty based on random-effects logistic regression.

	Outpatient services				Inpatient services			
	Not lagged		Lagged		Not lagged		Lagged	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
Unmet healthcare needs (ref. Met)	1.17 (1.02, 1.35)	0.021	1.24 (1.05, 1.45)	0.009	1.28 (1.00, 1.64)	0.046	1.55 (1.17, 2.06)	0.002
Age	1.07 (1.06, 1.08)	<0.001	1.05 (1.04, 1.05)	<0.001	1.07 (1.07, 1.08)	<0.001	1.05 (1.04, 1.06)	<0.001
Gender (ref. Male)	1.93 (1.72, 2.17)	<0.001	1.85 (1.62, 2.11)	<0.001	1.95 (1.72, 2.2)	<0.001	1.90 (1.66, 2.18)	<0.001
Education level (ref. less than lower secondary)								
Upper secondary and vocational training	1.03 (0.83, 1.27)	0.793	0.56 (0.44, 0.71)	<0.001	1.00 (0.81, 1.25)	0.978	0.54 (0.42, 0.69)	<0.001
Tertiary	1.42 (0.93, 2.17)	0.101	0.72 (0.44, 1.18)	0.195	1.35 (0.87, 2.09)	0.174	0.71 (0.43, 1.17)	0.176
Marital status (ref. Divorced or widowed)	0.83 (0.72, 0.97)	0.019	0.66 (0.56, 0.79)	<0.001	0.83 (0.71, 0.97)	0.023	0.72 (0.6, 0.87)	<0.001
Rural/urban residence (ref. Rural)	0.90 (0.80, 1.01)	0.075	0.80 (0.7, 0.92)	0.002	0.89 (0.79, 1.01)	0.069	0.80 (0.69, 0.92)	0.001
Current work status (ref. Not working)	0.94 (0.85, 1.03)	0.177	1.00 (0.9, 1.12)	0.990	0.91 (0.82, 1.01)	0.090	0.98 (0.87, 1.1)	0.758
Household per capita consumption group (ref. low)								
Low to middle	1.00 (0.88, 1.13)	0.973	0.90 (0.78, 1.04)	0.150	0.97 (0.85, 1.12)	0.713	0.87 (0.75, 1.02)	0.079
Middle	0.93 (0.82, 1.06)	0.256	1.03 (0.89, 1.19)	0.674	0.93 (0.81, 1.07)	0.313	1.03 (0.88, 1.20)	0.718
High	0.93 (0.81, 1.06)	0.263	1.14 (0.99, 1.33)	0.076	0.91 (0.8, 1.05)	0.214	1.12 (0.96, 1.32)	0.148
Hukou status (ref. Agricultural)	0.41 (0.36, 0.47)	<0.001	1.16 (1.00, 1.34)	0.043	0.42 (0.37, 0.49)	<0.001	1.10 (0.95, 1.27)	0.223
Public health insurance coverage (ref. Not covered)	0.94 (0.79, 1.11)	0.475	0.78 (0.65, 0.95)	0.012	1.01 (0.84, 1.21)	0.906	0.77 (0.63, 0.93)	0.008

UHN, unmet healthcare needs; OR, odds ratio; CI, Confidence Interval.

inpatient needs (Supplementary Figure S2), 'not having enough money' was the main cause (2011, 61.08; 2013, 61.29, 2015, 57.48%).

4. Discussion

To the best of our knowledge, this is the first study to assess the effect of UHN on the development of frailty. This study uses nationally representative data and cohort analysis to show that both unmet outpatient and inpatient healthcare needs increase frailty risk in China's middle-aged and older population. Nevertheless, this effect was pronounced only in rural China.

Given the multiple adverse outcomes associated with frailty, such as falls and fractures, hospitalisations, reduced quality of life, complications and early mortality (26), it will undoubtedly be among the most serious global public health challenges in the coming century (10). China has the world's largest older population, with the Seventh National Census showing 264 million people to be 60 years old and over. The rapid expansion of the aging population has brought about a concomitant rise in the frequency of frailty, placing increased pressure on healthcare systems (27, 28). As frailty increases the need for medical services, the unmet need for services also increases. Previous studies have shown that frailty increases UHN (29). However, UHN also increase the risk of frailty, which could be caused by several possible mechanisms. First, UHN in older adults have been found to be associated with deteriorating physical health. UHN usually brings about delay of disease treatment, the miss of the best treatment period of the disease, and even the subsequent aggravation of diseases (30, 31). Frailty itself is also a risk factor of disease aggravation, and UHN inevitably brings about an increased risk of frailty. Second, UHN have also been found to be associated with worse psychological health. UHN often lead to deteriorating health, which could affect the quality of life and lead to more depressive symptoms in several ways like adding chronic pain, limiting the ability to move and carry out valued activities, participating in social activities, or even taking care of themselves and their basic needs. Witnessing their deteriorating health might also add to feeling more negative emotions and helplessness about their situation and the future (32). In addition, frailty often coincides with chronic disease, and even multimorbidity. For older populations suffering chronic diseases, UHN often means insufficient or inadequate management, which could increase risk of co-occurence of chronic conditions and frailty (33, 34). These suggest that reducing UHN is crucial for delaying the onset of frailty and consequently promoting healthy aging.

The Chinese government has made tremendous efforts to reduce UHN by improving the accessibility of medical services and providing affordable and equitable healthcare for all residents. These efforts center around expanding healthcare insurance coverage, increasing the accessibility of basic public health services for all, establishing a national essential medicines system, improving basic healthcare delivery within the primary care system and reforming public hospitals (35, 36). However, although years of medical service

TABLE 3 Association between UHN and frailty based on Cox regression with time-varying exposure.

	Outpatient services		Inpatient services	
	Odds ratio (95%CI)	*P*-value	Odds ratio (95%CI)	*P*-value
Unmet healthcare needs (ref. Met)	1.23 (1.05, 1.44)	0.010	1.48 (1.11, 1.99)	0.008
Age	1.02 (1.01, 1.02)	<0.001	1.02 (1.01, 1.02)	<0.001
Gender (ref. Male)	1.34 (1.21, 1.48)	<0.001	1.34 (1.2, 1.48)	<0.001
Education level (ref. Less than lower secondary)				
Upper secondary and vocational training	0.88 (0.73, 1.05)	0.161	0.88 (0.73, 1.05)	0.164
Tertiary	1.21 (0.83, 1.76)	0.331	1.19 (0.82, 1.74)	0.358
Marital status (ref. Divorced or widowed)	0.73 (0.63, 0.84)	<0.001	0.73 (0.63, 0.84)	<0.001
Rural/urban residence (ref. Rural)	0.95 (0.85, 1.06)	0.332	0.95 (0.85, 1.06)	0.356
Current work status (ref. Not working)	0.98 (0.88, 1.09)	0.735	0.99 (0.88, 1.1)	0.790
Household per capita consumption group (ref. Low)				
Low to middle	0.88 (0.77, 1.02)	0.082	0.88 (0.77, 1.02)	0.083
Middle	0.93 (0.81, 1.07)	0.341	0.93 (0.81, 1.08)	0.343
High	0.85 (0.73, 0.99)	0.043	0.85 (0.73, 1)	0.044
Hukou status (ref. Agricultural)				
Non-agricultural	1.12 (0.99, 1.28)	0.072	1.12 (0.99, 1.27)	0.083
Other	0.82 (0.47, 1.44)	0.491	0.83 (0.47, 1.45)	0.509
Public health insurance coverage (ref. Not covered)	0.71 (0.60, 0.83)	<0.001	0.71 (0.6, 0.83)	<0.001

UHN, unmet healthcare needs; HR, hazard ratio; CI, Confidence Interval.

TABLE 4 Sensitivity analysis*.

	Unmet healthcare needs (ref. Met)	
	HR (95%CI)	*P*-value
Without imputation		
Outpatient	1.26 (1.04, 1.53)	0.016
Inpatient	1.47 (1.03, 2.11)	0.036
Without loss up		
Outpatient	1.19 (0.98, 1.45)	0.087
Inpatient	1.58 (1.13, 2.20)	0.007

HR, hazard ratio; CI, Confidence Interval.
*Cox regression with time-varying exposure were used to calculate relative risks. The adjusted confounders includes age, gender, marital status, Hukou status, education level, rural or urban residence, public health insurance coverage, current work status and household per capita consumption.

TABLE 5 Subgroup analysis of urban/rural residence*.

	Unmet healthcare needs (ref. Met)	
	HR(95%CI)	*P*-value
Urban		
Outpatient	1.24 (0.95, 1.60)	0.110
Inpatient	1.49 (0.86, 2.56)	0.152
Rural		
Outpatient	1.23 (1.01, 1.50)	0.037
Inpatient	1.47 (1.04, 2.08)	0.028

HR, hazard ratio; CI, Confidence Interval.
*Cox regression with time-varying exposure were used to calculate relative risks. The adjusted confounders includes age, gender, marital status, Hukou status, education level, rural or urban residence, public health insurance coverage, current work status and household per capita consumption.

system and medical insurance reform have positively impacted health service provision to residents, we found that the incidence of UHN, especially for inpatient services, has increased. This may be attributable to an increase in absolute demand as the population ages. We analyzed the reasons for not having their healthcare needs met and found that the perception that the "illness is not serious" was the main cause for unmet outpatient needs, followed by "not having enough money" and that "not having enough money" was the main cause of unmet inpatient healthcare needs. Firstly, these findings indicate that the health literacy and health awareness of older residents need to be improved. Secondly, as older people progressively become less able to work, their ability to pay for the use of medical services also decreases. Therefore, it is necessary to intervene to increase their medical security.

Notably, the impact of UHN on frailty is more significant in rural than in urban areas of China. A likely cause of this is the lower income level of rural older populations, which arises because, while the urban population has retirement wages, the rural population do not and suffer an irreversible decline in income as ability to work decreases (37, 38). Moreover, the ongoing population outflow from rural areas can weaken family cohesion and economic support to the elderly from their children may be lacking (39, 40). In addition, rural residents generally have less health literacy and health awareness than urban residents (41). All of these factors not only increase UHN in rural areas but cause worse overall health in older populations in rural than urban areas, making the onset of frailty more sensitive to the effects of UHN in rural China.

In summary, this study identifies a targeted means of frailty-reduction: reducing UHN. This reduction could be achieved by further improving the medical security system, strengthening social solidarity and family function and increasing medical service utilization. Especially in rural areas, we need more policy actions to gradually establish a more equitable long-term care mechanism and ensure the active supply of medical services, as this will reduce UHN and thus reduce the occurrence of frailty.

This study has several limitations. First, the use of self-report data will have introduced recall bias. For example, self-report of the

deficits used to calculate the FI may not be accurate, affecting the accuracy of the frailty level estimation. Second, respondents who became frail but died before 2018 have not been included in our analysis. Given the association of frailty with mortality, excluding them may have introduced survival bias. Third, the FI amalgamates numerous indicators. Observations for many indicators were missing from individual participants' interview data, which led to sample loss. Nevertheless, we applied a cohort design and conducted several sensitivity analyses to overcome and check for this bias. Fourth, the prevalence of and reasons for UHN were not measured in 2018, making the results less informative about the current situation in China than they would be with more recent data. Finally, the reference group in this study was respondents without UHN, which included both those who were ill but receiving medical services and those who were not ill. We could not draw any conclusions about whether there was an increase in frailty risk for those with a given serious illness who had their healthcare needs unmet. However, based on our analysis, this study clearly indicates that UHN are an important predictive factor for frailty onset.

5. Conclusions

This study clearly demonstrated that UHN put middle-aged and older populations in China, especially in rural areas, at greater risk of becoming frail. Therefore, reducing UHN would be a valuable intervention to promote healthy aging in middle-aged and older populations. As population aging becomes an ever-greater challenge, it is urgent and essential to strengthen the equity and accessibility of the medical insurance and health delivery systems.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: All the original data could be obtained from the official website of CHARLS (http://charls.pku.edu.cn/).

Author contributions

JL, JC, and HL designed and conducted the research. JL, DW, and JC analyzed the data and interpreted the results. JL, DW, and HL prepared the first manuscript and had primary responsibility for the final content. All authors critically reviewed, interpreted the results, and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1064846/full#supplementary-material

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Youth perceptions toward managing elderly care among low-income household families using the My-Elderly-Care-Skills Module

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Background: Caregivers of elderly people need the right education and empowering skills to manage their own health needs and the elderly people they care for.

Objective: The study aimed to explore youth perceptions of the My-Elderly-Care-Skills Module intervention and its perceived feasibility.

Methods: This study involved youth respondents (18–30 years old) from low-income households who are accountable to providing care for independent older people (60 years or above) living in the same house. A qualitative study using a case study design was used to assess youth perceptions based on the content of the My-Elderly-Care-Skills module, by focusing on its implementation usage and usefulness for the care of the elderly. A total of 30 youths voluntarily participated in the online training workshop during the COVID-19 pandemic movement restriction order period. There were multiple sources of data, such as video recorded on reflection of care given at home, text messages in a WhatsApp group, and in-depth interviews during small group online meetings. Data were recorded and transcribed verbatim for common themes before a theme analysis was conducted. Inductive content analysis was performed after the saturation point was met.

Results: Thematic analysis derived two domains of feasibility: operational and technical feasibility. There were three themes under operational practicality (improving awareness, addressing the caregiving skills needs, and seeking resources for knowledge) and three themes for technical practicality (easily used and informative, skill in effective communication, and program fulfillment).

Conclusion: It was verified that it is feasible for young caregivers of the elderly to participate in the My-Elderly-Care-Skills training intervention as it helps in improving knowledge and skills performance in managing and caring for the elderly.

KEYWORDS

youth, perception, elderly care, training, aged care

Introduction

Aging, health, and quality of life are closely intertwined. In Malaysia, the elderly are classified as those aged 60 or above (1). In 2020, the elderly population in Malaysia was 3.5 million, 10.7% of the total population, and this number is predicted to triple by 2040 when one in every five Malaysians will be aged 60 or above (2). The percentage of the elderly is projected to reach 15%

of the total population in 2030, making Malaysia one of the most rapidly aging nations in the world (2). The current life expectancy for Malaysians is 72 years for men and 75 years for women (2), which is still far behind the life expectancy of 80 years in developed countries.

Elderly care and management strategies for promoting the wellbeing of both the elderly and their caregivers are still in the infancy stage in Malaysia. Most studies focused largely on the elderly and not on their caregivers (3). A recent systematic review assessing the gap in bridging health and social care of caregivers identified only 15 publications in Asia over the past 5 years that discussed the impact of interpersonal communication, social works intervention, and communication barriers faced by caregivers of the elderly (4). In addition, most studies concentrated mostly on awareness, education, and tasks of informal elderly caregiving in a familial setting, and scarcely focused on health problem-solving, dietary and nutritional requirements, and satisfaction with comfort, hygiene, daily activity, and safety of the elderly who lives alone or in the same home as the caregiver (4).

For statistical purposes, the Malaysian Youth Development Research Institute (IYRES) defined youth as the population between the ages of 15 and 30 (5). The numbers of the youth in Malaysia are as follows: 5,242,700 males and 4,709,900 females (5). The proportion of youth to the elderly is higher in Malaysia compared to the rest of Asian countries. As part of the sandwich generation and with an extended family living arrangement, most youths stay in the same house as their elderly relatives, either their own parent or a family member. Youths are the catalyst for the nation's future by spearheading the changes in the country's leadership. Their role in providing elderly care should be enhanced by better skills. They should also be better equipped to deal with the responsibilities of being part of the sandwich generation. Malaysia is transforming into a high-income nation through the Fourth Industrial Revolution (IR4.0), which demands a change in daily life, working style, communication, and how the future is evaluated (6). One of the most important aspects of IR4.0 is the realignment of the purpose of education, in that it should go beyond increasing knowledge to also help individuals understand how the learned information can be applied in daily life.

Based on the literature review of the evidence provided by previous studies, the researchers found that most of the studies only focused on the elderly respondents and not on their caregivers, especially in the case of young caregivers (7). Lack of awareness among the youth about the importance of elderly care was encountered and they were normally less interested in gerontology education (8). Lack of disclosure of care and the importance of taking care of elderly health was taught at universities, colleges, schools, and non-governmental organizations (NGOs). Poor awareness and scarce training make the youth less skilled in the care of the elderly and at the same time affects the quality of life, social support, and psychological wellbeing of the caregivers of the elderly, as well as elderly satisfaction.

Malaysia still lacks research on the various issues involved with professional care for the elderly, such as training modules for the elderly, and training of the skills needed by caregivers of the elderly and the disabled population. Most available skills were focused on hospitality skills, sewing, cooking, retail, and vocational training (9). Therefore, it is necessary to develop a specific module that promotes social participation in active aging and helps caregivers and the elderly to improve their quality of life, social support, and psychological wellbeing. The module should aim to empower youth to engage in training and vocational training (TVET) and to make them aware of the importance of empowering TVET in helping to improve the national economy and practicing lifelong education. Malaysia is still attempting to reach a high number of skilled workers to be comparable to developed countries, such as Taiwan, South Korea, Singapore, Germany, and the United Kingdom, which are some of the countries that consider TVET as one of the main focuses in education (10). A scoping review on informal caregivers recently reported that most training interventions helped in the caregivers' needs, specifically in improving knowledge, self-efficacy, and competency (11, 12). A qualitative approach study among the caregivers of the elderly mostly reported on their physical and mental readiness, and knowledge related to elderly care and support (4, 13). There is limited literature on exploring perceptions, especially among the youth in caring for the elderly. Therefore, the present study aims to explore youth perceptions of caring for their elderly relatives concerning the training intervention modules given to them and their perceived feasibility.

Methodology

The study employed the case study as a type of qualitative research to explore youth perceptions of using the My-Elderly-Care-Skills module online training in caring for the elderly in relation to the training intervention modules given to them. Using the qualitative case study methodology enables researchers to conduct an in-depth exploration of intricate phenomena within some specific context (14, 15). The study was conducted during the Malaysia Government Movement Control Order (MCO) at a time when several phases had been enacted nationwide to curb the COVID-19 pandemic and had put various sectors of the economy in jeopardy (16). The MCO caused many activities reliant on services to allow people to work and learn from home through the utilization of online platforms. We adopted an e-learning technique to teach the My-Elderly-Care-Skills module and to train youth in caring for their elderly relatives at home during the MCO. We aimed to provide accredited training based on the module developed and tested among the youth as on-the-job training and to provide a support system to help youths secure jobs in elderly care in the community or institutional care. The case study approach is particularly useful to employ when there is a need to obtain an in-depth appreciation of an issue, event, or phenomenon of interest, in its natural real-life context (15).

We reported the qualitative research output following the suggested guideline (17, 18) and added it in the Supplementary file 1 for reference. Each focus group discussion consisted of five respondents and each session lasted approximately one to one and a half hours for each group, as described in the Supplementary file 2. Each respondent was used as case study data. The My-Elderly-Care-Skills module was created by adopting elderly care guidelines developed (19, 20) for educating the elderly and their caregivers on the various aspects of caregiving needs for the elderly. The research team used the guidelines and developed online presentations, interactive lectures, videos on caregiving skills, frequently asked questions, and tips for quick assessment. The module was divided into two set packages, i.e., the education package and the competency skills in managing the elderly package. The education package was divided into four domains: (i) the right of youth to obtain health information for self-care; (ii) healthy lifestyle approaches

for wellbeing and active aging; (iii) preventing abuse and mental health resilience; and (iv) social support approach toward healthy aging. The competency skill in the elderly health care management package was divided into four domains: (i) youth role as an elderly healthcare volunteer; (ii) physical and mental health care for the elderly; (iii) tips to prioritize the needs of the elderly and seeking additional resources; and (iv) elderly health monitoring plan for the volunteers. These packages were designed to provide basic guidelines for providing care to the elderly and enhancing the competency skills of the caregivers. Researchers used the Google Meet application instead of a face-to-face workshop from March to October 2021 (during the COVID-19 pandemic's critical phase). Young caregivers of the elderly from all over Malaysia were invited to attend an elderly health empowerment webinar. The workshop was advertised *via* the Community Health Department, Faculty of Medicine University Kebangsaan Malaysia website in collaboration with the National Elderly Development Association (NEDA Malaysia.org), which is a registered non-profit organization, as well as the university's various official social media accounts.

Setting and participants

The study was conducted during the height of the COVID-19 pandemic under the movement and quarantine restrictions imposed by the Malaysian Government's Movement Control Order (MCO) in 2020 and 2021. A case study design was used to explore the youth's perception of using the My-Elderly-Care-Skills module and its feasibility as a guide for improving caregivers' competency and feasibility analysis (technical and operational feasibility) for an assessment of the practicality of using the module. Each youth who participated in the training was invited as a case study respondent. Respondents were the youth who is the main caregiver of the elderly and living in the same home as the elderly relative. The selection was based on the respondent's ability to participate in the two-day My-Elderly-Care-Skills Module workshops and their ability to provide sufficient data on their experience and the effectiveness of the module in empowering their competency skills. The inclusion criteria were: Malaysian citizens who can speak and understand Malay or English, have access to a smart device with a stable internet connection, age between 18 and 30 years, are from low-income household families (< RM4,850 (USD1050) per month or known as B40 category) (1, 2), and are caregivers to a dependent elderly person(s) staying together in same living arrangement. All respondents consented to participate in the study. We selected the youth who used the My-Elderly-Care-Skills module for 3 months and completed the 2-day online training course. There were 30 youths selected purposively to give a response to a key question during our data collection period.

Study instrument

The respondents were interviewed at the end of the intervention using the online platform (Google Meet application) for ∼5–15 min each in an individual in-depth interview using an online focus group discussion (FGD) technique. The groups were formed based on the respondents' residential state: north, south, central east, and west of the Malay Peninsula to ensure they had the same language dialect and social-cultural background. Monthly monitoring was also conducted *via* video calls, video recordings, and WhatsApp conversations over a period of 3 months since its implementation. The qualitative method in the study used the lived experience of the youth to assess the experience of young caregivers in caring for their elderly relatives and thematic analysis was performed to interpret the data to answer the study's objective. The questions were constructed as semi-structured, i.e., open-ended and closed questions.

- How do you find the My-Elderly-Care-Skills module and training in helping your understanding and skills in improving healthcare for the elderly?
- What did you learn after attending the training webinar over the past 2 days?
- Did this training webinar help you in caring for the elderly?
- What challenges do you face in using the information given in the module?

TABLE 1 List of materials used and the roles of the researchers and respondents.

	Researchers	
Respondents	Facilitator (RS)	Moderator (NSM)
1. My-Elderly-Care-Skills module 2. Laptop/desktop computer 3. Good Internet access	1. Laptop/desktop computer 2. Good Internet access 3. My-Elderly-Care-Skills module presentation, lecture note, video, and questionnaire to be given to trainees 4. planned activities for the program to be carried out.	1. My-Elderly-Care-Skills module 2. Laptop/desktop computer 3. Good Internet access 4. Lead the training program 5. Prepare poster slides to be posted during the training program.

Data collection tools

WhatsApp messages, recorded videos, and Google Meet recordings during the interview were transcribed and used in the present study. Table 1 listed the tool used and its function. Each respondent needed to have a training module (e-book), and a computer with internet access. The researcher (RS) provided online training on the use of the module and acted as the facilitator. Another researcher (NSM) acted as a moderator during the training and also conducted the focus group discussions as well as transcribed them verbatim.

WhatsApp

- WhatsApp is a free messaging platform that sends and receives texts, images, audio, and video files as well as web addresses to and from individuals and groups; it also served as an important e-learning platform. The researchers formed a WhatsApp group for the "Caregiving Training and Education for the Elderly Workshop" to facilitate communication of the My-Elderly-Care-Skills module usage and sharing experiences. NSM compiled all the respondents' reflection feedback, acknowledged

their contribution, and introduced them to one another for sharing their experiences and opinions in caring for the elderly.

Video recording

- Participants were requested to produce a short video while caring for the elderly for the researchers to assess their feedback experience in the implementation of the module for the daily task of caring for their elderly relatives at home.

Google Meet

- Google Meet was selected as the medium for focus group interviews as it is a simple and free platform. Participants were requested to enter the Google Meet room according to the schedule provided by the researchers. Everyone was allocated ∼5–15 min to reflect on their experience and the challenges faced.

Data collection procedure

Data were collected in three phases over a period of 4 weeks. At the start of phase one, informed consent was obtained from the respondents, and they were briefed on the purpose and duration of the study before proceeding to the interview session. Focus group discussion interviews were conducted for an average of an hour to an hour and a half with five respondents at each time during phase two, which was conducted over 6 days (4–9 October 2021). During each FGD, everyone was given ∼5–15 min to voice their opinions. Six focus group discussions were done with 30 respondents. Each respondent's view was treated as a case study. Each session was recorded and transcribed for data recording purposes. At the end of 3 months, we asked the respondents to submit a short video with their reflection about the training and usage of the module.

Data analysis methods

Data analysis was performed after verbatim recordings had been transcribed. Researchers constructed three boxes that were divided into themes, subthemes, and verbatim outcomes; following which, keywords collected in the verbatim outcomes were collected as themes. It is a form of pattern recognition used in analysis whereby themes that emerge from the data become the categories for analysis. The process involves the identification of themes with relevance specific to the research focus, the research question, and the research context that allows data to be both described and interpreted for meaning (21). All researchers worked together to explore the verbatim transcripts and reached a consensus for thematic analysis based on the feasibility component: technical and operational practicality (Table 2).

Validity and reliability

All six FGD interviews were moderated by NSM and assisted by RS. To ensure the validity of the research, data from the FGD (video interviews using Google Meet), WhatsApp group chats, and reflection videos on the module's feasibility, were used as a triangulation approach to achieve consistency and uniformity to answer the research question. The study set a primary research question as to how the youth perceived caring for their elderly relatives by using information gained during the online training of the My-Elderly-Care-Skills modules. The key questions were developed by the research team as listed in the Supplementary file 3. They were listed to address our concern on feasibility assessment that was not covered in the quantitative study design questionnaire. In exploring the respondents' perception of using the module, we related the key question with the content of the module as summarized in Figure 1. In assessing for reliability, we distributed the verbatim transcripts among the other researchers (RMY and HY) who were not involved in the interviews to find similar patterns. The interview questions and thematic analysis techniques were cross-referenced with experts (HY and RMY) who have experiences of over 25 years of qualitative study design for validation before and after the interviews were conducted. To ascertain reliability, reduce misinterpretation on the researchers' part, and fill in data gaps, the transcriptions of the interviews were shared with the respondents for them to review and a follow-up discussion was conducted to determine if the researchers understood them correctly.

Research findings and discussion

This section evaluated the findings of the interviews based on the 30 respondents who participated. The result was arranged to answer the study objective, which was to explore youth perception of the My-Elderly-Care-Skills Module intervention and its perceived feasibility. Demographic details of the respondents are outlined in Table 3.

Respondents' profiles

The age of the respondents ranged from 19 to 29 years. The majority were Malays (n = 28/30), women (n = 25/30), and grandchildren (n = 21/30). Most of them cared for their elderly relative, whose ages ranged from 60 to 81 years old. The majority needed moderate care monitoring as the elderly suffered multiple illnesses that required proper treatment compliance to drugs, physiotherapists, clean wounds, and clinic follow-up. Most caregivers spent ∼1–3 hours per day managing elderly care needs. Approximately three-quarters (22/30) of respondents of the study were grandchildren.

Thematic analysis

We assessed the youth's perception of the feasibility of using the My-Elderly-Care-Skills module in managing their elderly relative at home. Referring to Table 2, our finding achieved three themes under operational practicality and three themes for technical practicality. We reached the point of saturation after the fourth FGD and continued to proceed until all six FGDs were completed. Our approach was based on inductive understanding focusing on the perception of the module's feasibility in the care of the elderly.

TABLE 2 Flow of thematic data analysis.

Step 1	Step 2	Step 3
Read and underline keywords	List the underlined keywords	Unify the obtained keywords by forming a theme
Example of verbatim recording	Subtheme	Theme
. . . all the information that I got, the youth need to take care of five main things in the care of the elderly. Among them are comfort, food, cleanliness, daily activities, and safety... (R3)	Acquired knowledge through training	Knowledge Enhancement (operational practicality)
...applying the five main focuses in planning for the elderly to my mum. [*sic*] The five main focuses are in terms of comfort, food, cleanliness, daily activities, and safety at home...(R7)		
...I need to take care of the quality and quantity of his food and ensure safety i.e. no small toys for his grandson along his journey because he is worried about being stepped on and so on.... (R3)	Addressing the caregiving skills needs	The benefit of elderly care (operational practicality)
...I am more aware and know the importance of taking care of the emotional and mental health of the elderly...(R13)	Improve awareness	Awareness (operational practicality)
...this program is also very good because it cares about the mental and psychological health of the elderly... (R10)	i. Easy to use and informative. ii. Skills in effective communication. iii. Program fulfillment.	Program Completion (technical practicality)

Table 4 depicts the quotes representing the themes for two domains of feasibility: operational and technical feasibility. Three themes under operational practicality were grouped as improving awareness, addressing the caregiving skills needs, and seeking resources for knowledge. Another three themes for technical practicality were categorized as easily used and informative, skill in effective communication, and program fulfillment.

Technical feasibility: Easily used and informative

Respondents provided positive feedback of the workshop. The workshop was described as clear for them to understand and follow step-by-step even though they had not previously learned about the subject in school. They attempted to try the techniques provided in the module at home while managing their elderly relatives. Respondents stated that the knowledge they gained from the workshop was beneficial and they were able to apply the provided healthcare management tips in their daily activities.

Technical feasibility: Skills in effective communication

Respondents stated that the training workshop was invaluable in their gaining new knowledge on caregiving as well as planning the care and treatment for the elderly, particularly on the communication aspect. They felt that they were better equipped to manage the elderly in their care, particularly from the communication and emotional need aspects. The workshop training, delivered as an online platform, helped them to understand all aspects a caregiver needs in order to improve caregiving quality and better fulfill the needs of the elderly relative with multiple co-morbidities who is in their care. The majority of the respondents indicated that the workshop helped to increase their knowledge and technical skills in caregiving from the physical and mental aspects, as well as their role as caregivers.

Technical feasibility: Program fulfillment

The majority of the respondents agreed that the training module provided good educational materials and taught them how to obtain more information on the best practices to manage and care for the elderly.

Operational feasibility: Acquired knowledge through training

The majority agreed that they gained new knowledge on caregiving for the elderly in terms of physical, mental, and healthcare requirements as well as tips on evaluating the health status of the elderly. The respondents gained additional knowledge on elderly care and management needs for illness monitoring, which improved their caregiving planning. A proper time plan guide helped them to improve their wellbeing. Awareness of the benefit of proper time management and understanding the specific needs of the elderly with illnesses boosted the caregiver's confidence and continuity of care for the elderly. The finding noted that the My-Elderly-Care-Skills module was well accepted by all respondents and provided important knowledge in caregiving for the elderly. They acknowledged that the training helped them to improve the quality of the caregiving they provide for their elderly relatives.

Operational feasibility: Improve awareness

Respondents reported that they felt that as caregivers to the elderly they needed to learn how to better manage their emotions and improve their communication skills. They also reported that they must be prepared to address the physical, emotional, and mental health needs of the elderly while dealing with their fussy whims, cantankerousness, and reclusiveness. They claimed that the module and the training helped them realize the importance of early exposure to elderly caregiving so that they could be prepared to fulfill their caregiving responsibilities. According to the respondents, the module helped them to become more conscious of their responsibility in caring for elderly emotional, physical, and mental health as well as their healthcare needs. They claimed to have felt empowered to share their knowledge and experiences within their communities.

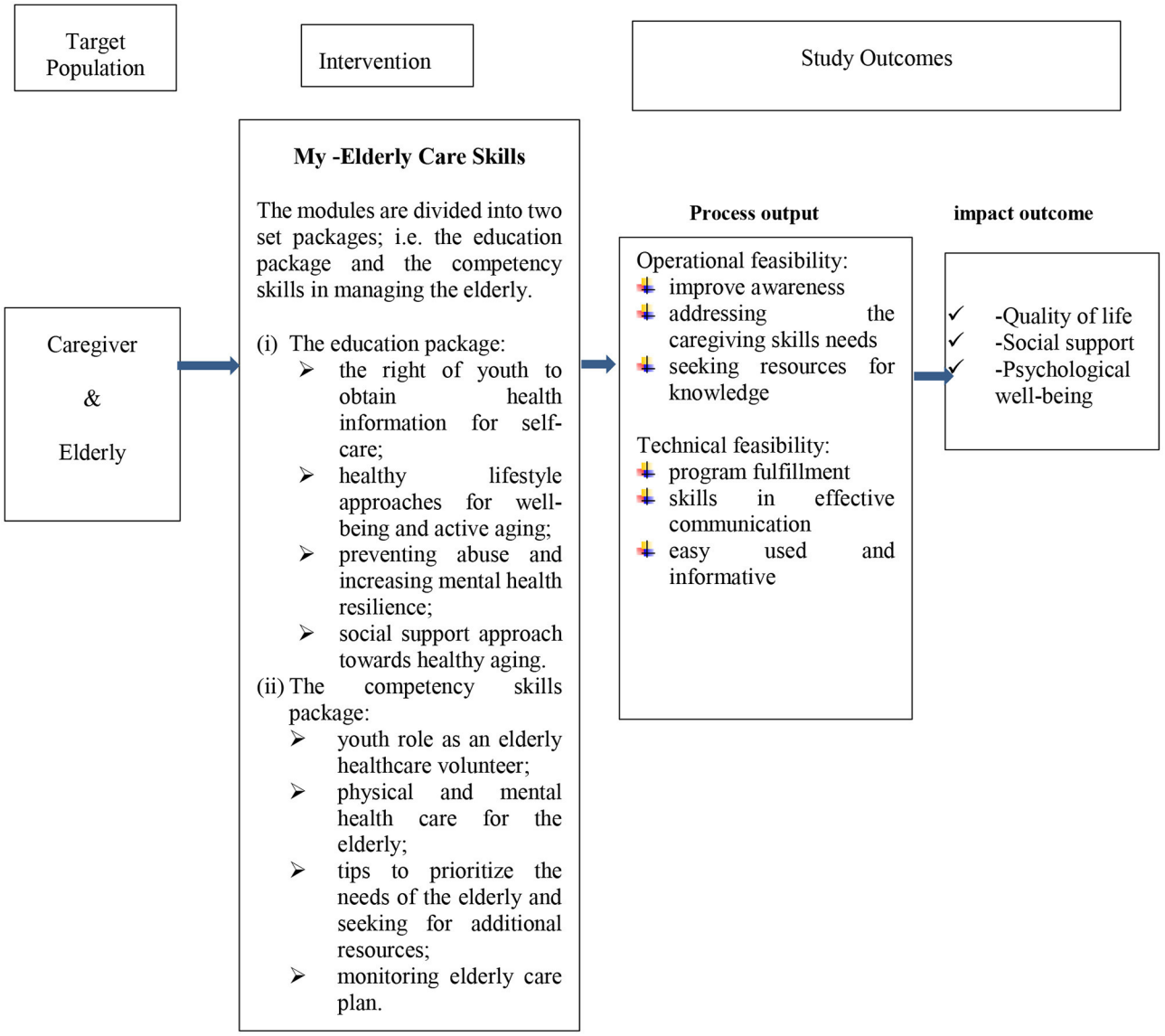

FIGURE 1
Visualization of study framework and output.

Operational feasibility: Addressing the caregiving skills needs

All respondents claimed to be aware that caregiving for the elderly is not an easy task. They described it as requiring responsibility, trust and being a task that must be taken seriously by the caregivers. They claimed to feel more prepared to deal with the emotions and behaviors of the elderly in their care after the workshop. They reported feeling more equipped as a caregiver to manage and care for the elderly after the workshop by using the techniques they learned, especially in terms of quality of care.

Discussion

In assessing the perceptions that the youth have on how to manage the elderly they care for in their homes, it became clear that more efforts are needed to empower young caregivers by providing them with the flexibility of ready-to-use materials, especially when there is limited access to formal training or institutional centers. Even though Malaysia is an aging nation, proper training for skill empowerment is limited and expensive, making it difficult for the country to prepare for an efficient treatment of its aging population, especially during disasters and economic downturns. In general, elderly care education and training is often a globally discussed and debated topic as the world faces an increased demand for the care of elderly populations (20). The creation of the My-Elderly-care Skills module is one of the steps that can be taken in helping the community to increase its knowledge about the care and health of the elderly while being able to achieve the government's desire to nurture the community, especially in helping the youth of low-income families practice lifelong education.

The results of the study showed that after attending the My-Elderly-care Skills workshop, the respondents were able to increase their knowledge related to the care and management of elderly health

TABLE 3 Respondents' profiles.

ID	Age	Gender	Ethnicity	Age of elderly in their care (years old)	Elderly health status		Relationship with the elderly in their care	Length of the period for care for the elderly (hours per day)
					Needs moderate daily care monitoring (has multiple chronic illnesses that need to comply with treatment)	Needs basic care in monitoring (has a mild illness and can manage themselves)		
R1	24	Female	Malay	63	/		Child	3
R2	24	Female	Malay	80		/	Child	3
R3	20	Female	Malay	72	/		Child	3
R4	24	Female	Malay	60		/	Grandchild	3
R5	24	Female	Malay	83		/	Child	3
R6	24	Female	Malay	78	/		Grandchild	3
R7	21	Female	Malay	81		/	Grandchild	3
R8	23	Female	Chinese	65	/		Grandchild	3
R9	24	Female	Malay	74		/	Child	3
R10	24	Female	Malay	63	/		Grandchild	3
R11	22	Female	Malay	80		/	Child	3
R12	24	Female	Malay	74	/		Grandchild	4
R13	20	Female	Malay	63	/		Grandchild	3
R14	26	Male	Malay	70		/	Grandchild	3
R15	25	Female	Malay	73		/	Grandchild	3
R16	24	Female	Malay	60	/		Grandchild	3
R17	21	Female	Malay	77		/	Child	5
R18	23	Male	Malay	63	/		Grandchild	5
R19	29	Female	Malay	68	/		Grandchild	3
R20	24	Female	Malay	65	/		Grandchild	3
R21	19	Male	Malay	60		/	Grandchild	4
R22	23	Female	Malay	67		/	Child	3
R23	24	Female	Malay	67	/		Grandchild	3
R24	27	Female	Malay	61		/	Grandchild	4
R25	25	Male	Malay	63	/		Grandchild	3

(Continued)

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TABLE 3 (Continued)

ID	Age	Gender	Ethnicity	Age of elderly in their care (years old)	Elderly health status		Relationship with the elderly in their care	Length of the period for care for the elderly (hours per day)
					Needs moderate daily care monitoring (has multiple chronic illnesses that need to comply with treatment)	Needs basic care in monitoring (has a mild illness and can manage themselves)		
R26	27	Female	Indian	62	/		Grandchild	5
R27	27	Female	Malay	61	/		Grandchild	4
R28	25	Male	Malay	60	/		Grandchild	4
R29	23	Female	Malay	78	/		Grandchild	4
R30	24	Female	Malay	78	/		Child	4

and were able to better plan the elderly care needs for the sake of mutual wellbeing. Knowledge is the main aspect of life to guarantee quality of life. In a recent national study, which used quantitative methods, with 1,153 Malay respondents aged 40–59 years, it was found that the quality of life among the elderly is very dependent on the caregivers of the elderly and that knowledge is the main aspect in helping the caregivers provide the best care services (22). Quality of life has a relationship with the increase or decrease in wellbeing in the life of caregivers and the elderly (23, 24).

Our present study explored the perceptions of young caregivers for the elderly during the COVID-19 pandemic. To present we have not seen any publication providing online training on the care of the elderly in the Asian region. Feedback from the respondents who participated showed a potential platform for training the younger generation and how they can use an online platform that focuses on elderly care. As many countries are facing the aging phenomenon, enhancing digital education will facilitate disseminating skills training for all in need. Our neighbor country Thailand shares almost similar socio-cultural practices and has developed a social health care program for the elderly in the community known as the Excellent Happy Home Ward (EHHW), which was carried out in the Lopburi Province, Thailand (25). The EHHW program involves taking care of the physical and mental health of the elderly and empowering the elderly in the use of information technology to help improve their support system and at the same time increase the level of knowledge of the elderly and caregivers of the elderly in the community. However, it required the caregiver to go to the center to obtain the training rather than be at home while managing their elderly relative.

Our findings showed that the benefit of the module is that it can be used for empowering caregivers in providing care for the elderly. Many researchers believe that the current trend of caring for the elderly depends a lot on young people who are not married, and it can also be seen that women are often chosen as caregivers for the elderly (22, 23). Our finding supports earlier evidence that women are more involved in elderly care. The elderly also often expect help and support from daughters because they are seen as easy to communicate with and easy to ask for help compared to sons who are seen as busy with work and have to shoulder multiple responsibilities, such as being responsible as the head of the family, as a father, as an employee, as a husband and as a child to their elderly parents (22). This phenomenon can have implications for the career, family, and national development of women who become tasked with various responsibilities. Indirectly it will have an impact on the wellbeing of the lives of the youth and the elderly (23, 24).

In this study, the researchers also found that six respondents stated that their role as caregivers of the elderly was not just living with the elderly as a companion, but the care of the elderly included emotional care, physical care, managing medication, ensuring mental and emotional health, as well as managingtheir own health status as they realized that they are the ones responsible for taking care of and managing elderly wellbeing. Our findings supported the perception of various ethnic groups that children and family members play a very important role in elderly caregiving and that children need to have a responsible attitude to repay the sacrifices of parents. There was also the notion that they too will also become old at some later point and maybe need caregiving from their own children (26, 27). A recent study also reported that the caregivers acknowledged their parents had sacrificed a lot to raise children–their children (26). It was clear

that young caregivers of disabled elderly need family development support to make them emotionally and physically balanced, and need assistance in their interpersonal care so that they are ready to assume the role and responsibility of caregiving. Emotional care is key for the mutual wellbeing of the caregiver and the elderly under their care (28).

The results of the thematic analysis also showed that awareness among caregivers of the elderly was one of the priority needs. A previous study conducted on five senior respondents aged 60 or over, seniors living alone, and seniors experiencing physical, emotional, as well as financial, and material neglect in Negeri Sembilan and Selangor found that the communication gap between the caregivers and the elderly is caused by the lack of awareness of their role as caregivers of the elderly. There is no doubt that those caring for the elderly go through various challenges, including the changing nature of the elderly, who need love, attention, and friendliness from caregivers and the people living around them to achieve wellbeing in their daily lives (29). Our study found that nine out of 30 respondents indicated that the workshop was instrumentally able to increase their awareness of responsibilities as caregivers to their elderly. A previous study among the Malays also found that people who chose to be caregivers to the elderly tended to have a strong sense of responsibility and empathy (26).

Japan, Sweden, China, and Singapore are developed countries that have been facing elderly problems earlier than Malaysia, and they reported that the elderly are never left out of their country's various levels of planning, and that establishing close relationships with children, families, and caregivers of the elderly has always been a priority (3, 7, 13, 20, 26). Promoting visiting each other often, calling when living far away, and helping elderly people from nearby neighborhoods living in their community helped in enhancing community participation (30). However, Malaysia is facing rapid aging as it has progressed from an agricultural to an industrialized country that urges the migration of people to urban areas, which in turn leads the young population to live with family. The focus and spiritual attitudes of children, family members, communities, and guardians are shifting from looking after the welfare of the elderly. This coupled with the rate of economic improvement, lack of jobs, and the ever-increasing pressures of life have caused many communities to be less concerned about the problems of others, especially the elderly (31).

Our study aimed at improving knowledge and skills in the care of the elderly, and we hope it will open job opportunities for youth in providing elderly care services at an institutional-based level, home care or in visiting services once they are competent after attending the training and using the My Elderly-care Skills module. The module motivates the youth and the elderly to stay healthy and ensures quality of life, social support, and mental health wellbeing. It uses a digital platform that attracts engagement in the empowerment of caregivers in venturing into Vocational Education and Training (TVET) and does not focus on education alone. The present study involved nine freshly graduated students who showed interest for lifelong learning even with simple 2 days of online training based on the My Elderly-care Skills module. This finding supported intergenerational relationships and psychological and social support in the care of the elderly as presented by a case study in Kota Kinabalu. That study found the need to build a holistic module based on the National Elderly Policy (DWEN) and that there is a need for improvements in the national action plan so that the production of modules is more integrated to guarantee the wellbeing and quality of life of caregivers and the elderly (32).

The My-Elderly-Care Skills module was created with a proof of concept to raise awareness on the importance of elderly caregiving. It also imparted skills and knowledge to caregivers of the elderly and improved the wellbeing of caregivers to the elderly from the quality of life, social support, and psychological aspects. The module was constructed based on the social health intervention theory (33) that is divided into role boundaries, the burden of demand, and conflicts as part of the experience of a caregiver for the elderly that has to undertake various responsibilities simultaneously (i.e., as an employee, spouse, parent, child, student, and caregiver) in improving the quality of life, social support and wellbeing of both the elderly and their caregivers.

Thus, the My-Elderly-Care Skills module can be used to promote reciprocity between the elderly and their caregivers. According to the social health intervention theory, the wellbeing of the elderly and their young caregivers depends upon their quality of life, social support, and psychological wellbeing, with the latter two affecting the first (24, 34, 35). The elderly and their caregivers who received social support had a high level of psychological wellbeing and were less stressed. Thus, good social support will increase the psychological wellbeing and quality of life of both the elderly and their caregivers in the long run. Using digital platforms as media for training helped in bigger-scale participation for awareness and knowledge dissemination. However, competency skills are more appreciated with physical interaction training (36). The emotional aspect of caregiving addressed by the respondents in this study, such as fussiness, irritability, and reclusiveness, need to be prioritized in areas of problem-solving ability, self-care, and resilience against life's pressure and demands. Young caregivers and the elderly who are less stressed are in a better place emotionally when compared to those who are struggling under the burden of various responsibilities and life's demands that affect their psychological wellbeing. The youth of the 21st century fall under the sandwich generation that needs to bear various responsibilities simultaneously. The style of caring for the elderly at this point is not the same as before due to the phenomenon of changes in terms of family structure, modernization, and urbanization. Therefore, the caregivers of the elderly need help and support from formal or informal institutions to correctly manage the care of elderly relatives and not put any pressure on them in achieving better wellbeing in their families. As more of them have to take up the role of caregivers to the elderly, they must be equipped with the best knowledge and skills in preparation for Malaysia's aging phenomenon, which is due to start in approximately 2030. In the present study, we used multiple approaches based on the time and setting of a similar case study. Using multiple case studies approach using a depth case study helped in improving saturation and validity (14, 15).

Limitation

The study had a limitation in exploring the perception experience in the aspect of technical feasibility related to environmental support. The study was conducted online, and the researchers had no responsibility for the respondent's internet connection at home. All respondents described caregiving activities based on their home setting. The study was conducted during the critical phase of the

TABLE 4 Summary of the results for theme development in relation to the feasibility domain.

Feasibility domain	Themes	Quotes
Technical feasibility	Easily used and informative	*"I used inputs given to me which is very clear to follow, and I am satisfied . . . "(R20) [sic]* *"I learned that skills in caregiving for the elderly in the present era are very challenging and need the training to catch up with our skills. (R23)" [sic]* *"I learned so many new things in how the best caregiving methods for the elderly that tailored to my cultural beliefs. . . "(R18) [sic]* *". . . so many things I learned during the workshop. I was never exposed to or learned while I was in school. In other words, it was easy and valuable new knowledge for me..."(R21)* *". . . gave me new insights on so many new information on how to best care for the elderly and the relevant techniques . . . " (R22)* *". . . gained so much valuable information on managing and caregiving for the elderly..."(R25)* *"I gained a lot of new information on how to care for the elderly. I now know better about the aging process, and the tips on health evaluation, and how to plan caregiving for the elderly has been most helpful . . . "(R7)* *"I gained a lot of new information on how to manage caregiving for the elderly, especially on the health, physical, and mental care aspects . . . "(R10)*
	Skills in effective communication	*"I have been exposed to the proper way of caring for the elderly, particularly on the best way to communicate with people who are older than me. It helped me gain new knowledge to prepare myself to care for and treat the elderly . . . "(R4)* *"I gained more knowledge on managing and caregiving for the elderly. I learned how I can communicate better, be more mindful of their emotions and feelings . . . " (R6)* *"I gained exposure to the right and proper ways on how to be a caregiver for the elderly..."(R2)* *"I learned how to communicate more effectively with the elderly . . . "(R28)* *"I learned how I can communicate better with them and be more mindful of their feelings and emotions . . . "(R29)* *"I learned about the techniques in caring for the elderly to be more effective with proper application on the physical and mental aspects from the training . . . " (R11) [sic]* *"the moderator and facilitator provided good explanations and in-depth exposure to the role of youth in caregiving. I also appreciate the sharing experiences by other caregivers of the elderly . . . " (R12) [sic]* *"I learned and helped me to add my knowledge on caring for the health of the elderly either on the physical or mental aspects . . . "(R27) [sic]*
	Program fulfillment	*". . . this is a wonderful program that emphasized the importance of caring for the elderly"s mental and psychological health . . . the program should be expanded to the wider community so that the physical and mental health of the elderly in this country are better-taken care of by the people who love them the most . . . " (R9)* *"... the program is a proactive measure in educating the community on proper caregiving for the elderly . . . " (R16)* *". . . the program has a positive impact on the community, especially for youths like myself . . . " (R23)* *". . . an effective way to educate the community on proper caregiving for the elderly . . . " (R25)* *". . . understand some of the main focus when planning healthcare for the elderly, such as comfort, diet, hygiene, daily activities, and safety in the home to fulfill the needs of the elderly as best as possible . . . " (R10) [sic]*
Operational feasibility	Acquired knowledge through training	*"I gained new knowledge on caregiving for the elderly on aspects, such as the physical, emotional, and spiritual..." (R1)* *"the training exposed me to the physical and mental changes experienced by the elderly which led to their health problems . . . "(R18) [sic]* *"I can understand better now what should be my role as a child who will care for my father"s mental and physical health later on . . . the tips on evaluating my father"s health will help me plan on how I can be the best caregiver for my father . . . "(R24)* *". . . the best knowledge I gained is on the five main factors I must pay attention to while being a caregiver to my parents. That is my parents" comfort, nutrition, hygiene, daily activities, and safety. (R3) [sic]* *"Now I will apply the five main focuses in planning for elderly caregiving for my mother. The five factors are comfort, nutrition, hygiene, daily activities, and safety at home. (R7)* *"This is my first time exposed to the best practices in managing and caring for the elderly as well as the actions that I can take when I am stressed while caring for my ill grandparent . . . " (R26)* *"I gained tremendous valuable input and information on caregiving for the elderly, especially for those with health and mobility issues like my father who has diabetes and had suffered from stroke. . . " [sic]* *"I gained so many valuable inputs like providing right and consistent attention while being a caregiver to the elderly . . . " (R8)* *"I obtained so many inputs on how to manage emotions, communicating techniques and so on . . . " (R15)* *"I find that many inputs and information on the best practices to care for the elderly . . . " (R9)*
	Improve awareness	*". . . I am more aware and mindful of the emotional and mental care needed by the elderly . . . " (R13)* *". . . to pass on the awareness to the greater community as a caregiver to the elderly . . . " (R18)* *"...modules we have just seen that there are actually many elements that youth need in caring for the elderly, among them in terms of emotional, physical, and mental health because the elderly..."* (R14) *". . . it made me more mindful of our responsibility as a caregiver . . . " (R18) [sic]* *". . . to be more attentive, such as giving their medication according to the prescribed time to reduce their discomfort . . . " (R8)* *". . . I realized the importance of managing emotions and better communication approach . . . " (R5) [sic]* *". . . to prepare me physically, emotionally, and mentally when dealing with their fussiness, grouchiness, and reclusiveness . . . " (R10)* *". . . gave me early exposure on how to get further information to prepare myself to be a caregiver to the elderly in the future..." (R17)* *". . . equipped with the knowledge needed to care for the elderly so we can take care of our parents and grandparents . . . " (R19)*
	Addressing the caregiving skills needs	*"I must take care of the quality and quantity of their food, making sure that none of the grandchildren's toys are in the way that can trip them or hurt them in any way..." (R3)* *"I must ensure that their daily routine, such as wound cleaning and dressing at the health clinic, is on time and to include light physical activities" (R3)* *". . . to monitor my father's present health status and ensure that he is taking the medications as instructed by the hospital doctor . . . " (R13)*

(Continued)

TABLE 4 (Continued)

Feasibility domain	Themes	Quotes
		"I will be more focused on their mental and emotional health" (R13) *"I realized that I need to take a bigger role in taking care of their emotional needs so that they are comfortable and not offended … " (R14)* *"I am feeling more comfortable and still can help to relief my father's aches and pains after doing such physically demanding jobs … " (R24) [sic]* *"the training guided me on how to help to be the better person facing with problem-solving while taking care of my Grandma … " (R20) [sic]* *"… to create a daily schedule so that their day-to-day activities go smoothly. It would also help me monitor the medication schedules better … " (R29)* *" I apply what I learned at the workshop and it helps me to reduce the conflicts that I have with my mother. Now I understand her better and how loneliness from getting older affects her … " (R28)* *"… better equipped to deal with their moods because older people to be quite sensitive, some of the things we say can easily hurt their feelings … " (R30) [sic]* *"… can reduce the burden of caregiving once we know the right techniques in caring for the elderly … " (R19)* *"… helped me to manage the elderly in my household better and more efficiently … " (R25)*

COVID-19 pandemic where the majority of places were imposed with a movement restriction order (MCO). The majority of the youth who participated in the study were trapped as the caregiver of the elderly as many of them were unemployed during the economic hardship of the pandemic period. No available formal training on the care of the elderly was obtained by any of the respondents before the module training. Therefore, we explored their experience during this critical period using the My-Elderly-Care-Skills module using existing guidelines and without providing any environmental support on technical components, such as internet access and access to a computer. It was challenging to fully understand the rigor required in qualitative research in view to replicate the thematic analysis as done in our study, especially when we conducted our research using an online platform. We could not appreciate in depth the emotions or feedback reflected because we did not have any contact with the respondents' surrounding environmental support.

Conclusion

Exploration of the perceptions of the youth who have been trained to use the MY-Elderly-Care-Skills module in managing elderly care shows an important aspect of the technical and operational feasibility component. There were three themes obtained under operational feasibility, which were knowledge enhancement, the benefit of the care of the elderly, and improving awareness. The three themes for technical feasibility were the program completion in relation to digital communication barriers and the interactive approach. Future studies on applying digital education as a health promotion approach should focus on environmental support in the implementation of digital health education.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by UKM PPI/111/8/JEP-2021-754. The patients/participants provided their written informed consent to participate in this study.

Author contributions

NM, RS, RMY, and HY participated and approved the study design. All researchers are women. NM, RS, and RMY contributed to designing the study. NM collected the data and conducted the FGD assisted by RS. NM and RS analyzed the data. NM, RS, and HY wrote the final article. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1042124/full#supplementary-material

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Depression and oral health-related quality of life: A longitudinal study

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Objectives: Geriatric oral health-related quality of life is a relatively new but rapidly growing concept as it is directly related to the general wellbeing and self-esteem of older adults. This study assessed the impact of worsening depression symptoms on oral health-related quality of life using representative nationwide data of Korean older adults.

Methods: This study comprised a longitudinal sample of older adults aged ≥60 from the Korean Longitudinal Study of Aging (2016–2020). After applying the exclusion criteria, 3,286 participants were included in the study. Depression status was determined through the biennial assessment of the short-form Center for Epidemiologic Studies Depression Scale (CESD-10); oral health was measured using the Geriatric Oral Health Assessment Index (GOHAI). We employed the lagged general estimating equations to assess the temporal effect of the CESD-10 score change on the GOHAI score.

Results: A decrease in CESD-10 score over a 2-year period was significantly associated with a decrease in GOHAI score in men and women: $\beta = -1.810$ and $\beta = -1.278$, respectively (p-values < 0.0001). Furthermore, compared to the same or improved CESD-10 score, worsening of the score on 1–2 points detected the $\beta = -1.793$ in men and $\beta = -1.356$ in women, and worsening on ≥3 points: $\beta = -3.614$ in men and $\beta = -2.533$ in women.

Conclusions: This study found that depression exacerbation is negatively associated with oral health-related quality of life in later life. Further, a more significant worsening of depression symptoms was correlated with lower scores for oral health-related quality of life in our study population.

KEYWORDS

CESD, GOHAI, older adults, geriatrics, KLoSA, Korea

1. Introduction

The world is progressing toward an aging population owing to the annual increase in average life expectancy. More medical researchers have focused on the burden that comes with an aging population and have defined processes leading to healthier and more successful aging (1). This increased emphasis on the aging population highlights the importance of careful consideration and attention to the health and quality of life of older adults.

Health-related quality of life is a multidimensional construct (2, 3) that includes oral health-related quality of life (4, 5), drawing the attention of researchers to geriatric dentistry (6). Oral disorders significantly affect the wellbeing and life satisfaction of older adults (7). In the age group >60 years, conditions associated with oral health problems are one of the leading causes of general morbidity (8). A decrease in social activity, somatic pathology, and a difficult financial situation impede full-fledged dental care for older people. Appropriate and timely access to oral health care is warranted to assess these problems and improve the overall quality of life.

In particular, South Korea (hereafter, Korea) reported that older individuals with poor oral health are more likely to experience depressive episodes (9). A cross-sectional study by Mun et al. emphasized the impact of depression and oral dryness on oral health-related quality of life (10). Globally, depression is a major public health concern and a leading cause of adverse health outcomes. Individuals with depression experience various symptoms, including reduced physical activity; some patients even show an extreme form of inactivity due to catatonia (11). Hence, researchers and clinicians have made efforts to prevent, reduce, and ameliorate depressive symptoms in populations.

The association between depression and oral health-related quality of life has been addressed in several cross-sectional and longitudinal studies (12); however, little attention has been paid to the time-changing aspect of depression status concerning the geriatric worsening of oral health-related quality of life. Extant literature hypothesizes that comparable biological and behavioral mechanisms are associated with both depression and oral health (13). However, several studies have explicitly examined the bidirectional relationship between depression and oral health and reported controversial results.

Therefore, the impact of the time-changing depressive symptoms on oral health-related quality of life among older Korean adults remains understudied. Moreover, some previous studies present limitations given their cross-sectional design and lack of representative samples. Thus, we hypothesized that individuals with worsening depression over time are more susceptible to experiencing a worse oral health-related quality of life. Furthermore, the greater the exacerbation of depression, the worse the oral health outcomes. Using the short-form Center for Epidemiologic Studies Depression Scale (CESD-10) and the Geriatric Oral Health Assessment Index (GOHAI), we systematically explored the effect of depression status changes on oral health-related quality of life among Korean older adults, based on a nationwide, longitudinal study after adjusting for assumed confounders that might affect the results.

2. Methods

2.1. Data source and sample

The data examined in the current study was extracted from the Korean Longitudinal Study of Aging (KLoSA), a longitudinal panel survey performed every even-numbered year since 2006. KLoSA provides the data of a representative nationwide sample of older adults over 45 years. The total number of participants surveyed in 2006 was 10,254, with the sample retention rate in 2020 of 63.3%. The main objective of the KLoSA is to provide data that can facilitate the collection of information on the demographic, economic, social, and psychological status and health conditions of middle- and old-aged people and the development of effective policies. In this study, we used data from the last three waves (2016, 2018, and 2020), as GOHAI was first employed in the survey in 2018. The application of exclusion criteria (participants aged <60 years, missing data of variables, and lack of follow-up) led to the inclusion of 3,286 participants (1,488 men and 1,798 women) in the baseline year.

2.2. Depression status

The short-form Center for Epidemiologic Studies Depression Scale (CESD-10) was used to measure depressive symptoms. The CESD-10 is a validated construct used as a screening tool to identify major depressive symptoms in older adults worldwide and in Korea (14, 15). Respondents were asked to answer 10 questions about their condition. Responses were made using a binomial scoring system, coded 0–1 (no/yes), and calculated as a total score of 10 points. Higher scores indicated greater distress and higher severity of depressive symptoms. The continuous variable of depression status change was categorized into two groups as the change of CESD-10 score over time: (1) same or improved and (2) worsened; the analyses were conducted assuming continuous changes in the recorded values within the two groups.

2.3. Oral health-related quality of life

The outcome variable, "oral health-related quality of life," was identified using the Geriatric Oral Health Assessment Index (GOHAI), which has been introduced for general use to measure the quality of life related to oral health and has proven its validity and reliability in adult samples worldwide, including Korea (16) and other Asian countries (17, 18). The GOHAI is based on responses to a 12-item self-administered questionnaire measured on a 6-point scale (0–5 points), while three positive questions are calculated by reversing the scores. A higher GOHAI score indicates a higher quality of life related to positive oral health, with the highest possible score of 60 points. To analyze the relationship between the change in depressive symptoms and the GOHAI score, changes in both scales over the previous year were recorded.

2.4. Covariates

We added data on sociodemographic characteristics and health-related factors as potential covariates in this study. Sociodemographic characteristics included gender (men and women), age (60–64, 65–69, 70–74, and ≥75 years), educational level (middle school or below and high school or above), marital status (married and not married), and income level per month in quartiles (low, middle-low, middle-high, and high). Additionally, we considered the participants' regions of residence (urban and rural areas). Health-related factors included the number of chronic medical conditions, smoking status (non-smoker and smoker), handgrip strength (normal and abnormal), cognitive function (normal and abnormal), and body mass index (BMI). KLoSA provides data on comorbidities, including hypertension, diabetes mellitus, cancer, lung disease, heart disease, and cerebrovascular disease. We grouped them into three categories depending on the number of diseases a participant had (none, 1, or ≥2 diseases). Handgrip strength was measured in kilograms considering sex-specific thresholds (<24 kg for men and <15 kg for women). Cognitive function was assessed through the Mini-Mental State Examination (MMSE) score; with a total score of 30, the MMSE's cut-off level for cognitive impairment is below 24. Furthermore, we considered participants' life satisfaction (bad, normal, and good).

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TABLE 1 Baseline characteristics of the study population according to Geriatric Oral Health Assessment Index (2016 → 2018).

Variables	Geriatric Oral Health Assessment Index									
	Men					Women				
	N	%	Mean ± S.D.		*P*-value	*N*	%	Mean ± S.D.		*P*-value
Total (*N* = 3,286)	1,488	100.0	38.61	8.46		1,798	100.0	38.27	8.19	
Change in CESD-10 score					<0.0001					<0.0001
Same or improved	1,055	70.9	39.61	8.68		1,203	66.9	39.37	8.28	
Worsened	433	29.1	36.19	7.38		595	33.1	36.04	7.55	
Age					0.0097					<0.0001
60–64	285	19.2	41.239	8.54		393	21.9	41.489	7.55	
65–69	359	24.1	40.326	8.03		420	23.4	39.612	7.61	
70–74	311	20.9	38.344	7.71		370	20.6	38.165	7.66	
≥75	533	35.8	36.214	8.46		615	34.2	35.354	8.31	
Region					0.1531					0.2669
Urban area	611	41.1	39.321	8.25		734	40.8	39.04	7.86	
Rural area	877	58.9	38.121	8.58		1,064	59.2	37.736	8.38	
Educational level					0.0013					<0.0001
Middle school or below	440	29.6	36.018	8.76		1,036	57.6	36.506	8.30	
High school or above	1,048	70.4	39.703	8.09		762	42.4	40.664	7.41	
Employment status					0.2128					0.5645
Employed	636	42.7	40.097	7.94		420	23.4	39.631	8.13	
Non-employed	852	57.3	37.506	8.67		1,378	76.6	37.853	8.17	
Marital status					0.8013					0.7178
Married	1,352	90.9	38.811	8.47		1,123	62.5	39.251	7.77	
Not married	136	9.1	36.654	8.10		675	37.5	36.633	8.61	
Household income per month					0.0450					0.5128
Quartile 1 (low)	387	437.0	36.167	9.06		742	41.3	36.636	8.64	
Quartile 2	412	390.0	38.287	7.78		426	23.7	38.761	7.33	
Quartile 3	411	391.0	40.302	8.36		381	21.2	39.793	7.49	
Quartile 4 (high)	333	270.0	40.6	7.47		249	13.8	39.956	8.40	
Chronic disease					0.1459					0.6289
None	553	37.2	39.687	8.03		637	35.4	39.143	7.99	
1	521	35.0	38.668	8.47		688	38.3	38.222	8.01	
≥2	414	27.8	37.111	8.80		473	26.3	37.156	8.59	
Smoking status					0.0013					0.0612
Non-smoker	471	31.7	39.584	8.32		1,737	96.6	38.366	8.13	
Smoker	1,017	68.3	38.164	8.50		61	3.4	35.475	9.43	
Handgrip strength					0.0056					0.0023
Normal	1,196	80.4	39.334	8.25		1,485	82.6	39.024	7.93	
Abnormal	292	19.6	35.664	8.68		343	19.1	34.708	8.50	
Cognitive function					<0.0001					<0.0001
Normal	1,156	77.7	39.843	8.12		1,213	67.5	40.001	7.65	
Abnormal	332	22.3	34.331	8.23		585	32.5	34.675	8.13	

(Continued)

TABLE 1 (Continued)

Variables	Geriatric Oral Health Assessment Index									
	Men					Women				
	N	%	Mean ± S.D.		*P*-value	*N*	%	Mean ± S.D.		*P*-value
Total (*N* = 3,286)	1,488	100.0	38.61	8.46		1,798	100.0	38.27	8.19	
BMI					0.7552					0.7872
Normal	1,429	96.0	38.728	8.38		1,713	95.3	38.382	8.18	
Abnormal	59	4.0	35.831	9.87		85	4.7	35.965	8.22	
Satisfaction of life					0.0002					<0.0001
Bad	157	10.6	34.459	8.21		261	14.5	34.375	8.76	<0.0001
Normal	970	65.2	38.354	8.27		1,143	63.6	38.183	7.83	
Good	361	24.3	41.119	8.27		394	21.9	41.094	7.76	

TABLE 2 Generalized linear model using the generalized estimating equations with Geriatric Oral Health Assessment Index in 2018.

Variables	Geriatric Oral Health Assessment Index					
	Men			Women		
	β	S.E.	*P*-value	β	S.E.	*P*-value
Change in CESD-10 score						
Same or improved	ref.			ref.		
Worsened	−1.810	0.3018	<0.0001	−1.278	0.2577	<0.0001

2.5. Statistical analysis

Lagged generalized estimating equation (GEE) analyses were performed and controlled for covariates to provide estimates for the GOHAI according to the 2-year change in CESD-10 scores. To examine gender-specific differences, all statistical analyses were performed separately for men and women. The GEE model allows for repeated measurement analysis of longitudinal panel survey data and considers the correlation within the subject to generate regression coefficients (β), standard errors (S.E.), and the corresponding *p*-value.

Subgroup analyses were performed to determine the relationship between the CESD-10 and GOHAI. We estimated the lagged GEE analyses for depression transitions for each GOHAI question. Furthermore, we performed a sensitivity analysis to determine the relationship between specific changes in the CESD-10 score (worsening on 1–2 points and ≥3 points) and the GOHAI. All differences were considered statistically significant with *p*-values of <0.05. Data analyses were performed using the SAS 9.4 software (SAS Institute Inc., Cary, NC, USA).

3. Results

The sex-stratified baseline characteristics of the study population are presented in Table 1. A total of 3,286 individuals were included in the survey during the baseline year (1,488 men and 1,798 women). In the unadjusted analysis, the mean difference in depression status groups and GOHAI scores was ∼3 points for men and women.

Table 2 presents the findings of the lagged GEE model analysis of the association between changes in CESD-10 and GOHAI scores. We noted that, in both men and women, compared to the same or improved depression status, worsened depression showed regression coefficients of −1.810 in men and −1.278 in women, which were highly significant at *p*-values < 0.0001. A decrease in CESD-10 score was significantly associated with a decrease in GOHAI score in both genders.

The findings of the independent subgroup analysis of the variables associated with the effect of changes in depression symptoms and GOHAI scores are presented in Table 3. The results indicated that men with worsened depressive symptoms aged ≥75 years and women in the 70–74 age group showed statistically significant regression coefficients: $\beta = -1.862$ in men and $\beta = -1.790$ in women, respectively. Furthermore, low handgrip strength was strongly associated with lower GOHAI scores in the group with worsened depressive symptoms: $\beta = -2.009$ in men and $\beta = -2.468$ in women.

Table 4 shows the lagged GEE model analysis results for the effect of a decreased CESD-10 score on each GOHAI question. The question related to the limitation of contact with other people due to teeth or dentures showed the most significant association with worsening depression: $\beta = -0.270$ in men and $\beta = -0.319$ in women. However, little to no discomfort while eating was associated with an improved depression status ($\beta = 0.367$ in men and $\beta = 0.328$ in women).

The sensitivity analysis results for the 2-year lagged transitions in terms of CESD-10 score changes on the GOHAI score are presented in Table 5. Compared to the same or improved CESD-10 score, worsening of the score by 1–2 points detected regression coefficients

TABLE 3 Subgroup analysis using the GEE of Geriatric Oral Health Assessment Index with depression status in 2020.

Variables	Geriatric Oral Health Assessment Index							
	Men				Women			
	Change in CESD-10 score							
	Same or improved	Worsened			Same or improved	Worsened		
	β	β	S.E.	*P*-value	β	β	S.E.	*P*-value
Age								
60–64	Ref.	−2.008	1.0770	0.062	Ref.	−0.872	0.7237	0.228
65–69	Ref.	−0.395	0.8357	0.637	Ref.	−1.462	0.8568	0.088
70–74	Ref.	−0.133	0.8945	0.882	Ref.	−1.790	0.7159	0.012
≥75	Ref.	−1.862	0.7840	0.018	Ref.	−0.831	0.6293	0.187
Region								
Urban area	Ref.	−2.397	0.7124	0.001	Ref.	−1.790	0.6185	0.004
Rural area	Ref.	−0.034	0.5762	0.953	Ref.	−0.999	0.4563	0.029
Employment status								
Employed	Ref.	0.010	0.7164	0.989	Ref.	−1.020	0.8673	0.239
Non-employed	Ref.	−1.709	0.5812	0.003	Ref.	−1.213	0.4099	0.003
Handgrip strength								
Normal	Ref.	−0.540	0.5060	0.286	Ref.	−0.745	0.4003	0.063
Abnormal	Ref.	−2.009	0.9684	0.038	Ref.	−2.648	0.8660	0.002

of −1.793 in men and −1.356 in women, and worsening by ≥3 points −3.614 in men and −2.533 in women, respectively.

4. Discussion

The substantial increase in the average life expectancy of people worldwide poses a challenge to public, social, and behavioral sciences, and medicine. Research has identified risk factors for poor oral health-related quality of life in older adults (19, 20). Strategies and interventions developed through a precise examination of the above-mentioned factors are expressly warranted to ensure that a greater proportion of our population ages without oral health-related discomfort.

The results contribute to the evidence that depression exacerbation during the previous 2 years is significantly associated with poor oral health-related quality of life. We found that the participants whose CESD-10 scores decreased had reported lower GOHAI scores than those whose depression status had remained the same or improved in the same period (Table 2). Furthermore, we found that the severity of depression exacerbation was negatively correlated with GOHAI scores in our study population. Those with a decrease in the CESD-10 scores of ≥3 points reported a greater decrease in overall geriatric oral health-related quality of life than those with a decrease of 1–2 points or with the same or improved depression condition (Table 5).

Our results are consistent with those of previous studies, namely, that depression was associated with a worsening of overall oral health-related quality of life. For example, one study found that the oral health impact profile was significantly associated with depression, stress, and self-esteem in community-dwelling middle-aged women (21). Although this was a cross-sectional study, the Pearson correlation coefficient of the correlation with depression ($r = -0.560$, $p < 0.001$) revealed a highly statistically significant outcome. Furthermore, another cross-sectional study involving participants with suspected dementia in Korea found that oral dryness and depression among older adults influenced oral health-related quality of life (10). A cross-sectional study using longitudinal data conducted in Germany by Hassel et al. reported that oral health-related quality of life was significantly linked to wellbeing and depression in later life, assuming that subjective health could mediate this relationship (22).

In the present study, a subgroup analysis of independent variables indicated that weak handgrip strength and worsened depression were related to lower oral health-related quality of life (Table 3). Previous research has observed an association between the GOHAI, its pain and discomfort dimension, and handgrip strength, suggesting that oral health problems associated with discomfort may be significant indicators of a decline in body muscle strength (23). The dependent subgroup analysis on the domains of the GOHAI revealed the link between the worsening of depression and limitation of social contacts due to oral problems, which supports the results of a cross-sectional study in Japan that assumed that depressive symptoms were significantly associated with social engagement, with greater associations in less mentally frail populations (24).

The etiology of the association between depression and oral health-related quality of life has not yet been well-elucidated. However, several possible biological (or bacterial and immunological) and behavioral mechanisms have been proposed. Changes in salivary immunity have been documented to be negatively associated with stressful life events (25). Therefore, a high life stress load would

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TABLE 4 Subgroup analysis using the GEE of Geriatric Oral Health Assessment Index questions with depression status.

Variables	Men				Women			
	Change in CESD-10 score							
	Same or improved	Worsened			Same or improved	Worsened		
	β	β	S.E.	*P*-value	β	β	S.E.	*P*-value
Geriatric Oral Health Assessment Index (questions)								
1. How often did you limit the kinds or amounts of food you eat because of problems with your teeth or dentures?	Ref.	−0.238	0.0664	0.0003	Ref.	−0.289	0.0518	<0.0001
2. How often did you have trouble biting or chewing different kinds of food, such as firm meat or apples?	Ref.	−0.221	0.0635	0.0005	Ref.	−0.237	0.0550	<0.0001
3. How often were you able to swallow comfortably?*	Ref.	0.279	0.0854	0.0011	Ref.	0.317	0.0691	<0.0001
4. How often have your teeth or dentures prevented you from speaking the way you want?	Ref.	−0.221	0.0684	0.0013	Ref.	−0.232	0.0555	<0.0001
5. How often were you able to eat anything without feeling discomfort?*	Ref.	0.367	0.0836	<0.0001	Ref.	0.328	0.0690	<0.0001
6. How often did you limit contact with other people because of the condition of your teeth or dentures?	Ref.	−0.270	0.0566	0.0006	Ref.	−0.319	0.0566	<0.0001
7. How often were you pleased or happy with the looks of your teeth and gums or dentures?*	Ref.	0.007	0.0818	0.9292	Ref.	−0.018	0.0677	0.7869
8. How often did you use medication to relieve pain or discomfort around your mouth?	Ref.	−0.202	0.0671	0.0027	Ref.	−0.227	0.0545	<0.0001
9. How often were you worried or concerned about problems with your teeth, gums, or dentures?	Ref.	−0.117	0.0644	0.0698	Ref.	−0.218	0.0559	<0.0001
10. How often did you feel nervous or self- conscious because of problems with teeth, gums, or dentures?	Ref.	−0.095	0.0658	0.1493	Ref.	−0.189	0.0555	0.0007
11. How often did you feel uncomfortable eating in front of other people because of problems with your teeth or dentures?	Ref.	−0.176	0.0641	0.0060	Ref.	−0.203	0.0537	0.0002
12. How often were your teeth or gums sensitive to hot, cold, or sweet foods?	Ref.	−0.161	0.0657	0.0143	Ref.	−0.226	0.0524	<0.0001

*Three positive questions were calculated by reversing the scores in main analysis.

seem to compromise either production or transport of the saliva secretion rate and given the prominent role of saliva in immune defense on mucosal surfaces (26), it may contribute to the onset of oral health problems. In addition, a positive association between the growth of lactobacilli and the use of anti-depressant medication when dental caries was considered an oral health outcome has been found (27, 28). The association between high lactobacillus counts and depressive symptoms suggests that depressed individuals are at a higher risk of developing caries and other dental diseases. The behavioral components were suggested to be related to the positive contribution of depression to poor oral health by acquiring and maintaining harmful oral habits (29, 30) and poor dental health (31).

The present study has several strengths and limitations. The main limitation of our study was that most of the data were self-reported and collected through surveys. Although we employed globally used and validated indexes for our main variables, we cannot exclude the risk of biased results. We also attempted to minimize the potential bias attributable to health selection by controlling for baseline health status. Second, the data of those who did not answer the essential covariate questions were excluded, which might have led to an underestimation of the conditions of some participants. Third, biological risk factors that might significantly affect the adjustment of variables may have been overlooked. Finally, causation could not be established due to the lack of a prospective design. We used the change in the depression condition between the two waves and analyzed its association with oral health-related quality of life in the subsequent wave to minimize the risk of reciprocal causation. However, the lack of data on GOHAI in previous years and poor oral-health-related quality of life might affect the severity of depression. Thus, future studies using a prospective design are needed to establish

TABLE 5 Generalized linear model using the generalized estimating equations with Geriatric Oral Health Assessment Index and the short form of Center for Epidemiological Studies Depression-10 scores change.

Variables	Geriatric Oral Health Assessment Index					
	Men			Women		
	β	S.E.	*P*-value	β	S.E.	*P*-value
Change in CESD-10 score						
Same or improved	Ref.			Ref.		
Worsened on 1–2 points*	−1.793	0.3146	<0.0001	−1.356	0.2665	<0.0001
Worsened on ≥3 points**	−3.614	0.6414	<0.0001	−2.533	0.4950	<0.0001

*Mild worsening.
**Severe worsening of depressive symptoms.

the causal relationship between changes in depressive symptoms and oral health-related quality of life.

Nonetheless, the strengths of our study include its longitudinal design, with the results representing the Korean older adult population of over 60 years. These findings can be applied to the general Korean population to establish healthcare policies or conduct future studies. Second, we used standardized tools to measure depression and oral health-related quality of life, which provides a substantial basis for future research. Finally, we used the change in depression rather than a timepoint depression estimation; thus, the results on depression as a changing over-time variable add novel information to the existing body of literature.

5. Conclusion

In conclusion, this study was conducted to assess the impact of changing depression conditions over time on geriatric oral health-related quality of life using longitudinal nationwide data of older adults in Korea. The findings of this study suggest that depression is negatively associated with oral health-related quality of life in later life. Participants with worsened depressive symptomology were more susceptible to poor oral health-related quality of life than those whose depression status remained the same or improved during the same period. The results also demonstrated that the severity of depression exacerbation was negatively correlated with GOHAI scores in our study population. Providing resources to assist older people with depression and on-time access to oral care may help prevent psychological distress and improve their chances of experiencing an improved oral health-related quality of life. Future studies addressing the underlying mechanisms of this association as well as the bidirectional preventive effects may provide valuable tactics for treating and preventing poor oral health-related quality of life.

Data availability statement

The datasets used during the study are publicly available in the Korean Longitudinal Study of Aging Repository via https://survey.keis.or.kr/klosa/klosa01.jsp. Any queries should be directed to the corresponding author.

Ethics statement

The KLoSA survey was approved by the National Statistical Office and Institutional Review Board of the Korea Centers for Disease Control and Prevention, with all methods following the relevant guidelines and regulations. As the KLoSA database is open for public use, ethical approval was not required for the study. All participants provided written informed consent to participate in the KLoSA survey and agreed to be used in further scientific research. The data were anonymized and de-recognizable with no personal information, with cautious protection on confidentiality. The patients/participants provided their written informed consent to participate in this study.

Author contributions

NN and S-IJ: conceptualization and visualization. NN, E-CP, and S-IJ: data curation and writing—review and editing. NN: formal analysis and writing—original draft. NN and E-CP: methodology. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Facilitators and inhibitors in hospital-to-home transitional care for elderly patients with chronic diseases: A meta-synthesis of qualitative studies

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Background: Chronic diseases are long-term, recurring and prolonged, requiring frequent travel to and from the hospital, community, and home settings to access different levels of care. Hospital-to-home transition is challenging travel for elderly patients with chronic diseases. Unhealthy care transition practices may be associated with an increased risk of adverse outcomes and readmission rates. The safety and quality of care transitions have gained global attention, and healthcare providers have a responsibility to help older adults make a smooth, safe, and healthy transition.

Objective: This study aims to provide a more comprehensive understanding of what may shape health transitions in older adults from multiple perspectives, including older chronic patients, caregivers, and healthcare providers.

Methods: Six databases were searched during January 2022, including Pubmed, web of science, Cochrane, Embase, CINAHL (EBSCO), and PsycINFO (Ovid). The qualitative meta-synthesis was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations. The quality of included studies was appraised using the Critical Appraisal Skills Programme (CASP) qualitative research appraisal tool. A narrative synthesis was conducted informed by Meleis's Theory of Transition.

Results: Seventeen studies identified individual and community-focused facilitators and inhibitors mapped to three themes, older adult resilience, relationships and connections, and uninterrupted care transfer supply chain.

Conclusion: This study identified potential transition facilitators and inhibitors for incoming older adults transitioning from hospital to home, and these findings may inform the development of interventions to target resilience in adapting to a new home environment, and human relations and connections for building partnerships, as well as an uninterrupted supply chain of care transfer at hospital-home delivery.

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KEYWORDS

older patients, chronic diseases, transitional care, discharge, qualitative research

Introduction

With the development of an aging population, chronic disease health problems are becoming increasingly prevalent and the coexistence of multiple diseases is becoming more severe among older adults worldwide (1). Approximately 50% of older adults are reported to have two or more chronic diseases (2). Compared to a single chronic disease, older adults with multiple diseases are associated with poorer quality of life, higher risk of adverse drug events, repeat care, and death (3), increasing the social and medical burden. In this context, with national efforts to reduce the burden of health care, coupled with increased hospital turnaround efficiency and shorter hospital stays, older adults with complex health problems often have more complex needs, requiring multiple health care providers to provide a wide range of health and geriatric care equipment in multiple care settings, as well as frequent transitions between hospital and home (4, 5). Approximately 1 in 5 older patients experienced adverse events during hospital-to-home transitions, including unplanned readmissions within a month of discharge, medication errors, and even death (6–8). These adverse events were associated with uncoordinated, discontinuous transitions of care across healthcare settings (9–12). Improving the safety and quality of care transitions had become a global concern (13, 14).

Transition is defined as the process of changing from one state, or condition to another, which is a complex, multidimensional process that encompasses awareness, engagement, and period (15, 16). Assisting patients in managing life transitions is a key function of nursing (16). The Transition from hospital to home is often a ternary process involving patients, families, and health care providers, and the common goal for the stakeholders involved is that older adults are able to make healthy transitions after discharge from the hospital in accordance with established goals or are supported in problematic transitions of care. According to Meleis' transition theory, healthy transitions are characterized by response patterns that include process indicators (e.g., coping skills) and outcome indicators (e.g., wellbeing). And some transition conditions at the individual level (e.g., cultural beliefs, attitudes, readiness and knowledge related to transition), community level (community resources and support), etc., and social level (e.g., social norms) can facilitate or inhibit healthy transitions (15).

To promote healthy and safe patient transitions, transitional care models have been developed to bridge the gap between patients in different healthcare settings and different levels of care by providing continuous, coordinated care (5, 17). However, there is some controversy about the effectiveness of implementing transitional care interventions (18, 19). Although studies have shown that transitional care has the potential to improve health system efficiency and reduce adverse events and lower patient readmission rates (20, 21), difficulties remain in improving user experience aspects and satisfaction (22, 23). User experience can improve the process and quality of healthcare delivery (4, 24–26). Several studies have focused on user experience and satisfaction in care transitions, and have received some review attention (23, 27–29). The more recent are Hestevik et al. (23), Chen et al. (29), Høy et al. (28), and Joo et al. (27). Høy et al. (28), and Hestevik et al. (23) explored the perspective of older adults and Joo et al. (27) included family caregivers in addition to patients. Chen et al. (29) reviewed the barriers and facilitators of transition care for stroke patients and their caregivers. This was a review of specific diseases. In contrast, the prevalence of multimorbidity in the elderly population is 55–98% (30), requiring us to focus on a broader population of chronic disease, not just the transition of patients with specific diseases. Høy et al. (28) drafted a protocol that focused on exploring patient preferences, challenges, and levels of involvement in care transitions. However, the protocol was only planned to include literature published after 2010. The main results of the more important his review have not been reported. Hestevik et al. (23) examined the experiences of older adults adjusting to daily life at home after discharge from the hospital, synthesizing the results of 13 studies as (i) experiencing an insecure and unsafe transition, (ii) settling into a new situation at home, (iii) what would I do without my informal caregiver? and (iv) experience of a paternalistic medical model. Joo et al. (27) reviewed seven studies to understand the experiences and perceptions of patients with chronic illnesses and their caregivers as they transitioned from a medical setting to home. They reported that the transition from hospital to home was influenced by the following barriers and facilitators: communication with multiple healthcare providers, self-management, and psychological stress and family caregiver support and nurse-provided patient-centered care. However, the study population was patients ≥18 years of age and older with chronic conditions. None of these reviews included studies of health care workers' perceptions of transitions of care for older adults. Without a doubt, patient experience is important for the quality of care during the transition and is considered one of the three cores of healthcare quality (31). Yet the transition of care is a triadic process involving patients, families, and health care professionals. Healthcare professionals, especially nurses, as the primary implementers and providers of transitional care, need to interact with other health care professionals, family members, and others in the transition of care to assess the biological, psychological, social, and emotional needs of the patient, and their perceptions and experiences also influence the patient's health transition (24, 32, 33).

Researchers have not identified a published systematic review examining the transition conditions of older adults from hospital to home that has included older adults, caregivers, and health care providers. To achieve this goal, researchers need to understand what facilitates and inhibits the transition process from the perspective of older adults, their family caregivers, and health care providers. The study aims to address this question: a more comprehensive understanding of what facilitates or inhibits the transition of older adults transitioning from hospital to home from multiple perspectives, based on Meleis' transition theory, is important for an evidence-based approach to developing interventions for care transitions.

Methods

Design

This is a systematic evaluation and meta-synthesis of qualitative research. Qualitative synthesis follows the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA).

The study aimed to address the following question: What facilitates or hinders the transition for older adults from hospital

to home? We used the SPICE framework (34) to formulate the review question. "Setting (where): healthcare facility, patient's home" "Perspective (for whom?): older adults transitioning from hospital to home, their caregivers, and health care providers" "Phenomena of interest: transition from hospital to home" "Comparison: not applicable" "Evaluation (with what results?): experiences, perceptions, facilitators, inhibitors."

Search strategy

A systematic electronic databases search was conducted during January 2022 for all English articles in six databases, including Pubmed, Web of Science, Cochrane, Embase, CINAHL (EBSCO), and PsycINFO (Ovid). There were no limitations on the year of publication. Searches were based on a combination of free-text keywords and indexed terms (MeSH) related to the terms: aged, elderly, chronic disease, transitional care, patient discharge, patient transfer, continuity of patient care, discharge, discharged home, transition, hospital-to-home, and qualitative research etc. (See Supplementary File 1 for search strategy).

Inclusion/exclusion criteria

Inclusion criteria: qualitative studies or mixed studies for which qualitative data could be extracted were included, including but not limited to phenomenological, root theory, and ethnographic studies; focus on multiple chronic conditions rather than one specific condition, as studies focusing on a single condition are too specific and not necessarily generalizable to older adults with multiple chronic conditions; all studies included older adults who were at least 60 years of age, as this is the World Health Organization definition of older adults; published in English.

Exclusion criteria: focus on the overall hospital/discharge experience rather than the transition experience from hospital to home; transition to a nursing home or specialized palliative care facility or rehabilitation center; conference proceedings or abstracts, review articles, editorials, clinical case reports, or review articles; articles collected using qualitative methods but analyzed using quantitative analysis; non-English language literature.

An initial search yielded a total of 3,129 articles. Two researchers independently screened and extracted literature by inclusion and exclusion criteria. The remaining 2,384 articles after removing duplicate literature. In addition, 117 papers remained after reading the titles and abstracts and 100 papers were deleted after reading the full text, for a total of 17 included studies. Seventeen papers were not deleted after quality assessment. The PRISMA flow chart was used in this process (Figure 1).

Quality appraisal

The Qualitative studies were appraised using The Critical Appraisal Skills Programme (2013) qualitative checklist comprising 10 items relating to rigor, credibility and relevance of qualitative studies (35). All items were scored as "yes" or "no" or "can't tell." Studies were scored as "high" or "medium" or "low" quality. Quality evaluations were performed by two independent authors, and when disagreements were encountered, a third author moderated. The final evaluation results are shown in Table 1.

Data extraction and synthesis

The study data extracted were: author, publication year, country, design, setting and sampling, method(s) of data collection, data analysis strategy and aims. Study findings were extracted from the findings/results section of each paper. Thematic synthesis was conducted using a three-stage process (36). Stage 1: the coding of the selected studies text line-by-line. Stage 2: a review of the coding with grouping to generate descriptive themes and subthemes. We drew upon Meleis's Transition theory (37) for data a narrative synthesis, specifically, the domain "transition conditions" to classify potential facilitators and inhibitors as personal, community or societal. Stage 3: the generation of abstract themes or analytic themes.

Results

A total of 17 studies were included, with studies from a total of nine countries: the United States ($n = 7$), Turkey ($n = 2$), Canada ($n = 2$), Australia ($n = 1$), Tran ($n = 1$), Norway ($n = 1$), Italy ($n = 1$), the United Kingdom ($n = 1$), and Ireland ($n = 1$). Six of the studies had theoretical or conceptual frameworks involving active recovery models, social-ecological perspectives, transition theory, social-ecological models of health behavior, positive deviance frameworks, and constructivism. The sample of participants varied across studies. Eleven of the 17 studies included older adults, 12 studies investigated the perspectives of their caregivers, and 3 studies explored the perspectives of health care providers. Each study was systematically assessed for study purpose, study methodology, sample size, study setting, and country in which the study occurred (Table 2). The methodological quality of the included studies was variable, with 2 being rated as high and 15 as moderate. None of the studies were excluded due to study quality issues.

In this review, Personal and community focused facilitators and inhibitors were identified that mapped to there themes: (1) Resilience in older adults; (2) Interpersonal connections and relationships; (3) Uninterrupted transfer of care supply chain (Table 3). These facilitators and inhibitors existed at the health care provider level, at the patient and family level, and at the health system level.

Resilience in older adults

Resilience in older adults refers to the ability of the elderly to accept the transition from hospital to home and to make sense of the benefits and losses associated with the transition. We identified several facilitators and barriers that were compatible with Meleis's personal and community transition conditions.

For older adults, the perceived benefits of going home include access to comfort, freedom (e.g., following one's own opinions in daily life without the constraints and supervision of organizations), safety (avoiding hospital-acquired infectious risks), and a sense of personal control (4, 25, 38). Care transitions can be a difficult and unsafe time for most participants (25, 38–40). Resilience as a force

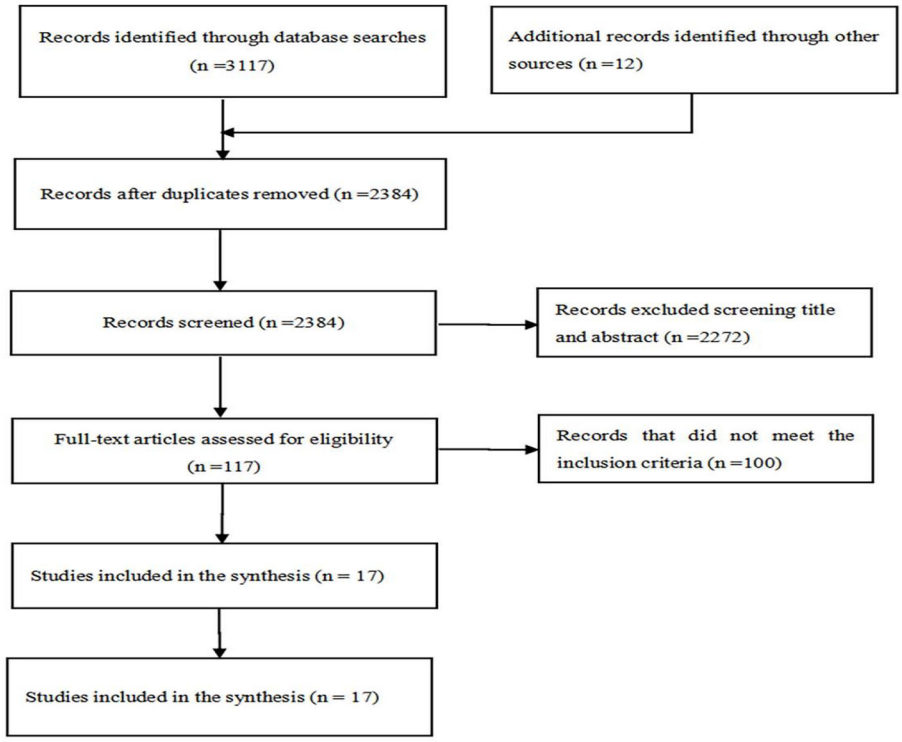

FIGURE 1
PRISMA flow diagram.

TABLE 1 Evaluation of methodological quality.

Included studies	Questions										Quality appraisal indicator
	①	②	③	④	⑤	⑥	⑦	⑧	⑨	⑩	
Dolu et al. (24)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	H
Dolu et al. (25)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Neiterman et al. (38)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Bull (41)	Y	Y	Y	Y	Y	?	?	Y	Y	Y	M
Bull and Jervis (42)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Backman et al. (43)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Allen et al. (4)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
La Manna et al. (39)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	H
Graham et al. (49)	Y	Y	Y	Y	Y	?	?	Y	Y	Y	M
Backman and Cho-Young (46)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Davis et al. (50)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Hvalvik and Reierson (48)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
McKeown (45)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Plank et al. (47)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Baxter et al. (44)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Foust et al. (26)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M
Nikbakht-Nasrabadi et al. (40)	Y	Y	Y	Y	Y	?	Y	Y	Y	Y	M

Y, Yes; N, No; ?, Can't tell. Quality appraisal indicator—"H" = High, "M" = Medium, "L" = Low. Adapted from Critical Appraisal Skills Programme (2013). ①: Was there a clear statement of the aims of the research? ②:Is a qualitative methodology appropriate? ③: Was the research design appropriate to address the aims of the research? ④: Was the recruitment strategy appropriate to the aims of the research? ⑤: Was the data collected in a way that addressed the research issue? ⑥: Has the relationship between researcher and participants been adequately considered? ⑦: Have ethical issues been taken into consideration? ⑧: Was the data analysis sufficiently rigorous? ⑨: Is there a clear statement of findings? ⑩: How valuable is the research?.

TABLE 2 Summary of included studies.

Author	Population and setting	Sample	Design	Aim (s)
Dolu et al. (24) 2021 Turkey	Healthcare providers. Both public and private community healthcare sectors in an urban area of Turkey.	$N = 13$ (5 general physicians and 8 nurses) The average age of healthcare staff was 41.6 years.	Qualitative study, purposive sampling, In-depth semi structured interviews, thematic analysis	To explore the perspectives of healthcare providers, including nurses and physicians, regarding transitional care from hospital to home in an urban area of Turkey
Dolu et al. (25) 2021 Turkey	Older patients and family caregivers. Patients' home.	$N = 25$ (14 older patients and 11 family caregivers) The mean age of the older adults was 79 years.	Qualitative exploratory descriptive study, purposive sampling, in-depth semi-structured interviews, thematic analysis, proactive rehabilitation model	To explore the perspectives of patients aged 65 years and over and their family caregivers transitioning from hospital to home in an urban area of Turkey.
Neiterman et al. (38) 2015 Canada	Older patients and family caregivers. Patients' home.	$N = 36$ (17 older patients and 19 family caregivers) The mean age of the older adults was 79 years.	Qualitative study, purposive sampling, semi-structured interviews, thematic analysis	To examine how the care transition was experienced, organized, and coordinated by patients and their informal caregivers at home.
Bull (41) 1992 America	Older adults and family members. Patients' homes.	$N = 55$ (17 older patients and 19 family caregivers) The mean age of the older adults was 67 years.	Qualitative study, purposive sampling, semi-structured interview, contant comparative method	To describes the period of transition from hospital to home based on the perspectives of the older adults and family members who experience it
Bull and Jervis (42) 1997 America	Older women and caregiving daughter. Participants' homes and private offices.	33 mother-daughter pairs at 2 weeks post-discharge (response rate 94%) and 32 pairs at 2 months post-discharge. The average age of the mothers was 73.9 years.	Qualitative study, grounded theory study, purposive sampling, semi-structured interviews, content analysis and constant comparison	To learn how older women and their caregiving daughters managed care following the mother's hospitalization because of a chronic illness.
Backman et al. (43) 2018 Canada	Patients with multiple chronic conditions and family members. Patients' home.	$N = 9$(4 older adults alone, 3 family members alone, and 2 older adult/family member together) Mean age of 77.6 years.	Descriptive qualitative study, participatory visual narrative methods, convenience sampling, thematic analysis, socio-ecological perspective	To engage older adults with multiple chronic conditions and their family members in the detailed exploration of their experiences during transitions across health care settings and identify potential areas for future interventions.
Allen et al. (4) 2018 Australian	Patients and caregivers. Patients' home.	$N = 26$ (19 Patients and 7 carers) Participants were aged on average 78.9 years.	Descriptive qualitative study, purposive sampling, semi-structured interviews, thematic analysis, constructivism	How do older people and their carers/families as care recipient service users, experience discharge and transitional care across the trajectories of acute, subacute and community care?
La Manna et al. (39) 2018 America	Older Patients. Patients' home.	$N = 96$ (Multimorbidity was prevalent among study participants) Mean age of 75.15 years.	Quantitative-qualitative, mixed-method design, inductive content analysis techniques, transition theory	To examine self-described hospital-to-home transition challenges encountered by older adults with a diagnosis of diabetes within the first 30 days following discharge
Graham et al. (49) 2009 America	Older person and cares. NR	Twenty focus groups ($n = 159$ caregivers included family members, friends, and paid informal caregivers) and focus group ($n = 5$, The five seniors selected were age 60 or older).	Qualitative study, purposive sampling, qualitative thematic analysis, social ecological model of health behavior	To assess the needs of patients and caregivers during the transition from hospital to home.
Backman and Cho-Young (46) 2019 America	Patients and informal caregivers. NR	$N = 8$ (Patients and informal caregivers). Mean age of 72.29 years.	Qualitative descriptive study semi-structured telephone interviews, convenience sampling, thematic analysis	To describe patients and informal caregivers' perspectives on how to improve and monitor care during transitions from hospital to home
Davis et al. (50) 2012 America	Health care professionals, clinicians, care teams, and administrators from the inpatient general medicine services at one urban, academic hospital; Two outpatient primary care clinics.	13 focus groups and two in-depth interviews with 75 health care professionals and administrators. The average age of healthcare staff was 42 years.	Cross-sectional qualitative study, purposive sampling, thematic analysis	To understand care transitions from the perspective of diverse healthcare professionals, and identify recommendations for process improvement.

(Continued)

TABLE 2 (Continued)

Author	Population and setting	Sample	Design	Aim (s)
Hvalvik and Reierson (48) 2015 Norway	The next of kin to an older patient (age 67 and older):such as spouse, sons, or daughters. NR	$N = 11$ (one son, two spouses, and eight daughters)	Phenomenological hermeneutic design, individual, narrative interviews, purposive sampling	To describe and illuminate the meaning of the next of kin's lived experiences during the transition of an older person with continuing care needs from hospital to home.
McKeown (45) 2007 Ireland	Older people (in their homes two weeks following discharge from acute hospital). Patients' home.	$N = 11$ (6 males and 5 females) The age of elderly entry ranged from 71–92 years old.	Qualitative study, phenomenological approach, semi-structured interview, purposive sampling	To explore the experiences of older people on discharge from hospital following assessment by the public health nurse
Plank et al. (47) 2012 Italy	Informal caregivers. Rehabilitation unit.	$N = 18$ (8 participating in individual interviews and 10 participating in post discharge focus groups, three caregivers attended both the interview and the focus group)	Qualitative phenome nological approach, in-depth interview, focus group, purposive sampling	To explore and understand the experience of new informal caregivers in Italy in the time of transition from hospital to home, focusing on their thoughts and reflections.
Baxter et al. (44) 2020 UK	Multidisciplinary staff. Six high-performing general practices and hospital specialtie.	$N = 157$(including doctors, nurses, healthcare assistants, allied health professionals, discharge coordinators, district nurses, community matrons, specialist nurses and receptionists/administrators).	Qualitative study, focus groups, interviews and brief observations, in semi-structured focus groups or interviews and meetings, opportunity and maximum variation purposive sampling, pen portrait approach, positive deviance framework	To explore how high-performing general practice and hospital teams successfully deliver safe care to older adults during transitions from hospital to home
Foust et al. (26) 2011 America	Older adults, carers, health providers. Patients' home and hospital	$N = 90$ (40 patients, 35 informal caregivers, and 15 clinicians). The mean age of patients was 64.8 years.	Descriptive qualitative, semi-structured Interview, content analysis, purposive sample	To describe the hospital-to-home transition from the three perspectives of home health patients, their informal caregivers, and home health care clinicians
Nikbakht-Nasrabadi et al. (40) 2021 Iran	Family caregivers. Either in their home or other else	$N = 15$ (family caregivers of patients with multiple chronic conditions).	Descriptive exploratory qualitative study, in-depth semi-structured, face-to-face interviews, purposive sample, content analysis	To explore the experiences of family caregivers of transitional care in diabetes with concurrent chronic conditions

against adversity involves positive thinking, lifestyle changes and engagement in self-management to readjust within an unstructured family environment, become independent and re-establish new routines (4, 25, 41–43). Adapting to a new environment at home and achieving a safe transition seem to benefit from personal traits such as motivation, initiative, and cooperation (4, 43, 44). One contributing factor was the personal belief that older adults want to be independent, which motivated them to find a personal strategy and solution to the dilemma of care transition and dependency.

During the care transition, older adults had difficulties with self-management in daily living, professional care and follow-up care, such as dressing, eating, bathing and transportation, medications, wounds, follow-up visits (4, 24, 38, 39, 41, 42, 45). Potential facilitators of transition were reinvention strategies used by older adults to meet independence and personal care needs, such as self-motivation, acting on previous experiences, developing schedules, engaging in activities of daily living and co-learning, proactively seeking help from others, integrating valid information, and mastering self-care skills (e.g., complex medication management) (4, 25, 41–43).

Inhibiting factors were negative perceived transitions as discontinuity and powerlessness, loss (25, 39, 41, 43, 46), which were related to the patient's health status, roles and relationships, daily life and hobbies, and gaps in self-care knowledge. Fear of leaving the hospital exacerbates disease progression in older adults due to unresolved physical symptoms (25). Patients with delayed self-recovery feel depressed and frustrated (39). Older adults presented a strong care dependency during transition. Participants indicated that maintaining daily life and managing complex health issues after returning home was a challenge (4, 24, 38, 39, 41, 42, 45) and that daily management and hobbies required forced changes (38, 41, 45). Gaps in knowledge when dealing with physical changes and adverse reactions can leave participants will be in a difficult situation (38, 39, 46).

Interpersonal connections and relationships

Interpersonal relationships and connections among older adults concentrated among family caregivers (including spouses, children, neighbors, friends, etc.), and health care providers. We identified several facilitators and barriers that were compatible with Meleis's personal and community transition conditions.

Patient-caregiver connections and relationships: a positive and strong relationship with caregivers was an important factor for a smooth transition for older patients. Caregivers actively empowered, advocated, and motivated patients in care transitions (4, 41–43, 45,

TABLE 3 Transition facilitators and inhibitors.

Theme	Transition conditions PC = Personal conditions, CC = Community conditions, SC = Societal conditions	References
Resilience in older adults;	**Facilitators**	
	• Coping strategies (PC): such as - Acting on past experience - Creating a schedule, adapting the home environment - Integrating effective information - Learning self-care skills	(4, 25, 41–43)
	• Personal Traits (PC):positive, cooperative	(4, 43, 44)
	Inhibitors	
	• Negative perception transition (PC)	(25, 39, 41, 43, 46)
	• Knowledge gap in managing symptoms (PC)	(39, 46)
Interpersonal connections and relationships		
Patient-caregiver connections and relationships	**Facilitators**	
	• A positive, caring relationship (CC)	(4, 43, 46)
	• Family caregivers actively empower, advocate, and motivate patients (CC): - Practical support e.g., life care, professional care - Emotional support e.g., courage, willingness to care	(4, 25, 41–43, 45, 47, 48)
	• Cultural concept of filial piety (CC)	(49)
	Inhibitors	
	• Residence status: especially widowed elderly living alone (PC)	(38, 45)
	• Physical and mental symptoms and financial burden of caregivers (PC)	(39, 40)
Patient/caregiver-healthcare provider connections and relationships	**Facilitators**	
	• Healthcare providers making efforts to understand patients (CC)	(44)
	• Caring from a healthcare providers (CC)	(4)
	• Patients and families participate in care decisions together (CC)	(4, 43)
	• Setting Navigator/Transitional Care Coordinator (CC)	(38, 46)
	Inhibitors	
	• Indifferent tone and attitude of health care providers (PC)	(40)
	• Use of terminology in conversation (PC)	(25, 26)
	• Ignore identity presentation and interaction (CC)	(4)
	• Organizational factors: such as specific time and workload constraints (CC)	(25, 43)
	• E-health literacy (CC)	(50)
Connections an relationships between health care providers	**Facilitators**	
	• Regular meetings (CC)	(44, 50)
	• Mutual trust between healthcare providers to support or quickly respond to requests (CC)	(44)
	• Communication media e.g., letters, electronic medical records or digital calls supported by technology (CC)	(46)
	Inhibitors	
	• Employee rotation and reorganization (CC)	(44, 50)
	• Hospitals and community organizations are independent (CC)	(44, 50)
	• Communication media e.g., letters, electronic medical records or digital calls supported by technology (CC)	(50)
Uninterrupted transfer of care supply chain	**Facilitators**	

(Continued)

TABLE 3 (Continued)

Theme	Transition conditions PC = Personal conditions, CC = Community conditions, SC = Societal conditions	References
	• Care coordination practices (CC), for example - Discharge coordinator: transition nurse - Multidisciplinary team to reach consensus on care transition delivery through meetings. - Patient and family participation in decision making, monitoring or supplementing the care transition process. - well-developed electronic systems and written information from a holistic perspective	(25, 38, 43, 44, 46, 47, 49)
	Inhibitors	
	• Lack of standardized processes and fragmented communication (CC)	(43, 46, 50)
	• Different positioning of healthcare providers (CC)	(44, 50)
	• Gaps in discharge planning (CC): handover of discharge t information	(24, 26, 46, 47, 50)
	• Approaches to care (CC), such as -Care provider-centered care -Organization of care (e.g., organizational responsibilities are not clearly defined)	(4, 38, 40, 43, 50)
	• Human resource limitations (CC), for example - Inadequate staffing - Insufficient staff knowledge and skill level - Family caregiver avoidance and misconceptions about caregiving responsibilities	(24, 38, 45, 47, 49)
	• Patients' residential distance (CC),	(45, 49)
	• Adherence to healthcare authority (PC)	(25)

47, 48), including closely monitoring older adults' health status; facilitating communication between older adults and health care providers; helping older adults improve their self-management; and focusing on the care delivery process to ensure a smooth transition. In addition, caregivers provided emotional support, such as hope, courage, and willingness to enter the caregiver role, so that patients felt dependent and confident as well as unabandoned (4, 43, 47). In some cultural settings, the value of filial piety became a double-edged sword and caregivers and patients had to live together. Cultural values and practices that do not allow elderly people to be sent to nursing homes constitute, at another level, a barrier to the use of formal care (49).

Caregivers experienced physical and emotional and financial stress when confronted with the complexity and number of chronic illnesses suffered by family members, combined with their own physical condition and work and patient cooperation, which may result in burnout and avoidance (39, 40). In addition, An important inhibiting factor was the patient's residential status (38, 45). Older adults who were widowed, especially those who live alone, were vulnerable to the loss of basic social relationships and connections, which not only exacerbated depression and isolation (45); they also tended to miss out on the symptom monitoring and care support provided by their families and put themselves at a disadvantage (38).

Interpersonal relationships and connections between older patients and families and healthcare providers was identified as potential facilitators and inhibitors of health transitions (4, 25, 38, 43, 44, 48). The nature of the relationship between older adults and health care providers was diverse and was described as collaborative and supportive (43), caring (4), trusting rapport (44), and skeptical (47, 48). Promoting meaningful patient/caregiver-provider relationships was a way for healthcare providers proactively spend more time with patients or families in an effort to understand the health status and care needs (44); to involve patients and families in healthcare decisions (4); to conduct regular follow-up visits (46); and, especially in cross-border situations, to establish intermediaries to navigate relationships, organize contacts to ensure patients know when problems arise whom to contact (38, 46).

Inhibiting factors were included: indifferent tone and attitude of medical provision (40); use of medical jargon in conversations; giving verbal information that may be forgotten and written information that is not readable (25, 26); neglected identity presentations and interactions (4); poor previous care and medical records (47); and organizational factors such as specific working hours and workload limitations (25, 43). A potential inhibiting factor lay in electronic communication devices (50). Older adults with limited e-health literacy had difficulty staying in communication with health professionals in digitally supported conversation and appointment systems and felt separated and alienated from their interpersonal relationships.

Establishing or maintaining valuable relationships among health care providers appeared to be important in facilitating the transition of older adults (44, 45). One barrier factor was the instability of relationships between healthcare providers, which was a matter of systems and organizational processes, such as regular staff rotation and reorganization, which meant that old familiar partnerships were broken up and had to be regrouped; the independence of hospitals and community health organizations from each other lacking feedback on patient transition status, channels for sharing and opportunities for cross-border learning, which reduced interpersonal interactions and contacts among healthcare providers and thus may not allow for timely tracking of patient transition status (44, 50). Communication media such as letters, electronic medical records, or digital calls supported by technology were considered potential facilitators or inhibitors that helped facilitate valuable contact between healthcare providers regarding patient follow-up care services (46) or relyed solely on electronic cases to

convey information or discharge processes, neglecting interpersonal communication (50). Trust was a cornerstone of many relationships among healthcare teams and an important facilitator of maintaining connections. Mutual support or rapid response to requests among healthcare members across settings helps strengthen relationships and connections (44). Regular meetings brought members of teams together, and such multidisciplinary meetings provided opportunities for socialization and interaction, not only to maintain contact and relationships, but also to support patients through verbal communication (44, 50).

Uninterrupted transfer of care supply chain

The theme of uninterrupted transfer of care supply chain centered on care coordination, approaches to care, and workforce factors. Potential facilitators and inhibitors corresponded with Meleis's personal and community transition conditions.

Care coordination was a facilitator of hospital-home care delivery for patients (25, 38, 43, 44, 46, 47, 49). An important manifestation of care coordination was the discharge coordinator, who was the central point of contact between the hospital and the community agency or family physician or general practitioner, especially the transition nurse, who was familiar with the way the health system works and provided a liaison for care coordination across hospitals/communities (25, 38, 43, 44, 46, 49). Whereas, communication was considered an important means of care coordination, multidisciplinary teams share information seamlessly between different team members and/or specialists through formal or informal meetings, raised relevant issues, and set transition goals and priorities to reach consensus on care delivery to avoid inconsistency and loss of trust (47). Other facilitators included involving patients and families in discharge planning decisions and discussions, the ability of patients and families to add and share more nuanced information as they move across health care settings to help care providers better understand the situation and make decisions (25, 46), or monitoring the entire care delivery process so that information was not misplaced (46, 48). Potential facilitators included well-developed electronic systems and written information with a holistic perspective so that staff in care transition delivery act on established plans and relevant symptom management knowledge and information (24).

Factors impeding care coordination included: lack of standardized processes and fragmented communication (43, 46, 50) differences in the positioning of hospital and community care providers' roles and thus priorities and goals, and possible conflicting values and understandings that impede care coordination (44, 50); other inhibiting factors included: gaps in discharge planning, where patients and caregivers were often passive and hastily accepted discharge plans (26); arbitrary and incomplete handover of discharge information, e.g., care provides giving verbal information that may be forgotten, and primary care providers or family physicians do not receive or delay receiving or receive incorrect, unclear discharge information or letters (24, 26, 46, 47, 50).

Approaches to care had the potential to inhibit transition. This included: approaches to care that promoted resident care dependence rather than greater patient self-management (4); care provider-centered care that did not take into account patient preferences and uniqueness (40, 43); and care organization (e.g., organizational responsibilities were not clearly defined (50), multiple care providers emerged in a confusing manner after discharge, and patients did not know who to contact when problems arose (38).

A potential inhibiting factor was human resources. With inadequate staffing, patients felt abandoned and helpless by the organization as they were unable to receive accurate care and assistance from medical staff at the right time or when they needed it most (38, 45). The limited level of knowledge and skills in the hospital-to-home delivery process, e.g., home health care providers were powerless in the face of new medical equipment due to gaps in continuing education (24). And family caregivers' ambiguous answers to questions about symptoms, questioning their ability to provide home care, and thus avoiding responsibility for home care or the misperception that it should be borne entirely by the health care provider, were often associated with limited discharge planning (24, 47).

In addition, other inhibiting factors including the distance patients live (45, 49) and adherence to medical authority (25) also hindered care delivery. If older adults were afraid to question care delivery methods and questions or live far from hospitals, communities, or in rural areas where there was a lack of primary care organizations, the lack of continuous supply of care services may affect patient transition.

Discussions

The ideal outcome for older adults transitioning from hospital to home is a healthy transition in which the physical, psychological, and emotional needs of older adults with follow-up care services are met and independence is gradually achieved. Our systematic review identified factors that may facilitate or inhibit healthy transitions from hospital to home for older adults, with implications for the development of transitional care services. Facilitators and barriers were mapped to three themes with an individual and community focus: Resilience in older adults; Interpersonal connections and relationships; Uninterrupted transfer of care supply chain. These themes resonate with the broader international literature (30, 51–54) on the losses and gains of care transitions (51, 52), elements that reduce readmission rates for older patients with chronic conditions (30, 53), and competencies needed for transitional care providers (54), such as: education and promotion of self-management, maintenance of relationships and promotion of coordination, communication and health care provider training.

For the topic of resilience in older adults, person-centered transition facilitators included older adults' values, positive personal attributes, and personal coping strategies in the face of self-management barriers. Chronic illness is a problem-based endeavor in which participants, with limited medical resources, often act on previous experiences, struggle to seek help, and employ self-management strategies to deal with health issues. Older adults want to be as independent as possible and stay at home for as long as possible. Personal strategies driven by beliefs to cope with self-management barriers emerge to make a smooth transition possible. Previous research had also found that older adults were struggling to find ways to master new situations that were useful and not burdensome for others (55). However, in the actual transition, there is a gap between the self-management performed

by older adults and the self-management imagined in the discharge instructions (56). The lack of knowledge and self-management skills led to uncertainty and anxiety in some participants. In addition, unresolved somatic symptoms, delayed recovery from self-care, difficulties in daily management and processing of information, and inadequate social support also had an impact on patients' psychological mood. These physically, psychologically, and socially diverse factors contribute to the uncertainty and powerlessness of patients' transitions. This is consistent with studies by Joo et al. (27) and Hardy et al. (57). MacLeod et al. (58) reported that resilience interventions currently designed for older adults are often not available *per se*, but seem to show life for resilience building by improving adaptive coping, changing complex emotional responses (e.g., anxiety, depression), and social support. Patients with chronic illness often need knowledge in order to objectively interpret the illness and cope effectively. In this context, patient education before discharge and intensive self-management training after discharge seem to facilitate patients' adaptation to the transition (30, 59, 60). Furthermore, in the theme of uninterrupted care supply transfer chain we mentioned the impediment of caregiver (family caregivers and medical caregivers) incompetence to care transition. Therefore, in addition to patients, formal and informal caregivers need to develop competencies to help patients with self-management education and training.

The two mindsets of older chronically ill patients regarding care transition gains and losses are intertwined and constantly dynamic. Participants can be seen to have gained some important developments in their care transitions, such as: regaining independence, sense of personal control, etc. However, unsurprisingly, some participants appeared to experience fewer gains, and their journeys contained more pronounced losses than others, reporting strong feelings of anxiety, depression, and becoming barriers to transition. Notably, although psychological problems such as anxiety and depression are common in patients after discharge, screening is not routinely performed at discharge. Common outcome indicators for most transitional care interventions remain objective indicators such as readmission rates and mortality (61), with limited attention to patient-related outcomes, such as complex emotional problems. A prospective study reported (62) that hospital-home transition, as a period when older adults are at high risk for depressive symptoms, screening for identification of depressive symptoms and assessment of coping skills at discharge may be a potentially preventive intervention. Esche et al. (52) showed that resilience, as a factor that must be considered when transitioning older adults from hospital home, requires early identification by nurses and help those patients with low resilience to succeed in the home environment. Thus, these facilitators and barriers have the potential to inform the development of resilience-specific interventions to promote the psychological, social, and physical wellbeing of older patients with chronic conditions during transitions of care. Furthermore, intervention development has to consider the potential contribution of conceptual models such as Meleis' transition theory, the active recovery model, and the social ecology of health promotion.

Connections and relationships between the elderly and their caregivers, healthcare providers, and healthcare workers play an important role in facilitating and inhibiting patient transition and engagement in care. Our study suggests that patient and family caregiver partnerships that fill supply gaps, navigate the health care system, and advocate on behalf of patients can improve the health wellbeing of older adults. Findings also highlight that contextual factors (e.g., cultural attributes, roles and responsibilities of family members, residential status, etc.) must be considered to support these important relationships. There is a link between interpersonal continuity and patient satisfaction with health care (63). The medical staff can act as a barrier or facilitator, depending on his communication skills and ability to involve patients in decision making. Our study showed that a cordial, trusting relationship with the provider was an important factor in facilitating transition and supporting patient involvement, which is consistent with a study by Stolee et al. (64), which reported similar characteristics of a beneficial patient-provider relationship, including trust and respect, and guided patient and family involvement in decision making related to treatment during the transition. Moreover, a study by Mitchell et al. found that cold, brief discourse was detrimental to the establishment and maintenance of the relationship. This is consistent with our study's findings. To facilitate communication and connection and improve relationships with healthcare professionals, information communicated verbally and in writing must be shared in language that is jargon-free and easily understood by service users and caregivers. Health care workers need biopsychosocial training including communication skills, the need to consider the risk of giving inadequate or marginalized elderly wellness, and the need to assess the ability and understanding of older adults to understand information to ensure that both parties are working at a uniform level and to correct inequalities in power between service users and providers, which is particularly important in the new person-centered care model promulgated by WHO and other health agencies (65, 66).

Our study also highlights the importance of maintaining relationships and connections among HCPs. Previous studies have shown that healthcare providers establish cross-border relationships that can overcome discontinuous letters and uncertainty at transition (67). Healthcare providers have also indicated that regular meeting interactions (formal or informal) provide opportunities and channels for knowledge sharing, information feedback, and interpersonal communication that not only help healthcare providers gain knowledge of each other's work environment and develop interpersonal relationships, but also build trust and mutual understanding of each other's roles of responsibility, thereby maintaining organizational stability and continuity of patient care treatment during hospital-to-home transitions and consistency of patient care during the hospital-to-home transition (68, 69). Participants perceived that healthcare professionals build trusting relationships that allow for rapid response to each other during care transitions. A previous study by Bryn et al. (70) demonstrated little effective tools to support trust among HCPs when collaborating across borders when in different locations and lacking shared electronic health records, and at the broader health care system level. Baxter et al. (44) suggested that supporting staff to build and maintain relationships should be prioritized from an organizational systems perspective, such as minimizing staff rotation or having the same values and beliefs among staff.

Transitions are uncertain and complex (37), and the transition of older adults from hospital to home is not a linear process, but one of cross-cultural challenges for two organizations with different values and priorities. Some participants indicated that the different

positioning and nature of services between hospitals and community agencies influence Healthcare workers' perceptions, expectations, and priorities for care transitions (25, 44, 50). Healthcare professionals need to be familiar with each other's roles and functions and clearly position themselves to minimize professional, cultural, and organizational differences (71). In fact, care plans and instructions between providers still conflict with each other. Previously Naylor et al.'s (11) transitional care model utilized transitional care coaches to facilitate care coordination through the advanced practice nurse and Coleman et al.'s (60) transitional care intervention model. Participants (25, 38, 43, 44, 46, 49) also reported that roles in the nursing process can facilitate care transitions and ensure an uninterrupted supply chain of care delivery. The importance of nurses as core healthcare practitioners and facilitators of transitional care continues to emerge. This is due to the professional status of nurses and their close interaction with patients, their familiarity with the way health systems work, and their leadership in collaboration. In the past few years, several Meta-analyses have shown that nurse-led transitional care, which respects patients' independence and decision-making power in care, is effective in increasing satisfaction, improving health status, reducing readmission rates, and is cost-effective and economically efficient (72, 73). Despite these developments, the inclusion of 17 studies in our review, only 3 of which investigated the views of medical caregivers, and no qualitative studies of transition nurses have been included, is a weakness of the existing literature. This supports our call for all stakeholders to be involved. Future research could therefore explore how nurses face barriers and experiences in collaborating across organizations.

Limitation

A systematic review of multiple perspectives of older patients, caregivers, and health professionals using Meleis' transition theory constructed our conceptualization of situational transitions and helped us classify facilitative and barrier factors with the help of the transition condition domain. However, we only included studies published in English in our review, so we may have missed relevant studies from non-English speaking countries, a potential language bias; there was a little theoretical framework in the studies and the timeline of the transition process varied, with some studies collected from the day patients were discharged and some 1 month or more after, and the heterogeneity of patient experiences and feelings limits the generalizability of the study to some extent. Finally, as this was a secondary analysis, we were unable to confirm our themes and consequences with the study participants.

Implications for practice

Identify individual and community-focused facilitators and inhibitors to inform the development of interventions to promote healthy transitions in older adults.

- Assess the psychological status of older adults at discharge in addition to the physical status of the patient.
- Healthcare staff need to improve capacity in addition to enhancing patient and family education.
- Build trusting relationships between health care providers, professionals, and older adults and their caregivers.
- Further explore the perceptions of health care workers, especially transition nurses, regarding transitions of care in order to improve transition care at the organizational system level.

Conclusions

This study identified potential transition facilitators and inhibitors for incoming older adults transitioning from hospital to home, and these findings may inform the development of interventions to target key areas of resilience in adapting to a new home environment, and human relations and connections for building partnerships, as well as an uninterrupted supply chain of care transfer at hospital-home delivery.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

MS and JW were responsible for the conception, design of the review, literature search and screening, analysis and interpretation of data, and drafted the manuscript. LL contributed to the data acquisition and interpretation and revised the paper. MZ, TX, and YQ contributed to data analysis and interpretation. RD contributed to the design of the review and revised of the manuscript. All authors approved the final version of the manuscript for submission and the type of the magazine.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1047723/full#supplementary-material

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Promoting the well-being of rural elderly people for longevity among different birth generations: A healthy lifestyle perspective

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Background: Wellbeing may have a protective role in health maintenance. However, no specific study clarified the particular protective effect of the subjective wellbeing of rural elderly people on survival probability. Few studies have examined the effect of the lifestyle of rural elderly people on their subjective wellbeing from different perspectives. We investigated whether improving subjective wellbeing increased the probability of longevity of rural elderly people and the effects of lifestyle behaviors on the subjective wellbeing of rural elderly people in different birth generations.

Materials and methods: Data were derived from the China Health and Nutrition Survey (CHNS), which is an ongoing open cohort study that adopts a multistage, random clustered sampling process. We used the data of elderly people who were aged 65 or over during 2006–2015 for analysis. The Kaplan–Meier method and log-rank test found that the survival probability of rural elderly people was significantly lower than urban elderly people. Based on a sample of rural elderly people, Cox regression and generalized estimating equations were performed as further analyses.

Results: A total of 892 rural elderly people aged 65 or over were included in the sample in 2006. High subjective wellbeing was a protective factor against death. The subjective wellbeing of rural elderly people born in the 1940s/1930s/1908–1920s birth generations first decreased then increased. For rural elderly people born in the 1940s, there were significant positive effects of a preference for eating vegetables and walking/Tai Chi on subjective wellbeing. For rural elderly people born in the 1930s, preferences for eating vegetables, reading, and watching TV all had significant positive effects on subjective wellbeing. Rural elderly people born in the 1908–1920s who preferred watching TV had more subjective wellbeing.

Conclusion: Improving subjective wellbeing extended the life span and reduced mortality risk in rural elderly people and may be achieved by the shaping of a healthy lifestyle, such as preferences for eating vegetables, walking/Tai Chi, and reading.

KEYWORDS

longevity, subjective wellbeing, lifestyle, cohort study, rural elderly

1. Introduction

The world's population is aging, and most countries are experiencing growth in the number and proportion of the elderly population (1). Approximately 9% of people worldwide were over 65 years old in 2021 (2). There are 190 million citizens over 65 years of age in China, which accounts for 13.5% of the total population (3). Active and healthy aging is the theme of the era. The English Longitudinal Study of Aging documented participants' experience of growing old in the context of active aging in the twenty-first century (4). Older adults are increasingly seen as contributors to development (5). Notably, China has the largest elderly population in the world (6), and the proportion of elderly Chinese aged 65 years and over in rural areas is 17.72%, which is 6.61% higher than urban areas (7). The average life expectancy of rural elderly people aged 65 and over is 16.69 ± 0.25 years, which is lower than the 18.33 ± 0.35 years of the urban elderly aged 65 and over (8). Rural revitalization pushes country prosperity forward. Improving the life expectancy of elderly people has become a key goal of the full life cycle of elderly care services. Chinese rural elderly people tend to report higher negative emotions than urban elderly people (9). Helping rural elderly people realize their pursuit of a better and happy life is a major concern of Chinese society.

Wellbeing may be good for the mind and the body (10). Higher subjective wellbeing is associated with good health (11). A longitudinal study demonstrated a significant association between subjective wellbeing and longevity (12–14), and eudemonic wellbeing increased survival (15). Several factors, such as educational level and lifestyle, significantly influenced the overall subjective wellbeing of older adults (16). A healthy lifestyle markedly increases life span and improves individuals' subjective wellbeing (17, 18). Lifestyle behaviors include physical activity, healthy diet, sleep, smoking, and drinking (19). Eating fruit and vegetable had positive effects on subjective wellbeing (20, 21). Physical activity was a protective factor for subjective wellbeing in older adults (22), and it reduced their risk of late-life depression (23). Many older adults would choose to make some changes to increase their wellbeing in their later life (24).

Life evaluation and wellbeing are relevant to health and quality of life as people age (15). Due to differences in the background of the times, age and birth generation are related to the prevalence and changes in lifestyle behavior (25). The present study compared the differences in life span between urban and rural elderly people based on an ongoing open cohort, the China Health and Nutrition Survey (CHNS). We tested two hypotheses. First, we examined whether improving subjective wellbeing increased the probability of longevity of rural elderly people. Second, we investigated the effects of lifestyle behaviors on the subjective wellbeing of rural elderly people of different birth generations.

2. Materials and methods

2.1. Participants and survey procedures

Data were derived from the CHNS, which is an ongoing open cohort study that adopts a multistage, random clustered sampling process. First, we chose nine provinces that varied substantially in geography, economic development, public resources, and health indicators. Second, two cities (one large and one small) and four counties (stratified by income, one high, one low and two middle income) were randomly selected per province. Third, two urban and two suburban communities were randomly selected within cities, and one community and three rural villages were randomly selected within counties. Finally, 20 households per community or village were randomly selected for participation. CHNS was approved by the Institutional Review Boards of the University of North Carolina at Chapel Hill and the Chinese Center for Disease Control and Prevention. All participants provided written informed consent for their participation in the survey.

This study used the CHNS data from 2006, 2009, 2011 and 2015. As shown in Figure 1, of the 1526 participants aged 65 or over in 2006, 892 lived in rural areas, and 634 lived in urban areas. Comparisons of the survival probability of the rural and urban elderly in 9-year follow-up (Figure 2A) found that the survival probability of rural elderly people was significantly lower than urban elderly ($p < 0.0001$). This study focused on a sample of rural elderly people who were followed up from 2006 to 2015, with a follow-up rate of 75.9%. The reason for loss to follow-up was death.

2.2. Measurements

2.2.1. Outcome variable

Subjective wellbeing refers to how people experience and evaluate their lives and specific domains and activities in their lives (26), which include emotional experiences and cognitive evaluations (life satisfaction). It was measured using four items: (i) How do you rate the quality of your life at present? (ii) I have as much pep as last year? (iii) I am as happy now as when younger? (iv) As I get older, things are better than I thought they would be. Each item was scored on five-point scale. After adjusting the reverse scoring, the total score was 4 to 20. Higher scores indicate higher subjective wellbeing. The Cronbach's α was 0.67–0.76 from 2006 to 2015, which indicated moderate reliability.

2.2.2. Lifestyles

Lifestyles included food and activity preferences, and items were rated on a five-point scale ranging from "dislike very much" to "like very much."

Food preferences were measured by asking participants "How much do you like this food: (i) fruits; (ii) vegetables; (iii) soft drinks and sugared fruit drinks?"

Activity preferences were measured by asking participants "How much do you like to participate in this activity: (i) walking, Tai Chi; (ii) body building; (iii) sports (ping pong, badminton, tennis, soccer, basketball, volleyball); (iv) reading; (v) watching TV; (vi) playing computer/video games, surfing the internet?" The first three activities are physical activities, and the last three activities are sedentary activities.

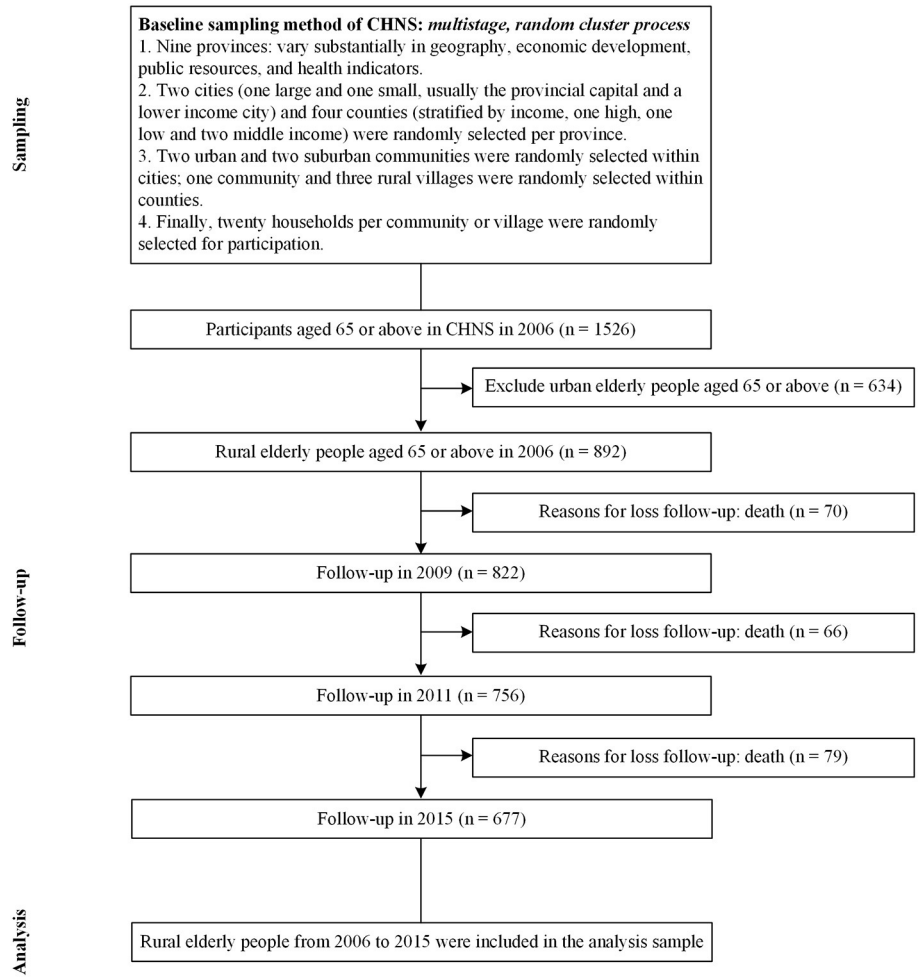

FIGURE 1
Flowchart.

2.3. Statistical analysis

Descriptive statistics are expressed as frequency and percentages and means and standard deviation. We estimated and graphed survival curves using the Kaplan–Meier (KM) method, which involves computing the probabilities of occurrence of events at a certain point in time (27), and the log-rank test was used to compare two survival curves. After validation of proportional hazards assumption, Cox regression was used to examine the relationship between subjective wellbeing and survival outcome. This relationship was further tested using "mean ± SD" of subjective wellbeing as a cutoff, which helped determine their causal relationship. Cox's semiparametric model is widely used in the analysis of survival data to explain the effect of explanatory variables on hazard rates (28). Generalized estimating equations (GEE) were performed to clarify whether food preferences and activity preferences influenced the subjective wellbeing of Chinese rural elderly people across different birth generations after accounting for sex and highest educational level. During the follow-up period, there were no missing demographic variables, such as age, sex, or highest educational level, for surviving rural elderly people, except for subjects who died. For missing lifestyle and outcome variables for survivors, we used the answers of the previous session among the surviving rural elderly people to replace the missing value of the same variables/items. Statistical analyses were performed using SAS 9.4. GraphPad Prism 7.00 and Microsoft Visio 2019 program were used to draw figures.

3. Results

Descriptive statistics of the sample from 2006 to 2015 are shown in Table 1. A total of 892 rural elderly people aged 65 or over were included in the sample: 153 people were born in the 1940s, 542 people were born in the 1930s, and 197 people were born in the 1908–1920s. More than half of the subjects were female, and males accounted for 44.84% of the sample. Of the 892 rural elderly people, 63.23% never attended school, 19.96% graduated from primary school, and 9.08% had a lower middle school degree. Due to deaths, there were 677 rural elderly people in 2015 after 4 rounds of follow-up. The average score of subjective wellbeing in the 4 rounds of the survey fluctuated between 11.92 and 12.47.

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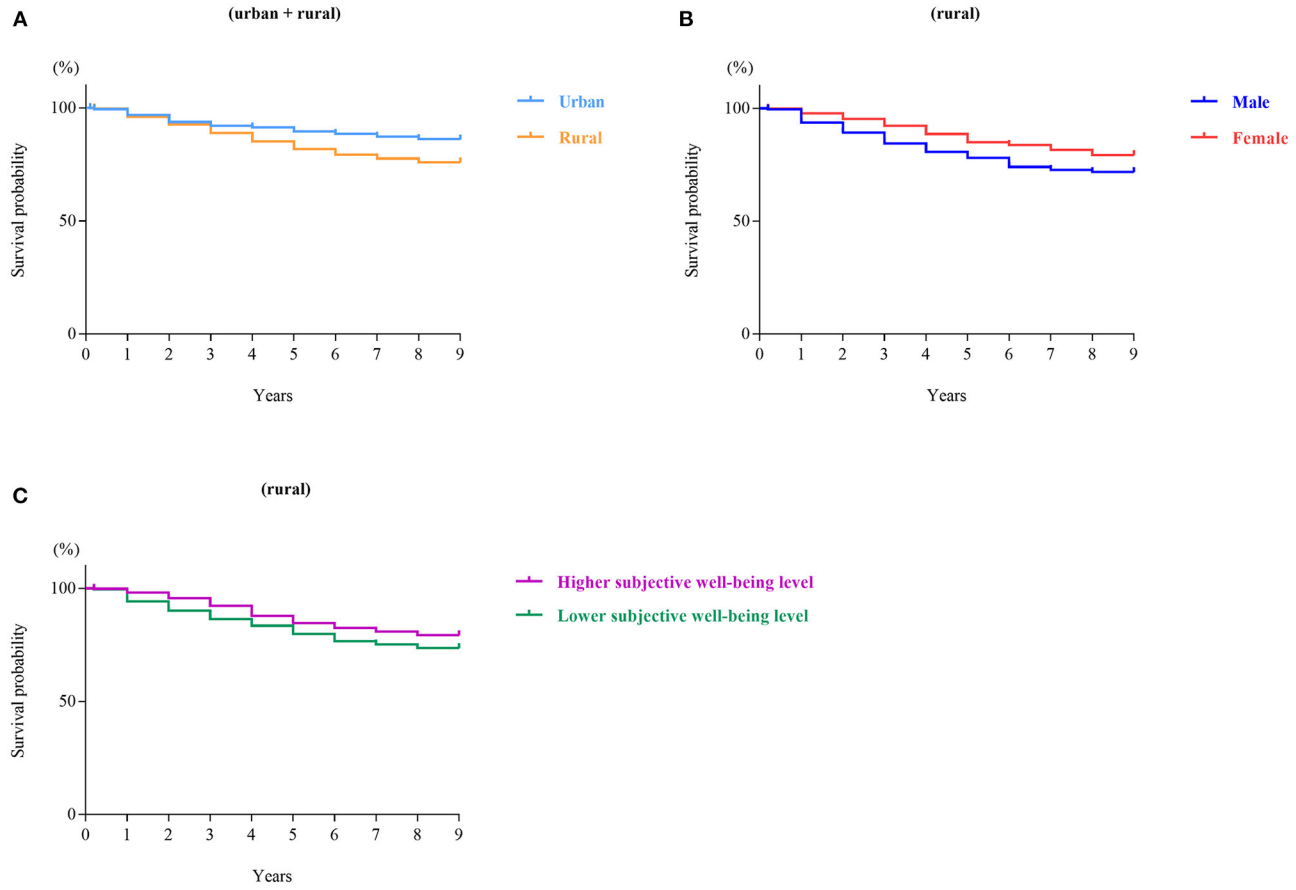

FIGURE 2
Survival curves among Chinese elderly people in urban/rural areas. **(A)** Urban + rural, **(B)** rural, **(C)** rural.

To evaluate whether sex and subjective wellbeing were associated with longevity in Chinese rural elderly people, Kaplan–Meier survival curves were generated using the 2006 data. As shown in Figure 2B, females lived longer than males ($p = 0.0046$). Figure 2C indicates that rural elderly people whose subjective wellbeing was higher than or equal to the average lived longer than rural elderly people whose subjective wellbeing was lower than the average ($p = 0.0368$). For the CHNS from 2006-2015, the categorical variables, which included sex and the bicategorical subjective wellbeing level with the mean plus standard deviation as a cutoff, were verified using the Kaplan-Meier survival curve method and the cumulative hazard function method, respectively, and both sets of curves for both variables were parallel and non-crossed. The influence of subjective wellbeing of continuous variables on survival outcomes was examined using the Schoenfeld residual method. The residuals fluctuated around 0, and there was no obvious change trend with the increase of time rank. The Pearson correlation coefficient between the Schoenfeld residual and time rank was not significant ($p = 0.221$). In summary, these data satisfied the proportional hazards assumption that the impact of covariates on survival possibility did not change over time, and the data are appropriate for a Cox regression analysis. After controlling for sex, Cox regression analysis suggested that high subjective wellbeing was a protective factor against death (HR, 0.90; 95% CI, 0.82–0.99), with a 10% lower risk of death when subjective wellbeing was higher than or equal to the average level. When subjective wellbeing was higher than or equal to the sum of the mean and standard deviation, there was a 69% lower risk of death (HR, 0.31; 95% CI, 0.11–0.85).

To further examine the trajectories in subjective wellbeing of rural elderly people in the four-wave survey by different birth generations, as shown in Figure 3, the horizontal axis corresponding to each birth generation group data point represents the minimum age of the group in 2006. The results showed that the subjective wellbeing of rural elderly people in the three groups of birth generations (1940s, 1930s, and 1908–1920s) all decreased then increased slightly. In the same round of surveys, the subjective wellbeing was lower for rural elderly people with an earlier birth generation than for rural elderly people with a later birth generation. This result suggests that the characteristics of birth background affect happiness.

Based on the above findings, we used GEE to analyze the factors that affected the subjective wellbeing of rural elderly people by different birth generations after controlling for sex and highest educational level (Table 2). Model 1 revealed that there was a significant positive correlation between a preference for eating vegetables and subjective wellbeing ($\beta = 0.874$, $p < 0.05$) among rural elderly people born in the 1940s. They had a greater

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TABLE 1 Descriptive statistics of the follow-up sample.

Variables	2006 (n = 892)		2009 (n = 822)		2011 (n = 756)		2015 (n = 677)	
	n	(%)	n	(%)	n	(%)	n	(%)
Birth generations								
1940s	153	(17.15)	147	(17.88)	141	(18.65)	133	(19.65)
1930s	542	(60.76)	509	(61.92)	474	(62.70)	425	(62.78)
1908–1920s	197	(22.09)	166	(20.19)	141	(18.65)	119	(17.58)
Sex								
Male	400	(44.84)	357	(43.43)	322	(42.59)	287	(42.39)
Female	492	(55.16)	465	(56.57)	434	(57.41)	390	(57.61)
Highest educational level								
None	564	(63.23)	564	(68.61)	511	(67.59)	463	(68.39)
Graduated from primary school	178	(19.96)	131	(15.94)	125	(16.53)	109	(16.10)
Lower middle school degree	81	(9.08)	71	(8.64)	67	(8.86)	57	(8.42)
Upper middle school degree	25	(2.80)	23	(2.80)	23	(3.04)	21	(3.10)
Technical or vocational degree	34	(3.81)	24	(2.92)	18	(2.38)	21	(3.10)
University or college degree	10	(1.12)	9	(1.09)	12	(1.59)	6	(0.89)
Master's degree or higher	0	(0.00)	0	(0.00)	0	(0.00)	0	(0.00)
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
Subjective wellbeing	12.47	(2.74)	11.97	(2.76)	11.92	(2.80)	12.03	(2.81)

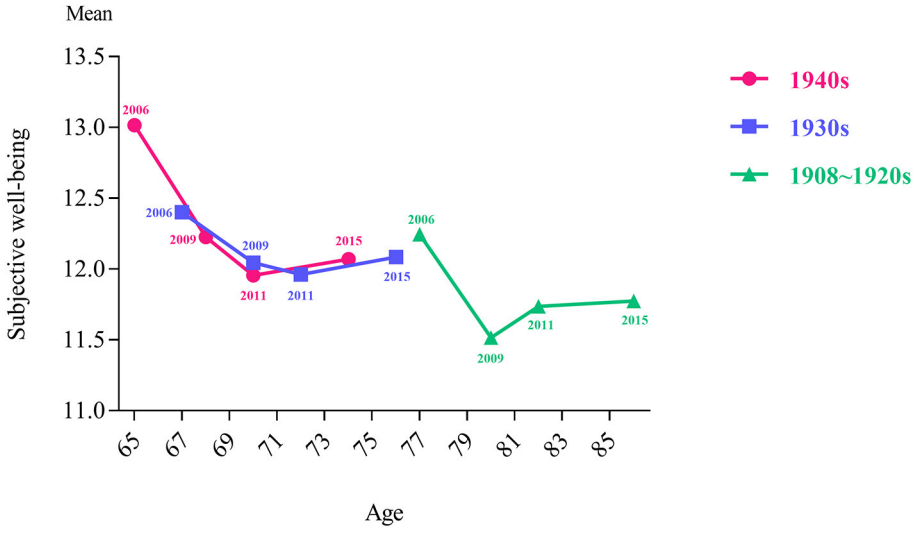

FIGURE 3
Subjective wellbeing level of Chinese rural elderly people in different birth generations during 2006–2015.

preference for walking or Tai Chi and a higher subjective wellbeing (β = 0.395, $p < 0.05$). Model 2 discovered that a preference for eating vegetables (β = 0.548, $p < 0.05$), preference for reading (β = 0.433, $p < 0.01$), and preference for watching TV (β = 0.416, $p < 0.001$) were all significantly positively associated with subjective wellbeing for rural elderly people born in the 1930s. For rural elderly people born in the 1908–1920s, Model 3-1 showed that a greater preference for watching TV was associated with a higher subjective wellbeing (β = 0.519, $p < 0.05$). We examined whether there was an interaction between the reading preference and educational level of rural elderly people of different birth generations. The results indicated that only rural elderly people born in the 1908–1920s had this interaction. Model 3-2 showed that a stronger reading preference and higher educational level were associated with higher subjective wellbeing (β = 0.374, $p < 0.05$).

TABLE 2 GEE analysis of subjective wellbeing of Chinese rural elderly people by different birth generation during 2006–2015.

Variables	1940s		1930s		1908–1920s			
	Model 1		Model 2		Model 3-1		Model 3-2	
	β	*p*	β	*p*	β	*p*	β	*p*
Intercept	8.428		8.004		8.778		9.060	
Food preferences								
Fruits	−0.204		0.087		−0.070		−0.091	
Vegetables	0.874	*	0.548	*	0.305		0.365	
Soft drinks and sugared fruit drinks	−0.287		−0.220		−0.340		−0.307	
Activity preferences								
Physical activities								
Walking, Tai Chi	0.395	*	0.187		0.304		0.218	
Body building	−0.002		−0.230		0.051		0.131	
Sports (ping pong, badminton, tennis, soccer, basketball, volleyball)	0.520		0.002		0.349		0.363	
Sedentary activities								
Reading	−0.174		0.433	**	−0.162		−0.565	
Watching TV	0.153		0.416	***	0.519	*	0.476	*
Playing computer/video games, surfing the internet	−0.223		−0.106		0.119		0.346	
Interaction effect								
Reading × highest educational level							0.374	*

Sex and highest educational level are taken as control variables in above models.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

4. Discussion

Positive attitudes toward life in general may be especially important in old age (29). Longevity is an indicator of active healthy aging, but the subjective wellbeing of older adults is an important factor in measuring successful healthy aging (30). Optimistic attitudes and subjective wellbeing in the daily life of older adults had a strong protective effect on all-cause mortality (31). The present study elucidated that subjective wellbeing was a protective factor for mortality in rural older adults. Subjective wellbeing above or equal to the average level decreased the death risk of rural elderly people by 10%, and subjective wellbeing above or equal to the sum of the average level and one standard deviation decreased the risk of death by 69%. These results suggest that drastically improving the subjective wellbeing of rural elderly people would decrease the number of deaths.

The subjective wellbeing of rural elderly people of different birth generations first decreased then increased slightly. This result may reflect the fluctuation of subjective wellbeing caused by the policy effect. Specifically, the subjective wellbeing of rural elderly people from 2006 to 2009 presented a downward trend in all three birth generations. The subjective wellbeing of rural elderly people from 2009 to 2011 and the declining trend of the 1940s and 1930s birth generations were slower than rural elderly people from 2006 to 2009, but the 1908–1920s birth generation showed an upward trend. As a transition point, this result may be because the Chinese government began to make special investments in the elderly care service system in 2009 and focused on supporting the construction of public elderly care service institutions and township nursing homes. The pilot reform of the new rural social endowment insurance for rural residents began in 2009, and social insurance for rural farmers was initiated. Research has detected that Chinese rural farmer who participated in the New Rural Cooperative Medical System enhanced their subjective wellbeing (32). Analogously, Medicare creates a safety net for vulnerable populations in the United States, which ensures a greater sense of economic and health security for older people and their families (33).

The trend of subjective wellbeing from 2011 to 2015 revealed that these trends for different birth generations are all on the rise. The changing trajectory of the subjective wellbeing of elderly people in rural China with age is likely to benefit from the continuous improvement of the Chinese elderly welfare system, such as China's Undertakings for the Aged during the 12th Five-year Plan (2011–2015), and the social elderly care service system construction plan (2011–2015). Previous studies demonstrated that social age-friendly policies were conducive to increased wellbeing of elderly people, such as the pension policy in Korea (34), social income policy in Turkey (35), internet access policy in South Africa (36), age-friendly city strategy in China (37), and ongoing construction of Chinese happy villages. We should pay attention to popularizing the policy needs of elderly people and their families and improve the policy literacy of this group. Notably, when seeking practical

and policy interventions for the social welfare of elderly people, the characteristics of elderly people of different birth generations and age stages should be considered.

Lifestyle is an important factor affecting happiness (38). For elderly people, the most commonly discussed lifestyle issues are diet and activity. Food is a necessity of life that has an important impact on mental health (39). Research has found that the eating behaviors and food preferences of adults predict their wellbeing (40). We elucidated the positive effect of a preference for eating vegetables on the subjective wellbeing of rural elderly people born in the 1940s and 1930s, but it had no significant effect on rural elderly people born in the 1908–1920s. This difference may be because rural elderly people of earlier birth generations have experienced resource poverty since childhood and have no specific dietary preferences, and dietary habits do not affect their subjective wellbeing. Preferences for eating fruits and drinking soft drinks and sugared fruit drinks had no significant effect on the subjective wellbeing of any birth generation in the rural elderly population. In contrast to vegetables on the dining table, fruits and drinks are not necessary for most rural elderly people and are considered additional consumption.

Leisure time physical activities improve wellbeing and alleviate depression and anxiety among elderly people (41–43). Our study demonstrated that the positive effect of walking/Tai Chi on subjective wellbeing was significant among rural elderly people born in the 1940s, but it was not significant in the other two birth generations. Younger rural elderly people may have had better activities of daily life abilities than older rural elderly people and paid more attention to physical exercise. Physical activity maintains the mobility and physical functions of elderly people and improves their community and social engagement (44, 45). We encourage rural elderly people with the necessary ability to participate in regular physical exercise of appropriate intensity, such as walking, performing Tai Chi, doing housework and aerobic exercise. Tai Chi is one of the most popular and frequently practiced sports among older Chinese people (46). For rural elderly people with poor activity ability, simple home-based health exercises may be performed according to their own physical conditions.

We observed that the positive effect of the preference for watching TV on subjective wellbeing was not significant in rural elderly people born in the 1940s, but it was significant in rural elderly people born in the 1930s and 1908–1920s. Barriers to participation in activities, such as sports, tend to increase with age (47). Senior rural elderly people tend to choose more sedentary activities, and watching TV is an option. Significantly, people experience abundant subjective wellbeing when they are engaged in interesting activities (48). We found that rural elderly people born in the 1930s who liked reading had a higher sense of subjective wellbeing than rural elderly people who do not like reading. A British survey found that leisure readers reported less stress and depression on average than non-readers (49). For elderly people, reading is a relatively relaxed leisure activity that promotes emotional health and brings a stronger sense of relaxation than other leisure activities (50). In addition to visual and performing arts activities, we advocate that communities perform reading activities in various forms, including reading clubs, essay competitions, and the appreciation of classical works. Providing opportunities for the community participation of elderly people in multiple dimensions reduces their social isolation and loneliness and improves their subjective wellbeing.

A major strength of the present study is that it was based on a large nationally representative sample, and we examined the longevity and wellbeing of rural elderly people in whom we were interested. The prospective study design of CHNS helped eliminate the potential recall bias that is an issue of special concern in most retrospective *post-hoc* analyses. The limitations of this study also merit consideration. First, the sample size of the rural elderly people involved in this study was relatively small. However, CHNS adopts a multistage, random clustered sampling process, the study participants were representative, and the results may be used as a reference for policy-making. Second, our sample was Chinese rural elderly people, and possible differences between Eastern and Western cultures should be considered when extrapolating the research results to other countries. Third, the choice of covariates was not sufficiently comprehensive. There are many factors associated with longevity and subjective wellbeing, such as health status for longevity and income for subjective wellbeing. However, this study focused on the perspective of food and activity preferences. Due to the few rural elderly people who answered the measures of present medical illness and income in the CHNS from 2006 to 2015, this study did not include this them in the model control, which is also a limitation of this study. Finally, CHNS is aimed at all age groups, rather than just the elderly, and the categories of activity preference choices may not be representative for the rural elderly.

5. Conclusion

The present study contributes additional evidence that improving subjective wellbeing extends life span and reduces mortality risk among rural elderly people. Improving the subjective wellbeing of rural elderly people may be achieved by shaping a healthy lifestyle, such as a preference for eating vegetables, walking/Tai Chi, and reading. We found that a higher educational level of rural elderly people and a greater enjoyment of reading were associated with higher subjective wellbeing. It is recommended that the implementation of facility, infrastructure, space and equipment be strengthened to promote wellbeing in rural regions.

Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics statement

CHNS was approved by the Institutional Review Boards of the University of North Carolina at Chapel Hill and the Chinese Center for Disease Control and Prevention. The patients/participants provided their written informed consent to participate in this study.

Author contributions

XL and Y-CC made contributions to data analysis and interpretation. XL, MG, SH, and ZF drafted the manuscript. XL, MC, TC, C-YL, and Y-CC revised it critically for important intellectual content. C-YL and Y-CC supervised the study. TC and Y-CC provides funding acquisition. All authors were major contributors in conception and design of the study, read, and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Effectiveness and safety of manual therapy for knee osteoarthritis: An overview of systematic reviews and meta-analyses

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Background: Manual therapy has been used as an alternative approach to treat knee osteoarthritis (KOA) for many years. Numerous systematic reviews (SRs) or meta-analyses (MAs) were published to evaluate its effectiveness and safety. Nevertheless, the conclusions of SRs/MAs are inconsistent, and the uneven quality needs to be critically appraised.

Objectives: To conduct a comprehensive overview of the effectiveness and safety of manual therapy for KOA and the quality of relevant SRs/MAs, thus providing critical evidence and valuable direction for future researchers to promote the generation of advanced evidence.

Methods: The pre-defined search strategies were applied to eight electronic databases from inception to September 2022. Suitable SRs/MAs were included in accordance with the inclusion and exclusion criteria. The methodological quality, risk of bias, reporting quality, and evidence quality were assessed by two independent reviewers who used respectively the A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR-2), the Risk of Bias in Systematic Reviews (ROBIS), the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 Version (PRISMA 2020), and Grades of Recommendations, Assessment, Development and Evaluation (GRADE) based on the method of narrative synthesis. We excluded the overlapping randomized controlled trials (RCTs) and performed a re-meta-analysis of the total effective rate.

Results: A total of eleven relevant SRs/MAs were included: nine SRs/MAs were rated critically low quality, and two were rated low quality by AMSTAR-2. According to ROBIS, all SRs/MAs were rated low risk in Phase 1 (assessing relevance) and Domain 1 (study eligibility criteria) of Phase 2. Three SRs/MAs (27.27%) were rated low risk in Domain 2 (identification and selection of studies). Ten SRs/MAs (90.91%) were rated low risk in Domain 3 (data collection and study appraisal). Five SRs/MAs (45.45%) were rated low risk in Domain 4 (synthesis and findings). And five SRs/MAs (45.45%) were rated low risk in Phase 3 (risk of bias in the review). By PRISMA 2020, there were some reporting deficiencies in the aspects of abstract (2/11, 18.18%), search strategy (0/11, 0%), preprocessing of merging data (0/11, 0%), heterogeneity exploration (6/11, 54.55%), sensitivity analysis (4/11, 36.36%), publication bias (5/11, 45.45%), evidence quality (3/11, 27.27%), the list of excluded references (3/11, 27.27%), protocol and registration (1/11, 9.09%), funding (1/11, 9.09%), conflict of interest (3/11, 27.27%), and approach to relevant information (0/11, 0%). In GRADE, the evidence quality was defined as moderate quality (8 items, 21.05%), low quality (16 items, 42.11%), and critically low quality (14 items, 36.84%). Among the downgraded factors, risk of bias, inconsistency, imprecision, and publication

bias were the main factors. A re-meta-analysis revealed that manual therapy can increase the total effective rate in KOA patients (risk ratio = 1.15, 95% confidence interval [1.12, 1.18], $p < 0.00001$; $I^2 = 0$, $p = 0.84$). There are four reviews that narratively report adverse effects, and no severe adverse reactions occurred in the manual therapy group.

Conclusions: Manual therapy may be clinically effective and safe for patients with KOA. However, this conclusion must be interpreted with caution because of the generally unsatisfactory study quality and inconsistent conclusions of the included SRs/MAs. Further rigorous and normative SRs/MAs are expected to be carried out to provide robust evidence for definitive conclusions.

Systematic review registration: https://www.crd.york.ac.uk/PROSPERO/#myprospero, identifier: CRD42022364672.

KEYWORDS

manual therapy, rehabilitation, knee osteoarthritis, systematic review, overview

1. Introduction

Knee osteoarthritis (KOA), the most prevalent form of osteoarthritis, is a chronic degenerative joint pathology characterized by progressive hyaline articular cartilage destruction, sclerotic changes of subchondral bone, and synovial inflammation (1, 2). It is a leading cause of disability and poor quality of life worldwide due to the symptoms and signs including chronic knee pain, stiffness, functional limitations, and muscle weakness (3, 4). Nearly 21% of patients undergoing KOA even suffer from a series of psychological problems such as depression and anxiety (5). The global prevalence of KOA has reached 22.9% in patients aged 40 or older, which represents tremendous personal and societal burdens (6, 7). The increased disease burden has not only strained severely the healthcare institution but has also affected the medical expenditure of patients (8). As life expectancy and obesity prevalence increase, the number of people living for prolonged periods with KOA is expected to grow in the foreseeable future (9). Thus, the management of patients with KOA attracts increasing attention from researchers.

At present, the primary treatment goals of KOA are to decrease pain, enhance physical function, and improve the quality of life (10). Doctors need to develop individualized and stepwise treatment strategies based on the actual situations of their patients. Current guidelines have evaluated over 50 treatments for KOA (11–14). Common interventions for KOA include patient education, weight management, exercise therapy, physical therapy, pharmacologic therapy, and surgery therapy (15, 16). Moreover, several innovative therapies for KOA, such as stem cell therapy (17), chondrocyte cell-sheet transplantation (18), injectable natural polymer hydrogels (19), geniculate artery embolization (20), and water-cooled radiofrequency ablation (21), have been proven effective by relevant studies. However, more rigorous clinical trials are needed to determine whether those treatments can be recommended in clinical practice. Drug analgesic intervention is still the primary therapy for KOA. The majority of the physicians generally prescribe medications for controlling the symptoms. Oral medications mainly contain acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and duloxetine. However, the long-term efficacy and side effects of pharmacotherapy are still uncertain (22). Some rehabilitation strategies for individuals with KOA are more likely to alleviate the pain in the long term and to delay functional decline than the existing drugs (1). And the proportion of patients who have multiple coexisting diseases simultaneously is rising steadily in older people (23, 24). The multimorbidity trend presents challenges to the pharmacotherapy of KOA. For example, in patients with severe gastrointestinal or cardiovascular conditions, the use of oral NSAIDs is not recommended owing to the adverse effects such as gastrointestinal events (irritation, ulceration, or bleeding) and cardiovascular events (myocardial infarct, cerebrovascular accidents, or hypertension) (11, 16). Therefore, many patients have gradually shifted from drug interventions to seeking rehabilitation techniques in recent years (25).

Rehabilitation techniques largely meet a tremendous need for conservative management to enhance physical functioning and quality of life (26). Manual therapy has been used as part of a multimodal rehabilitation management for KOA as it has the potential to improve symptoms. It can be defined as the application of a manual force to the patient by a trained practitioner to improve pain-related symptoms and mobility in areas that are restricted, such as skeletal muscles, joints, connective tissues, or nerve tissues (27). Manual therapy mainly includes soft tissue techniques, stretching, massage, active or passive mobilization, and manipulation techniques (28, 29), which have been popular therapeutic modalities for patients with KOA. Many randomized controlled trials (RCTs) have been conducted to investigate the effect of manual therapy in the treatment of KOA. Pozsgai et al. (30) reported that single manual therapy is effective immediately and in short term on alleviation of pain compared to sham manual therapy. Nigam et al. (31) reported long-term beneficial effects (up to 6 months) of manual therapy, and their results indicated that the addition of manual therapy provided clinically significant improvements in pain, disability, and functional activities than usual care alone in patients with symptomatic KOA. The exact mechanism of manual therapy is unknown, but it is postulated

that it may improve blood supply, enhance muscle strength, relieve inflammatory reactions, and also result in changes in the immune system, which may help improve pain and physical function in patients with KOA (32). To date, numerous systematic reviews (SRs) or meta-analyses (MAs) about manual therapy for KOA have been reported. However, the effectiveness and safety of manual therapy from related research still didn't reach a consistent conclusion. Owing to poor data quality and an insufficient benefit, the level of evidence for manual therapy is ambiguous, and many clinical practice guidelines have not yet recommended manual therapy as a routine treatment for KOA in clinical practice. Therefore, credible evidence of manual therapy for KOA is still needed.

An overview is a method of summarizing study evidence from different SRs/MAs into one usable and accessible document (33). It can provide a comprehensive description by assessing the methodological quality, reporting quality, risk of bias, and evidence quality of relevant SRs/MAs. To our knowledge, no overview of manual therapy for KOA has been published. Therefore, we conducted this overview to comprehensively evaluate the effectiveness and safety of manual therapy for KOA based on relevant SRs/MAs (Figure 1). This overview will provide critical evidence for clinicians, patients, or policymakers, as well as improvement guidance for SR/MA producers in the future.

2. Methods

2.1. Protocol and registration

The protocol of this overview was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (https://www.crd.york.ac.uk/PROSPERO/) with the registration number CRD42022364672.

2.2. Search strategy

Two reviewers (TF and ZJ) independently searched the literature in eight electronic databases, including PubMed, EMBASE, Cochrane Library, Web of Science, the Chinese National Knowledge Infrastructure (CNKI), the WanFang Database, Chinese Biological Medicine (CBM), and the Chongqing VIP Database, from inception to September 2022. In addition, relevant references for review articles, the research registries and gray literature such as academic dissertations and conference reports were further searched manually. There were no restrictions on the language or the publication status. The search terms mainly include "Osteoarthritis, Knee", "Osteoarthritis", "Knee osteoarthritis", "Knee pain", "KOA", "Manipulation, Osteopathic", "Massage", "Chiropractic", "Manual therapy", "Manipulation therapy", "Osteopathic manipulative treatment", "Meta-analysis", and "Systematic review". The search strategies were adjusted to suit the specific features of the electronic databases. The search strategy for PubMed was shown in Table 1. Detailed search strategies for electronic databases were summarized in Appendix A.

2.3. Inclusion criteria

2.3.1. Type of studies

SRs/MAs containing more than one RCT that used manual therapy for KOA were eligible.

2.3.2. Type of participants

According to the existing internationally recognized diagnostic criteria, patients who were diagnosed with KOA were included regardless of the differences in gender, region, age, ethnicity, disease duration, or severity.

2.3.3. Type of interventions

Manual therapy was the primary intervention measure, with no restrictions on types of manual therapy (such as massage, joint mobilization, manipulation, or other manual therapies). It could be treated with manual therapy alone or combined with the control intervention.

2.3.4. Type of comparators

The control interventions included sham (placebo) manual therapy, exercise therapy, usual care, western medicine, acupuncture therapy, no treatment, or other conventional treatments.

2.3.5. Type of outcome measures

The primary outcome was the total effective rate. The total effective rate was a compound outcome and total effective rate = (number of basically cured patients + number of markedly improved patients + number of improved patients) / total number of patients (34). The secondary outcomes included the Visual Analog Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score, WOMAC stiffness score, WOMAC physical function score, hospital for special surgery knee score (HSS), and stairs ascending-descending time. These outcome measures have been widely used as evaluation tools by clinical investigators to observe the efficacy of KOA. The VAS score is the most frequently used instrument to assess pain intensity in patients with chronic musculoskeletal pain (35). The WOMAC score is a patient-reported questionnaire that can be used to assess pain, stiffness, and physical function for osteoarthritis of the hip or knee (36). HSS score and stairs ascending-descending time are reliable and effective outcome measures for evaluating the physical function and performance of KOA (37, 38).

2.4. Exclusion criteria

The exclusion criteria were as follows: (a) SRs/MAs including non-RCTs; (b) SRs/MAs without quantitative synthesis; (c) The control interventions were treated with different types of manual therapy; (d) Network meta-analyses; (e) Duplicate publication; (f) Protocols of SRs/MAs; (g) SRs/MAs whose full text couldn't be accessed; (h) SRs/MAs without the outcomes mentioned above.

FIGURE 1
The process of this overview.

2.5. Study selection

According to the intended inclusion and exclusion criteria, two reviewers (TF and XQ) conducted literature screening independently. Two reviewers imported the retrieved results into Endnote X9.3 software to remove duplicates. Inconsistent articles were then excluded based on their titles and abstracts. Finally, eligible SRs/MAs were retrieved for full-text assessment. Any unresolved disagreements were resolved by a third reviewer (XW).

2.6. Data extraction

Two reviewers (TF and XQ) independently extracted data by using a pre-designed information extraction table, and the extraction items were as follows: the first author, publication year, country, language, number of included RCTs, total simple size, type of intervention and comparator, outcome measures, duration of treatment, quality assessment tool, data analysis methods, and overall conclusions. Two reviewers cross-checked the extracted content and consulted a third reviewer (XW) for any disagreements.

2.7. Quality assessment

The quality assessment of the overview mainly followed the Cochrane Handbook and the methods of relevant studies (39–43). The quality assessment mainly contained four aspects: methodological quality, risk of bias, reporting quality, and evidence quality. Two independent reviewers (TF and XW) evaluated the quality of the SRs/MAs. Before the evaluation, each item of the relevant assessment tools was intensively discussed to reach a consensus.

2.7.1. Assessment of methodological quality

A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR-2) (44) was applied to assess the methodological quality of included SRs/MAs. The AMSTAR-2 contains 16 items (Appendix B), including 7 critical items (items 2, 4, 7, 9, 11, 13, 15). Each item is evaluated as "yes", "partial yes", or "no" according to the standard. An overall assessment of SRs/MAs (high, medium, low, or critically low) is performed based on the evaluation of critical and non-critical items.

2.7.2. Assessment of risk of bias

Risk of Bias in Systematic Reviews (ROBIS) (45) was applied to assess the risk of bias based on 3 phases (Appendix C). Phase 1 assesses whether the proposed question matches the target question from participants, interventions, comparisons, and outcomes (PICO). Phase 2 consists of 4 domains: "study eligibility criteria", "identification and selection of studies", "data collection and study appraisal", and "synthesis and findings". Phase 3 is based on the evaluation of phase 2 domains for comprehensive assessment. The risk of bias of SRs/MAs is evaluated as "low risk", "high risk" or "unclear risk".

2.7.3. Assessment of reporting quality

Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 Version (PRISMA 2020) (46) was applied to assess the reporting quality of included SRs/MAs. The PRISMA 2020 consists of 27 items (Appendix D), covering seven aspects of SRs/MAs, including the title, abstract, introduction, methods, results, discussion, and other information. Each item is evaluated as "yes", "partial yes", or "no".

2.7.4. Assessment of evidence quality

The Grades of Recommendations, Assessment, Development and Evaluation (GRADE) (47) system was applied to assess the

TABLE 1 The search strategy for PubMed.

Query	Search term
#1	Massage [Mesh]
#2	Manipulation, Osteopathic [Mesh]
#3	Chiropractic [Mesh]
#4	Zone Therapy [Title/Abstract] OR Zone Therapies [Title/Abstract] OR Massage Therapy [Title/Abstract] OR Massage Therapies [Title/Abstract] OR Osteopathic Manipulative Treatment [Title/Abstract] OR Osteopathic Manipulative Treatments [Title/Abstract] OR Osteopathic Manipulation [Title/Abstract] OR Tuina [Title/Abstract] OR Manual Therapy [Title/Abstract] OR Manual Traction [Title/Abstract] OR Manipulation Therapy [Title/Abstract] OR Manipulative Therapy [Title/Abstract] OR Massage [Title/Abstract] OR Manipulation, Osteopathic [Title/Abstract] OR Chiropractic [Title/Abstract]
#5	#1 OR #2 OR #3 OR #4
#6	Osteoarthritis, Knee [Mesh]
#7	Osteoarthritis [Mesh]
#8	Knee Osteoarthritides [Title/Abstract] OR Knee Osteoarthritis [Title/Abstract] OR Osteoarthritis of Knee [Title/Abstract] OR Osteoarthritis [Title/Abstract] OR Osteoarthritides [Title/Abstract] OR Osteoarthrosis [Title/Abstract] OR Osteoarthroses [Title/Abstract] OR Arthritis, Degenerative [Title/Abstract] OR Arthritides, Degenerative [Title/Abstract] OR Degenerative Arthritides [Title/Abstract] OR Degenerative Arthritis [Title/Abstract] OR Knee Pain [Title/Abstract] OR KOA [Title/Abstract]
#9	#6 OR #7 OR #8
#10	Systematic reviews as topic [Mesh]
#11	Meta-analysis as topic [Mesh]
#12	Systematic review [Publication Type]
#13	Meta-analysis [Publication Type]
#14	Meta-analysis [Title/Abstract] OR Systematic reviews [Title/Abstract] OR Systematic review [Title/Abstract] OR Meta analysis [Title/Abstract] OR Meta analyses [Title/Abstract] OR Meta-analyses [Title/Abstract] OR Evaluation of system [Title/Abstract] OR System assessment [Title/Abstract] OR System evaluation [Title/Abstract] OR Systematic assessment [Title/Abstract]
#15	#10 OR #11 OR #12 OR #13 OR #14
#16	#5 AND #9 AND #15

quality of the evidence. Evidence based on RCTs begins as high quality, but confidence may decrease according to five aspects: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The quality of the evidence is graded "high", "moderate", "low", or "critically low" (Appendix E).

2.8. Data synthesis and analysis

The clinical characteristics of reviews and the results of AMSTAR-2, ROBIS, PRISMA 2020, and GRADE were summarized by tables or figures based on the method of narrative synthesis. GRADE profiler 3.6.1 software played an important role in assessing the evidence quality. Review Manager 5.4 software was used in the re-meta-analysis of the primary outcome. A dichotomous variable was represented by the risk ratio (RR) and 95% confidence interval (CI). When there is obvious heterogeneity ($I^2 > 50\%$), the random-effects model should be applied. When no significant heterogeneity ($I^2 < 50\%$), the fixed-effects model was used. A funnel plot was used to detect publication bias.

3. Results

3.1. Study identification and selection

A total of 798 records were accessed from eight electronic databases. After removing duplication, 185 records were excluded. After screening titles and abstracts, 586 records were excluded. Meanwhile, 27 SRs/MAs needed to be further screened by reviewing the full text. Finally, eleven SRs/MAs (48–58) were included in this overview (Figure 2). The reasons for exclusion were shown in Appendix F.

3.2. Characteristics of included SRs/MAs

Eleven reviews [four reviews (48, 49, 54, 56) in English and seven reviews (50–53, 55, 57, 58) in Chinese] were published from 2013 to 2022, including 5 to 29 RCTs whose number of subjects ranged from 451 to 2,920 individually. There are ten reviews (48–53, 55–58) from China and one (54) from Saudi Arabia. For the quality assessment tools, the Cochrane Collaboration Risk of Bias Tool was applied in five reviews (48, 49, 52, 53, 58), the PEDro scale was used in two reviews (54, 56), the Jadad scale was used in one review (50), and the Cochrane Collaboration Risk of Bias Tool combined with the Jadad scale were adopted in three reviews (51, 55, 57). As for intervention, all reviews compared manual therapy with controls, which included sham (placebo) manual therapy, western medicine, acupuncture therapy, exercise therapy, usual care, or conventional treatments. More details can be found in Table 2.

3.3. Methodological quality of included SRs/MAs

By AMSTAR-2, the methodological quality of nine reviews (48–53, 56–58) was assessed as critically low quality, and two (54, 55) were rated low. Their deficiencies were as follows: For item 2, ten reviews (48–53, 55–58) were not registered in advance, and the protocol wasn't published before conducting the study. For item 3, six reviews (49–51, 54, 56, 58) didn't explain the reasons for choosing RCTs to include the study. For item 4, only three reviews (48, 49, 54) described a comprehensive literature search strategy. Gray literature retrieval was ignored in some studies. For item 7, seven reviews (48, 50–53, 56, 57) didn't provide a list of excluded studies. For item 8, none of the reviews described the dose of intervention. For item 10, none of the reviews described the funding sources of the included RCTs. For item 12, ten reviews

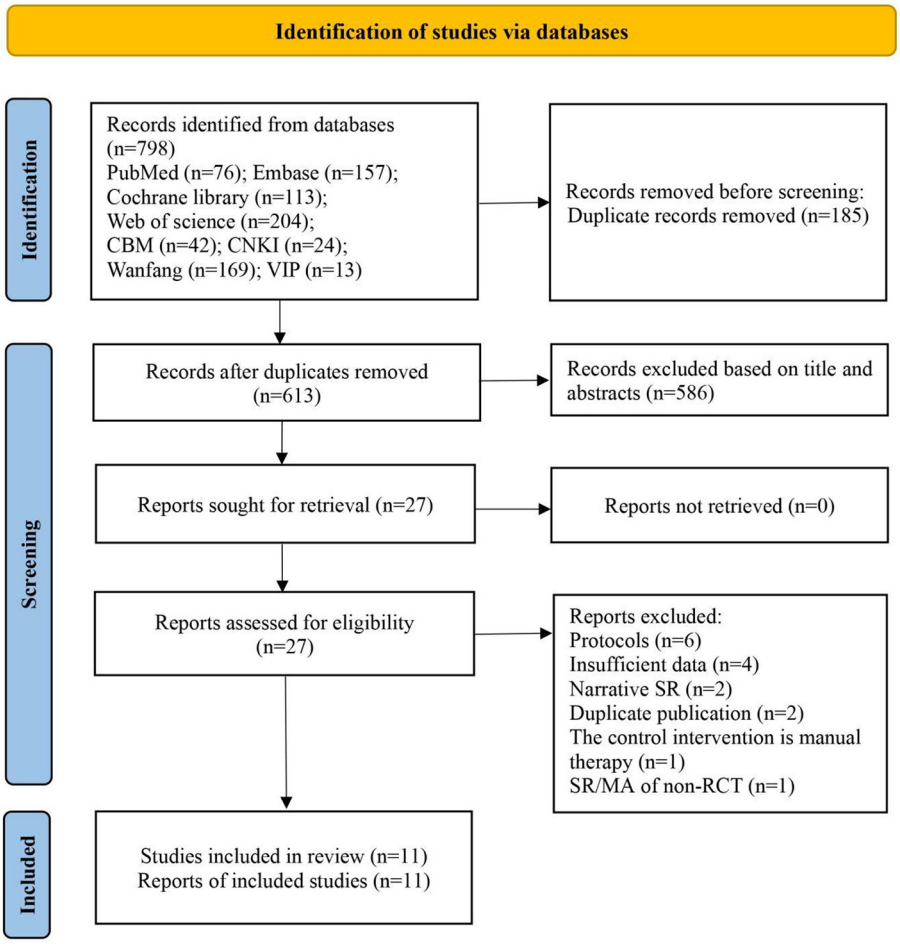

FIGURE 2
The PRISMA flow diagram of study selection.

(48–54, 56–58) ignored the potential impact of bias on the meta-analysis result in each trial. For item 14, five reviews (50, 52, 53, 57, 58) didn't explain reasons for heterogeneity reasonably. For item 15, six reviews (48, 49, 52–54, 58) didn't adequately explore the publication bias. For item 16, eight reviews (50–53, 55–58) didn't declare any conflicts of interest or provide the source of funding. More details were shown in Table 3.

3.4. Risk of bias of included SRs/MAs

According to the rules of ROBIS, all reviews were assessed as low risk in Phase 1 and Domain 1. For Domain 2, three reviews (48, 49, 54) (27.27%) were rated low risk, and eight reviews (50–53, 55–58) (72.73%) were assessed as high risk. For Domain 3, ten reviews (48, 49, 51–58) (90.91%) were rated low risk, and one (50) (9.10%) was assessed as high risk. For Domain 4, five reviews (48, 49, 54–56) (45.45%) were rated low risk, five reviews (50, 52, 53, 57, 58) (45.45%) were rated high risk, and one (51) (9.10%) was unclear risk. For Phase 3, five reviews (48, 49, 54–56) (45.45%) were rated low risk and six (50–53, 57, 58) (54.55%) were high risk. More details were shown in Table 4.

3.5. Reporting quality of included SRs/MAs

In general, there are some deficiencies in the reporting process. Many reviews (48–53, 55, 57, 58) didn't provide adequate information according to the abstract checklist (Q2: 18.18%). In terms of methods, all reviews didn't report comprehensively the information sources and search strategies in all databases (Q6: 0%; Q7: 0%). All reviews didn't mention preprocessing of merging data (Q13b: 0%). Partial reviews didn't report how to explore the heterogeneity (50, 52, 53, 57, 58) or analyze the sensitivity (52–58) (Q13e: 54.55%; Q13f: 36.36%). Partial reviews didn't explore the publication bias (48, 49, 52–54, 58) and evidence quality (49–51, 53, 55–58) (Q14: 45.45%; Q15: 27.27%). Besides, in the section on results, some reviews (48–53, 56, 57) didn't provide the list of excluded references and reasons (Q16b: 27.27%). All reviews didn't report the risk of bias in each meta-analysis result (Q20a: 0%) and partial reviews didn't report the results of heterogeneity sources (50, 52, 53, 57, 58) and sensitivity analyses (52–58) (Q20c: 54.55%; Q20d: 36.36%). Partial reviews didn't report the results of publication bias (48, 49, 52–54, 58) and evidence quality (49–51, 53, 55–58) (Q21: 45.45%; Q22: 27.27%). Furthermore, as for other information, only one

TABLE 2 Characteristics of the included SRs/Mas.

Authors (ref) country	Language	Number of included RCTs (simple Size)	Intervention	Comparator	Quality assessment tools	Duration of treatment	Outcomes	Overall conclusions (quote from the original paper)	Adverse effects
Wu et al. (48) China	English	12 (737)	MT	UC/SMT/CT/ Medication	Cochrane Collaboration Risk of Bias Tool	1–16 weeks	B; C; D; E	"Massage therapy may lead to some improvement in pain, stiffness, and functionality scores in the short term but not in long term"	Not reported
Xing et al. (49) China	English	8 (711)	MT	Medication	Cochrane Collaboration Risk of Bias Tool	2–4 weeks	A; B; C; D	"Therapeutic massage was more effective than oral NSAIDs in treating KOA. In relieving pain and stiffness and improving the function of knee joint, therapeutic massage was superior to NSAIDs"	Not reported
Zhang et al. (50) China	Chinese	8 (632)	MT	Medication/AT	Jadad scale	2–4 weeks	A	"The existing clinical evidence shows that massage alone can effectively alleviate the clinical symptoms of KOA patients and improve their quality of life"	Yes
Xu et al. (51) China	Chinese	17 (1,387)	MT	Medication/AT	Cochrane Collaboration Risk of Bias Tool; Jadad scale	2–6 weeks	A; E	"Compared with western medicine, both groups show equivalent effects on VAS score and adverse reactions, and Chinese Tuina was better than western medicine in improving WOMAC score. Chinese Tuina was better than the control group in improving the effective rate"	Yes
Tang et al. (52) China	Chinese	26 (2,920)	MT	AT/ET/CT/ Medication	Cochrane Collaboration Risk of Bias Tool	10 days-6 weeks	A; E; F	"The effect of massage on KOA was better, and the improvement of VAS score, WOMAC score, HSS score, etc. was not weaker than that of western medicine, traditional medicine, acupuncture or joint cavity injection"	Yes
Yu et al. (53) China	Chinese	6 (590)	MT	AT	Cochrane Collaboration Risk of Bias Tool	2–4 weeks	B; C; D	"In improving the stiffness of the joint, the traditional Chinese manipulation is superior to the acupuncture, and the effect of both and physical function is equivalent"	Not reported
Anwer et al. (54) Saudi Arabia	English	11 (494)	MT	ET	PEDro scale	2–24 weeks	B; D; E; G	"This review indicated orthopedic manual therapy compared with exercise therapy alone provides short-term benefiits in reducing pain, improving function, and physical performance in patients with KOA"	Not reported
Yu et al. (55) China	Chinese	29 (2,678)	MT	Medication/ AT/UC	Cochrane Collaboration Risk of Bias Tool; Jadad scale	10 days-8 weeks	A; B; C; D; E	"Chinese manipulation is effective in treating knee osteoarthritis, and the total effective rate is better than other conservative treatment. In the aspect of improving pain and stiffness, Chinese manipulation has advantages over acupuncture, Chinese manipulation is superior to western medicine in improving joint function"	Not reported
Xu et al. (56) China	English	14 (841)	MT	UC/AT/ET/ Medication	PEDro scale	2–12 weeks	B; C; D	"The preliminary evidence from our study suggests that manual therapy might be effective and safe for improving pain, stiffness, and physical function in KOA patients and could be treated as complementary and alternative options"	Yes

(Continued)

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TABLE 2 (Continued)

Authors (ref) country	Language	Number of included RCTs (simple Size)	Intervention	Comparator	Quality assessment tools	Duration of treatment	Outcomes	Overall conclusions (quote from the original paper)	Adverse effects
Cai et al. (57) China	Chinese	14 (1,174)	MT	Medication/ AT/CT	Cochrane Collaboration Risk of Bias Tool; Jadad scale	15 days-8 weeks	A; E	"The total effective rate of the evaluation criteria manipulation in the treatment of osteoarthritis of the knee significantly better than medicines and acupuncture treatment by Meta-analysis"	Not reported
Wang et al. (58) China	Chinese	5 (451)	MT	UC/ET/SMT	Cochrane Collaboration Risk of Bias Tool	4–48 weeks	E	"Manipulation therapy has therapeutic effect on alleviating knee joint pain and improving the knee joint activity both in short and long term"	Not reported

MT, manual therapy; AT, acupuncture therapy; ET, exercise therapy; UC, usual care; CT, conventional treatment; SMT, sham manual therapy; A, total effective rate; B, WOMAC pain score; C, WOMAC stiffness score; D, WOMAC function score; E, Visual Analog Scale (VAS); F, hospital for special surgery knee score (HSS); G, stairs ascending-descending time.

review (54) had been registered before conducting their study (Q24a: 9.09%; Q24b: 9.09%) and none of the reviews mentioned a revision of their protocol (Q24c: 0%). Most of the reviews ignored the descriptions of funding (49–58) and conflict of interest (50–53, 55–58) (Q25: 9.09%; Q26: 27.27%). None of the reviews mentioned access to relevant information (Q27: 0%). More details were shown in Figure 3.

3.6. Evidence quality of included SRs/MAs

The evidence quality of 38 items in eleven SRs/MAs was defined as moderate quality (8 items, 21.05%), low quality (16 items, 42.11%), and critically low quality (14 items, 36.84%). Risk of bias (38 items, 100%), inconsistency (20 items, 52.63%), imprecision (18 items, 47.37%), and publication bias (8 items, 21.05%) were the main downgraded factors. More details were shown in Table 5.

3.7. Outcomes and efficacy evaluation

3.7.1. Total effective rate

Six reviews (49–52, 55, 57) compared the effects of manual therapy with those of medication, acupuncture therapy, exercise therapy, usual care, or conventional treatment using the total effective rate. In all six SRs/MAs, manual therapy appeared to be more effective than control interventions in terms of the total effective rate. One review (52) reported a higher total effective rate with manual therapy than medication (RR = 1.13, 95% CI [1.06, 1.20], $p < 0.00001$) and exercise therapy (RR = 1.34, 95% CI [1.13, 1.59], $p = 0.0009$). Two reviews (50, 51) found that, as compared with medication or acupuncture therapy, manual therapy was associated with a higher total effective rate (OR = 2.03, 95% CI [1.43, 2.88], $p < 0.00001$; OR = 2.30, 95% CI [1.65, 3.22], $p < 0.00001$). Three reviews (49, 55, 57) showed a significant effect of manual therapy compared with medication, acupuncture therapy, usual care, or conventional treatment (RR = 1.14, 95% CI [1.07, 1.21], $p < 0.00001$; OR = 3.26, 95% CI [2.48, 4.29], $p < 0.00001$; OR = 2.46, 95% CI [1.57, 3.86], $p < 0.00001$). We conducted a re-meta-analysis on the total effective rate. A total of 53 RCTs (4,513 participants) were included after the overlapping RCTs were removed. The result showed no homogeneity among these studies ($I^2 = 0$, $p = 0.84$). The effect of manual therapy for KOA was better than that of control interventions on the total effective rate (RR = 1.15, 95% CI [1.12, 1.18], $p < 0.00001$; Figure 4). The funnel plot showed no obvious publication bias (Figure 5).

3.7.2. VAS score

Five reviews (48, 54, 55, 57, 58) reported lower scores for manual therapy on the VAS. One review (58) showed a favorable effect of manual therapy compared with usual care or sham manual therapy (long term: SMD = −8.92, 95% CI [−15.70, −0.88], $p = 0.03$; short term: SMD = −16.64, 95% CI [−22.15, −11.12], $p < 0.00001$). Another four reviews (48, 54, 55, 57) also found a significant effect of manual therapy compared to control interventions (SMD = −1.95, 95% CI [−3.78, −0.12], $p = 0.04$;

TABLE 3 Results of the AMSTAR-2 assessments.

Items	Wu et al. (48)	Xing et al. (49)	Zhang et al. (50)	Xu et al. (51)	Tang et al. (52)	Yu et al. (53)	Anwer et al. (54)	Yu et al. (55)	Xu et al. (56)	Cai et al. (57)	Wang et al. (58)
1	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2	N	N	N	N	N	N	Y	N	N	N	N
3	Y	N	N	N	Y	Y	N	Y	N	Y	N
4	Y	Y	PY	PY	PY	PY	Y	PY	PY	PY	PY
5	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
6	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
7	N	Y	N	N	N	N	Y	Y	N	N	Y
8	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY	PY
9	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
10	N	N	N	N	N	N	N	N	N	N	N
11	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
12	N	N	N	N	N	N	N	Y	N	N	N
13	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
14	Y	Y	N	Y	N	N	Y	Y	Y	N	N
15	N	N	Y	Y	N	N	N	Y	Y	Y	N
16	Y	Y	N	N	N	N	Y	N	N	N	N
Methodological quality	Critically low	Critically low	Critically low	Critically low	Critically low	Critically low	Low	Low	Critically low	Critically low	Critically low

Y, Yes; PY, Partial Yes; N, No.

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TABLE 4 Results of ROBIS assessments.

Review	Phase 1	Phase 2				Phase 3
	Assessing relevance	Domain 1. Study eligibility criteria	Domain 2. Identification and selection of studies	Domain 3. Data collection and study appraisal	Domain 4. Synthesis and findings	Risk of bias in the review
Wu et al. (48)	☺	☺	☺	☺	☺	☺
Xing et al. (49)	☺	☺	☺	☺	☺	☺
Zhang et al. (50)	☺	☺	☹	☹	☹	☹
Xu et al. (51)	☺	☺	☹	☺	?	☹
Tang et al. (52)	☺	☺	☹	☺	☹	☹
Yu et al. (53)	☺	☺	☹	☺	☹	☹
Anwer et al. (54)	☺	☺	☺	☺	☺	☺
Yu et al. (55)	☺	☺	☹	☺	☺	☺
Xu et al. (56)	☺	☺	☹	☺	☺	☺
Cai et al. (57)	☺	☺	☹	☺	☹	☹
Wang et al. (58)	☺	☺	☹	☺	☹	☹

☺: Low risk; ☹: High risk; ? : Unclear.

SMD = −0.80, 95% CI [−1.43, −0.17], p = 0.013; SMD = 0.98, 95% CI [0.23, 1.74], p = 0.01; SMD = 0.47, 95% CI [0.30, 0.64], p < 0.00001). Whereas, Wu et al. (48) indicated no significant reduction of VAS with 4 weeks compared to control groups (SMD = −0.09, 95% CI [−0.49, 0.30], p = 0.64). Xu et al. (51) and Tang et al. (52) showed no significant effect on the VAS of manual therapy compared to medication (SMD = −0.33, 95% CI [−0.93, 0.28], p = 0.29; SMD = −0.38, 95% CI [−1.52, 0.75], p = 0.51).

3.7.3. WOMAC pain score

Five reviews (48, 49, 54–56) reported significant effect on the WOMAC pain score of manual therapy compared to control groups (SMD = −0.79, 95% CI [−1.14, −0.44], p = 0.001; SMD = 0.68, 95% CI [0.23, 1.13], p = 0.003; SMD = −0.61, 95% CI [−0.95, −0.28], p = 0.0003; SMD = −1.96, 95% CI [−3.25, −0.68], p = 0.003; SMD = −2.06, 95% CI [−2.75, −1.36], p < 0.00001). However, Wu et al. (48) indicated no significant difference in WOMAC pain scores between the two groups after six to eight weeks (SMD = −1.24, 95% CI [−2.22, 0.28], p = 0.11). Yu et al. (53) found no significant difference on the WOMAC pain score between manual therapy and acupuncture therapy (SMD = 0.79, 95% CI [0.01, 1.57], p = 0.05).

3.7.4. WOMAC stiffness score

Five reviews (48, 49, 53, 55, 56) found a significant difference in WOMAC stiffness score compared to control groups. One review (48) revealed a statistically significant reduction in stiffness scores with 4 weeks (SMD = −0.60, 95% CI [−1.00, −0.20], p = 0.003) or 6–8 weeks of manual therapy (SMD = −0.80, 95% CI [−1.45, −0.16], p = 0.01). Besides, Another four reviews (49, 53, 55, 56) also found significant difference in improving stiffness scores between manual therapy and control groups (SMD = −0.90, 95% CI [−1.05, −0.75], p < 0.00001; SMD = 0.66, 95% CI [0.06, 1.27], p = 0.03; SMD = 0.50, 95% CI [0.13, 0.87], p = 0.008; SMD = −0.58, 95% CI [−0.95, −0.21], p = 0.002).

3.7.5. WOMAC function score

Five reviews (48, 49, 54–56) reported a favorable effect of manual therapy on WOMAC function score compared to control groups (SMD = 0.75, 95% CI [0.32, 1.18], p = 0.0007; SMD = −0.49, 95% CI [−0.76, −0.22], p = 0.0004; SMD = −0.85, 95% CI [−1.20, −0.50], p = 0.001; SMD = −12.48, 95% CI [−13.91, −11.05], p < 0.00001; SMD = −1.50, 95% CI [−2.14, −0.87], p < 0.00001). Nevertheless, Wu et al. (48) found no significant difference between the two groups after 4 weeks (SMD = −2.57, 95% CI [−5.39, 0.25], p = 0.07). Yu et al. (53) revealed no statistical difference in improving function score compared to acupuncture therapy (SMD = 0.59, 95% CI [−0.09, 1.26], p = 0.09).

3.7.6. HSS and stairs ascending-descending time

Tang et al. (52) found no significant difference on the HSS between manual therapy and medication (SMD = 6.41, 95% CI [−5.92, 18.74], p = 0.31). Anwer et al. (54) showed a significant effect on stairs ascending-descending time compared to exercise therapy (SMD = −0.88, 95% CI [−1.48, −0.29], p = 0.004) based on the insufficient number of subjects (total 48).

3.7.7. Adverse effects

Although none of the included reviews provides a quantitative comparison of adverse effects between manual therapy and the control group, four SRs/MAs (50–52, 56) narratively reported and discussed this aspect. The findings regarding adverse effects indicated that there were no severe adverse reactions in the manual therapy group.

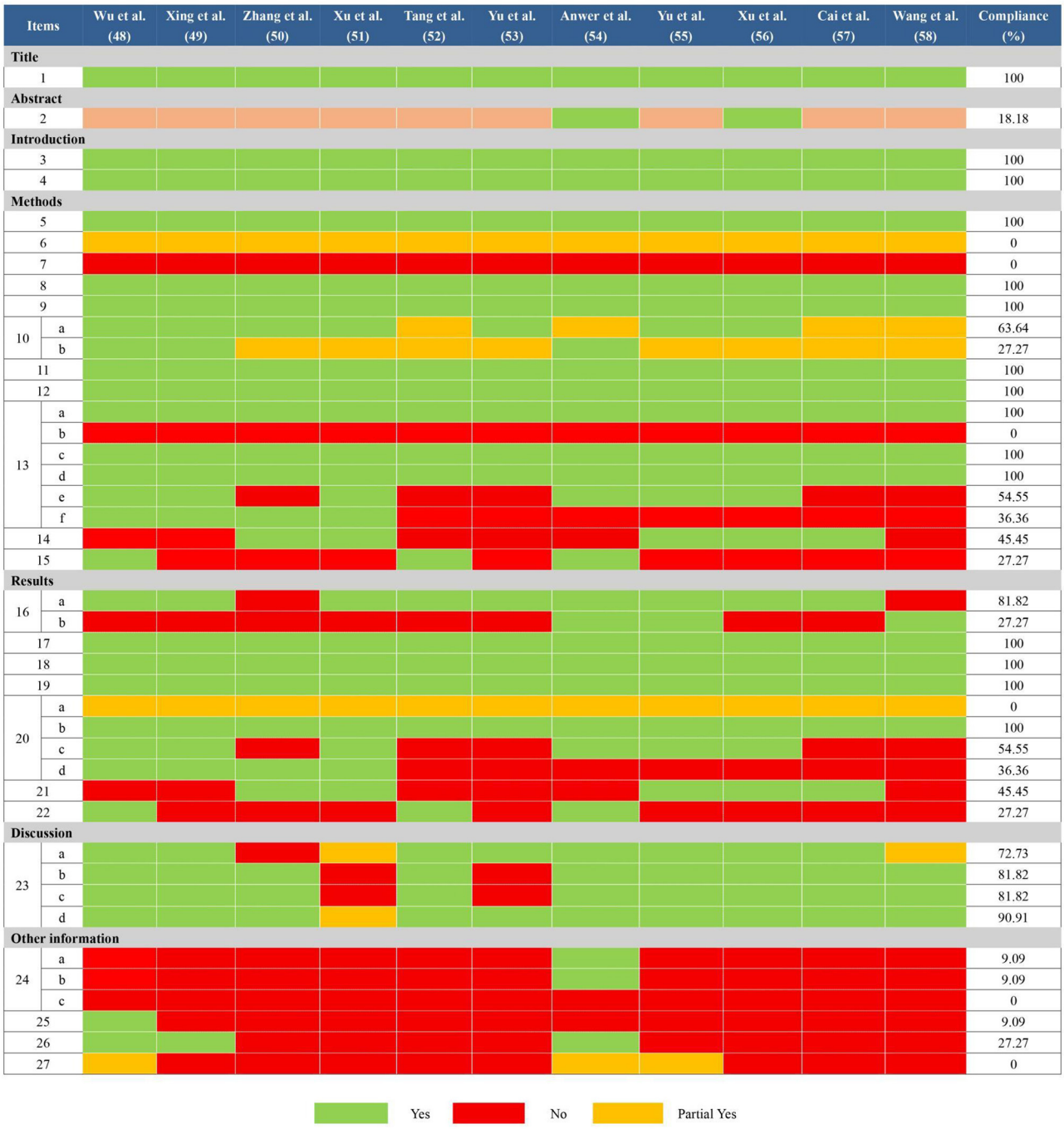

FIGURE 3
Results of the PRISMA 2020 assessments. Item 1: Title; Item 2: Abstract; Item 3: Rationale; Item 4: Objectives; Item 5: Eligibility criteria; Item 6: Information sources; Item 7: Search strategy; Item 8: Selection process; Item 9: Data collection process; Item 10: Data items; Item 11: Study risk of bias assessment; Item 12: Effect measures; Item 13: Synthesis methods; Item 14: Reporting bias assessment; Item 15: Certainty assessment; Item 16: Study selection; Item 17: Study characteristics; Item 18: Risk of bias in studies; Item 19: Results of individual studies; Item 20: Results of syntheses; Item 21: Reporting biases; Item 22: Certainty of evidence; Item 23: Discussion; Item 24: Registration and protocol; Item 25: Support; Item 26: Competing interests; Item 27: Availability of data, code, and other materials.

4. Discussion

4.1. Research significance of this overview

With the increased awareness of the adverse effects of drugs, there has been a heightened interest in complementary and alternative treatments for KOA (59, 60). Manual therapy has gradually derived a variety of applications for patients with KOA in recent years (61–65). Numerous trils (66–69) and SRs/MAs (48–58) have been performed to investigate the effectiveness and safety of manual therapy. However, a few SRs/MAs were reported in accordance with PRISMA 2020 or assessed for

quality of evidence by GRADE. The methodological quality and risk of bias of SRs/MAs were still uncertain. Therefore, it is inadequate to guide clinical practice based on individual SR/MA or low quality SRs/MAs with unconvincing conclusions. Under the circumstances, the establishment of a comprehensive overview of these SRs/MAs can more effectively guide clinical practice. Besides, the deficiencies and gaps in the overview may provide notable information and direction for future studies. Thus, it is significant and innovative to conduct a systematic overview based on these SRs/MAs.

4.2. Pivotal findings of this overview

Firstly, we found that manual therapy was significantly superior to the control group in terms of the total effective rate. But in terms of improving pain and function in KOA patients, the included reviews draw inconsistent conclusions, possibly due to different control interventions, treatment durations, disease severity, and the number of subjects. Some reviews conducted quantitative synthesis on different control measures or durations of manual therapy, but most of the included reviews did not differentiate specifically between these factors or lacked subgroup analysis. As for the safety of manual therapy, the results indicated that there were no severe adverse reactions in the manual therapy group, which revealed that manual therapy may be a safe complementary and alternative treatment. Nevertheless, the promotion and application of these results are limited by the overall quality of the included reviews. The methodological quality of included reviews were rated critically low or low quality. Partial reviews were assessed as high risk in Phase 2 and Phase 3 by ROBIS. Therefore, since definitive conclusions can't be drawn in accordance with published results, caution is warranted when recommending manual therapy as an alternative treatment for improving the symptoms of KOA patients. SRs/MAs with high methodological quality and low risk of bias are needed to evaluate the effectiveness and safety of manual therapy.

Secondly, there is much room for addressing quality during the SR/MA process. In the case of AMSTAR-2, only one review registered a protocol of preliminary design, which may affect the transparency of the study and increase the risk of bias. All the authors conducted literature searches in multiple databases, whereas most of them didn't apply a complete search strategy and provide a list of excluded studies. Partial reviews didn't reasonably explore the heterogeneity and publication bias. And some reviews didn't declare the source of funding. According to ROBIS, a few reviews were assessed as low risk, particularly in Domain 2 of Phase 2 and Phase 3. From the PRISMA 2020 results, the included reviews had different reporting flaws, including mainly these aspects: abstract, protocol and registration, preprocessing of merging data, heterogeneity analysis, sensitivity analysis, publication bias, evidence quality, the list of excluded references, funding source, conflict of interest, and the approach to relevant information. The poor reporting quality may exaggerate the effectiveness of manual therapy, which may diminish the value of the design. Based on GRADE, the evidence of low and critically low quality accounted for 78.95%. The risk of bias in the RCTs was the most common factor degrading the level of evidence. A large proportion of the RCTs had an unclear risk of bias for random sequence generation, allocation concealment, and blinding. Inconsistency may exist due to a large number of clinical characteristics and methodological differences in the RCTs, which could result in high heterogeneity. Moreover, the implausible study designs and small sample size may cause imprecision and publication bias. These deficiencies will provide a promising direction for future researchers to promote the generation of advanced evidence.

4.3. Implications for further studies

This overview introduces several challenges for producers of RCTs and SRs/MAs that should be taken into consideration: (a) Manual therapy appears to be superior to the control group in improving the total effective rate, but the effect on improving pain and physical function is still needed to be further explored. In addition, more normative SRs/MAs are required to evaluate the short and long term effects of manual therapy based on different durations. Researchers should pay attention to the dose-effect and time-effect relationships of manual therapy for KOA. (b) Reviewers should register or publish the research protocol of the preliminary design at PROSPERO, Cochrane, or a public publication in advance for a transparent process. (c) A comprehensive search strategy and a list of excluded studies with explanations should be provided. The gray literature should be taken into account when reviewers conduct searches. (d) The conflicts of interest and funding source should be mentioned in the article. (e) If the heterogeneity is significant, subgroup analysis or meta-regression should be conducted. Reviewers shouldn't also ignore the exploration of publication bias, sensitivity analysis, and evidence quality. (f) Most of the RCTs included in the SRs/MAs had an unclear risk of bias for blinding, allocation concealment, and random sequence generation. So reviewers should comply with the relevant guidelines in order to minimize the bias. (g) We have insufficient evidence on the adverse effects of manual therapy, and researchers should further investigate its safety.

4.4. Strengths and limitations

To our knowledge, this is the first overview of SRs/MAs that focuses on the effectiveness and safety of manual therapy for KOA. AMSTAR-2, ROBIS, PRISMA 2020, and GRADE tools were used to comprehensively appraise the published SRs/MAs in a rigorous way, which was in favor of the clinical application. The revelent results may provide valuable evidence references for clinical practice, and promote the generation of advanced evidence of manual for KOA. However, several limitations in this overview were analyzed in the following: Firstly, we did not explore the influence of detailed control interventions and manual therapy durations because of deficient reporting in many SRs/MAs. This overview can not fully present situations in long term effect of manual therapy. Secondly, most of the included studies were conducted in China, so more studies should be performed to investigate whether the relevant conclusions can be generalized to other populations.

TABLE 5 Results of the GRADE.

Outcome measures	No. of RCTs (No. of participants)	Interventions	Effect estimate 95% CI	*p*-value	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality of evidence	References
Total effective rate	7 (661)	MT vs. Medication	RR 1.14 (1.07, 1.21)	< 0.00001	−1①	0	0	0	0	M	(49)
	8 (632)	MT vs. Medication/AT	OR 2.03 (1.43, 2.88)	< 0.00001	−1①	0	0	0	0	M	(50)
	16 (1,307)	MT vs. Medication/AT	OR 2.30 (1.65, 3.22)	< 0.00001	−1①	0	0	0	0	M	(51)
	7 (728)	MT vs. Medication	RR 1.13 (1.06, 1.20)	< 0.00001	−1①	0	0	0	0	M	(52)
	2 (229)	MT vs. ET	RR 1.34 (1.13, 1.59)	0.0009	−1①	0	0	−1③	−1④	CL	(52)
	23 (2,144)	MT vs. AT/UC/Medication	OR 3.26 (2.48, 4.29)	< 0.00001	−1①	0	0	0	0	M	(55)
	12 (909)	MT vs. AT/CT/Medication	OR 2.46 (1.57, 3.86)	< 0.00001	−1①	0	0	0	0	M	(57)
VAS	4 (167)	MT vs. Medication/UC/SMT	SMD −0.09 (−0.49, 0.30)	0.64	−1①	0	0	−1③	0	L	(48)
	5 (361)	MT vs. Medication	SMD −0.33 (−0.93, 0.28)	0.29	−1①	−1②	0	−1③	0	CL	(51)
	3 (288)	MT vs. Medication	SMD −0.38 (−1.52, 0.75)	0.51	−1①	−1②	0	−1③	−1④	CL	(52)
	4 (300)	MT vs. UC/CT/LT	SMD −1.95 (−3.78, −0.12)	0.04	−1①	−1②	0	−1③	0	CL	(48)
	5 (141)	MT vs. ET	SMD −0.80 (−1.43, −0.17)	0.013	−1①	−1②	0	−1③	0	CL	(54)
	15 (1,434)	MT vs. AT/Medication/UC	SMD 0.98 (0.23, 1.74)	0.01	−1①	−1②	0	0	0	L	(55)
	6 (437)	MT vs. AT/CT/Medication	SMD 0.47 (0.30, 0.64)	< 0.00001	−1①	0	0	0	0	M	(57)
	2 (244)	MT vs. UC/SMT	SMD −8.29 (−15.70, −0.88)	0.03	−1①	0	0	−1③	0	L	(58)
	4 (283)	MT vs. UC/SMT	SMD −16.64 (−22.15, −11.12)	< 0.00001	−1①	0	0	−1③	0	L	(58)
WOMAC pain score	6 (590)	MT vs. AT	SMD 0.79 (0.01, 1.57)	0.05	−1①	−1②	0	0	0	L	(53)
	6 (426)	MT vs. UC/SMT	SMD −1.24 (−2.22, 0.28)	0.11	−1①	−1②	0	0	0	L	(48)
	3 (132)	MT vs. ET	SMD −0.79 (−1.14, −0.44)	0.001	−1①	0	0	−1③	−1④	CL	(54)
	14 (1,192)	MT vs. AT/Medication/UC	SMD 0.68 (0.23, 1.13)	0.003	−1①	−1②	0	0	0	L	(55)

(Continued)

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TABLE 5 (Continued)

Outcome measures	No. of RCTs (No. of participants)	Interventions	Effect estimate 95% CI	*p*-value	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Quality of evidence	References
	11 (657)	MT vs. Medication/UC/AT	SMD −0.61 (−0.95, −0.28)	0.0003	−1①	−1②	0	0	0	L	(56)
	5 (227)	MT vs. UC/CT/SMT	SMD −1.96 (−3.25, −0.68)	0.003	−1①	−1②	0	−1③	0	CL	(48)
	2 (135)	MT vs. Medication	SMD −2.06 (−2.75, −1.36)	< 0.00001	−1①	0	0	−1③	−1④	CL	(49)
WOMAC stiffness score	4 (345)	MT vs. Medication	SMD −0.90 (−1.05, −0.75)	< 0.00001	−1①	0	0	−1③	0	L	(49)
	6 (590)	MT vs. AT	SMD 0.66 (0.06, 1.27)	0.03	−1①	−1②	0	0	0	L	(53)
	13 (1,132)	MT vs. AT/Medication/UC	SMD 0.50 (0.13, 0.87)	0.008	−1①	−1②	0	0	0	L	(55)
	11 (657)	MT vs. Medication/UC/AT	SMD −0.58 (−0.95, −0.21)	0.002	−1①	−1②	0	0	0	L	(56)
	5 (227)	MT vs. UC/CT/SMT	SMD −0.60 (−1.00, −0.20)	0.003	−1①	−1②	0	−1③	0	CL	(48)
	6 (426)	MT vs. UC/SMT	SMD −0.80 (−1.45, −0.16)	0.01	−1①	−1②	0	0	0	L	(48)
WOMAC function score	4 (460)	MT vs. AT	SMD 0.59 (−0.09, 1.26)	0.09	−1①	−1②	0	0	0	L	(53)
	10 (882)	MT vs. AT/Medication/UC	SMD 0.75 (0.32, 1.18)	0.0007	−1①	−1②	0	0	0	L	(55)
	11 (657)	MT vs. Medication/UC/AT	SMD −0.49 (−0.76, −0.22)	0.0004	−1①	−1②	0	0	0	L	(56)
	3 (132)	MT vs. ET	SMD −0.85 (−1.20, −0.50)	0.001	−1①	0	0	−1③	−1④	CL	(54)
	3 (225)	MT vs. Medication	SMD −12.48 (−13.91, −11.05)	< 0.00001	−1①	0	0	−1③	−1④	CL	(49)
	6 (426)	MT vs. UC/SMT	SMD −1.50 (−2.14, −0.87)	< 0.00001	−1①	0	0	0	0	M	(48)
	6 (287)	MT vs. UC/CT/LT	SMD −2.57 (−5.39, 0.25)	0.07	−1①	−1②	0	−1③	0	CL	(48)
HSS	2 (210)	MT vs. Medication	SMD 6.41 (−5.92, 18.74)	0.31	−1①	−1②	0	−1③	−1④	CL	(52)
Stairs ascending-descending time	2 (48)	MT vs. ET	SMD −0.88 (−1.48, −0.29)	0.004	−1①	0	0	−1③	−1④	CL	(54)

MT, manual therapy; AT, acupuncture therapy; ET, exercise therapy; UC, usual care; CT, conventional treatment; SMT, Sham manual therapy; RR, risk ratio; OR, odds ratio; SMD, standard mean difference; 95% CI, 95% confidence interval; ①The design of the experiment with a large bias in random, distributive hiding or blind; ②The confidence interval overlaps less, the heterogeneity lly small, and the I^2 is larger; ③Confidence interval is not narrow enough; ④ Fewer studies are included and there may be greater publication bias; M, moderate quality; L, Low quality; CL, Critically low quality.

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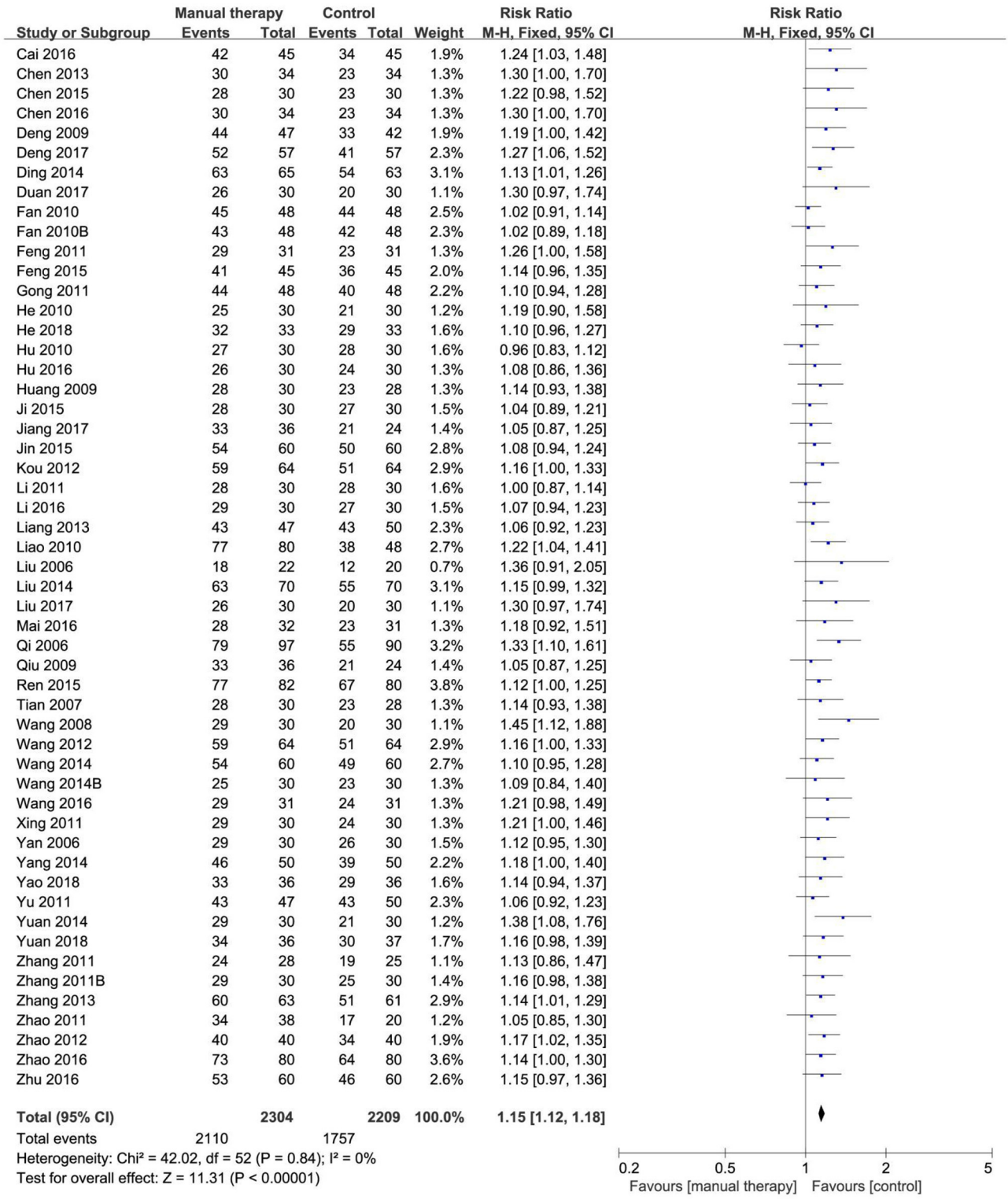

FIGURE 4
Forest plot of total effective rate.

5. Conclusion

Manual therapy may be clinically effective and safe as a nonpharmacological intervention for KOA. Nevertheless, because of the generally unsatisfactory study quality and inconsistent conclusions of the SRs/MAs, this conclusion must be interpreted with caution. Further rigorous and normative SRs/MAs are

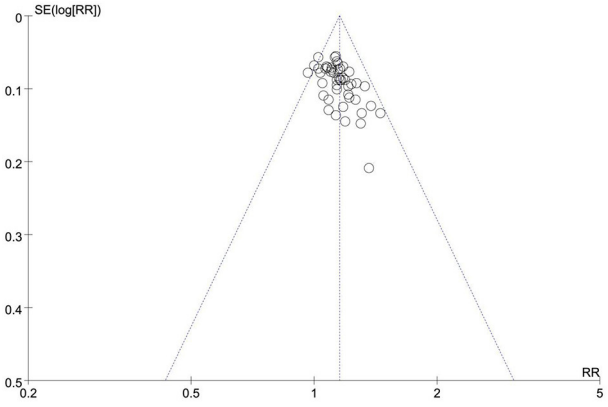

FIGURE 5
Funnel plot of total effective rate.

expected to be carried out to provide robust evidence for definitive conclusions.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

Study conception and design: TF, LZ, and XWe. Final approval of manuscript materials: TF, LZ, and XWe. Collection and assembly of data: TF, XWa, ZJ, and XQ. Data analysis and interpretation: TF, CS, BQ, and YZ. Manuscript writing: TF and XWa. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1081238/full#supplementary-material

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The impact of pandemic-related social distancing regulations on exercise performance—Objective data and training recommendations to mitigate losses in physical fitness

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Introduction: In the context of the COVID-19 pandemic in Germany, governmental restrictions led to the closure of sports facilities for several months. To date, only subjective and fitness-tracking related data on physical activity during the pandemic are available. Using data of a chip-controlled fitness circuit, training data as a measure of physical performance before and after the lockdown during the first wave of the COVID-19 pandemic will show the impact of the training interruption on exercise performance in middle-aged and older adults. The re-training data are analyzed, to extract practical recommendations.

Methods: Objective training data of 17,450 participants [11,097 middle-aged (45–64 yrs), 6,353 older (≥65 yrs)] were exported from chip-controlled milon® fitness circuit systems before and after the first COVID-19 related lockdown in Germany. The change in the product of training weight (sum of lifting and lowering the training weight) and repetitions on the leg extension resistance exercise device (leg score) between the last three training sessions before the lockdown and the first ten training sessions after individual training resumption as well as the last training session before the second lockdown in October 2020 was analyzed.

Results: Participants who trained with high intensity before the lockdown, experienced deleterious effects of the training interruption (middle-aged group: −218 kg, older group: ∼−230.8 kg; $p < 0.001$ for change in leg score from to post-lockdown) with no age effect. Participants training with a leg score of more than 3,000 kg did not resume their leg score until the second lockdown.

Conclusion: The interruption of training in a fitness circuit with combined resistance and endurance training due to the lockdown affected mainly those participants who trained at high intensity. Apparently, high-intensity training could not be compensated by home-based training or outdoor activities. Concepts for high-intensity resistance training during closure of sports facilities are needed to

be prepared for future periods of high incidence rates of infectious diseases, while especially vulnerable people feel uncomfortable to visit sports facilities.

Trial registration: Identifier, DRKS00022433.

KEYWORDS

social distancing, aged, exercise training, physical fitness, physical activity, health promotion, COVID-19 pandemic

1. Introduction

The first wave of the COVID-19 pandemic had a great impact on the health care system and the social life in Germany. Since no vaccines were available in 2020, a high number of patients with SARS-CoV-2 infections suffered from severe courses, which led to an overload of the health care system, especially in Intensive Care Units. Until 2023, about 37.5 Mio. cases were reported during several COVID-19 waves in Germany, which were caused by different mutations of the virus (1, 2). To reduce the rate of infection during the first wave of the COVID-19 pandemic, the German government enacted a hard lockdown from March to June 2020, which included not only the temporary closure of retail shops, cultural events, and restaurants, but also all sports facilities.

Due to their high risk for severe courses of a COVID-19 infection, older adults voluntarily limited their life space and physical activity substantially to protect themselves from infection (3). As physical activity is of high importance to promote health, wellbeing, physical fitness, and participation in older people (4–11), short- and long-term side effects of the restrictions are of great concern.

Physical activity decreased during the pandemic-related lockdown, especially in formerly very active adults, in many countries (8, 12–14). As known from bed rest, step reduction, and detraining studies, recovery of muscle mass and aerobic capacity, which are reduced by inactivity, require a longer period of time in older, compared with younger adults (15–19). Low skeletal muscle mass is well-documented as a cause of diverse negative outcomes, such as functional impairment and morbidity in older adults (5, 20).

To date, only self-reported (8, 12, 13, 21) and activity tracking data (14) on changes in individual physical activity and exercise behavior during the pandemic were published. Chip-controlled fitness circuits give access to objective measures of exercise training performance, which we postulate as a surrogate of physical fitness, before the lockdown and after training resumption.

The aim of this observational study is to describe how individual exercise training performance on resistive and aerobic exercise training devices changed following the first lockdown period in different age groups and in respect to baseline training intensity. Further, predictive factors for a pronounced decline, as well as factors enhancing the recovery of exercise training performance after the lockdown will be identified in regression models.

2. Material and methods

2.1. Study design and data base

This observational study uses data from the milon® fitness circuit system (milon industries, Emersacker, Germany). Apart from age and gender of the participant, the system stores the following training data: workout weight in concentric, eccentric, and adaptive mode, as well as while lifting and lowering the weight, the number of repetitions per set, the number of sets, as well as the duration of the training activity on each device. On the ergometric devices, power and training duration are documented. If an appropriate belt is worn, heart rate (HR) is also registered. A regular training in a milon® fitness circuit includes 60 s for each resistance exercise, 30 s time intervals to change between two devices and 240 s for the endurance training devices. Sets can be repeated as desired. In this analysis, only data from the leg extension, the seated row devices for resistance training of a larger upper-body muscle group, and the cycle ergometers were included.

Data of participants with a training registration during the 4 weeks before the lockdown were exported anonymously from the milon® care cloud, owned by milon industries, in consideration of the general data protection regulation of the European Union. The data analysis was approved by the ethics committee of the medical faculty at the Carl von Ossietzky University of Oldenburg before the beginning of data extraction (2020-061) and the study was registered at the German clinical trials registry (DRKS00022433).

2.2. Study population

Overall, data sets of initially 43,843 participants above the age of 45 years with training data in February 2020 (1 month before the first lockdown) were exported until October 2020 from the milon® care cloud. The participants were divided into a "middle-aged" (45–64 yrs) and an "older" (≥65 yrs) age group.

2.3. Outcomes

For the resistive exercise devices, training performance was measured with a score, calculated from the product of training weight (sum of weight for lifting and lowering) and overall number of repetitions during one training session (leg score, rowing score). The scores reflect the total weight lifted per training session and allow a comparison in spite of different training habits (low

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training weight, many repetitions vs. high training weight, few repetitions). For the endurance exercise data, we calculated an endurance score [HR divided by work rate (WR)] to account for a higher HR when performing the same WR, which indicates lower physical capacities.

The changes for the leg score were the primary outcome of the analysis. Secondary outcomes were changes in the rowing and the endurance scores.

2.4. Data analysis

As measure for baseline training performance, scores were averaged from the last up to three training sessions in February 2020, as available. Three training intensity groups (TIG; low, moderate, high) were determined, applying the tertials of the leg score before the first lockdown (pre-COVID-$19_{legscore}$) as cut-off values. The time course of the changes of the leg, rowing and endurance scores before the lockdown are described for the first ten individual training sessions after the re-opening of the fitness circuits to show potential losses of performance. To assess the progression of recovery, the last session before the second lockdown (starting on November 2nd in 2020) was included as well. Only participants with available data for the leg extension device for the described time points, as well as individuals who additionally trained with the rowing resistive exercise device and a cycle ergometer, were included in the analysis. The first registered training was used to calculate the individual training interruption in days. In the generalized, additive regression models all available training sessions from February to October 2020 were included.

2.5. Statistical analysis

A mixed linear regression model, including gender (male, female), age group (older, middle-aged), training session (session 1–10 after the lockdown) and TIG (low, moderate, high) was used to describe the changes in the leg, rowing and endurance scores, before and after the lockdown.

In addition, three generalized additive regression models were constructed to predict the difference between the pre-COVID-19_{score} and the first post lockdown training score for the leg, rowing, and endurance scores. The set of covariates was gender, age (in years), average training weight (sum of weight lifted and released), duration of training set, average number of repetitions in a set, number of training sets, pre-COVID-19_{score} for leg score, rowing score, endurance score, and number of days paused. The variable selection was performed stepwise backwards using the Akaike Information Criterion (AIC).

The increase of the leg score, as the most important indicator for the weight bearing muscles, after training resumption relative to the pre-COVID-19_{score}, was modeled in a generalized additive mixed regression. All post lockdown trainings were included as repeated measurements and the number of completed trainings was included as a random effect per person. For the fixed effects, the same set of covariates as in the previous models was eligible, plus the number of completed trainings. Variable selection was

TABLE 1 Participants' characteristics by age groups and training intensity groups.

Age group	Pre-COVID-$19_{Legscore}$ mean ± SD (median) [kg]	Rowing score mean ± SD (median) [kg]	Endurance score mean ± SD (median) [$min^{-1}.W^{-1}$]	TIG according to pre-COVID-$19_{Legscore}$ [kg]	Cut off values [kg] to define TIGs	*n*	Gender		Age [years] mean ± SD	Training break [days] mean ± SD
							Female [*n* (%)]	Male [*n* (%)]		
Middle-aged *n* = 11,097	1,395.14 ± 830.16 (1,237.67)	1,601.61 ± 947.73 (1,426.00)	1.26 ± 0.48 (1.16)*	Low	<976.00	3,701	3,050 (17.5%)	651 (3.7%)	56 ± 5	84 ± 31
				Moderate	976.00–1,548.22	3,697	2,558 (14.7%)	1,139 (6.5%)	55 ± 5	84 ± 32
				High	>1,548.22	3,699	1,591 (9.1%)	2,108 (12.1%)	55 ± 5	85 ± 32
Older *n* = 6,353	1,182.22 ± 716.90 (1,050.00)	1,343.33 ± 828.73 (1,190.33)	1.49 ± 0.67 (1.34)#	Low	<816.00	2,124	1,502 (8.6%)	622 (3.6%)	73 ± 6	86 ± 31
				Moderate	816.00–1,324.33	2,110	1,209 (6.9%)	901 (5.2%)	72 ± 5	85 ± 32
				High	>1,324.33	2,119	783 (4.5%)	1,336 (7.7%)	71 ± 5	85 ± 32

TIG, training intensity group; SD, standard deviation, *n = 5,444, #n = 2,696 (numbers reduced for endurance score as only 49%, respectively 42% of participants wore the belt to measure the heart rate.

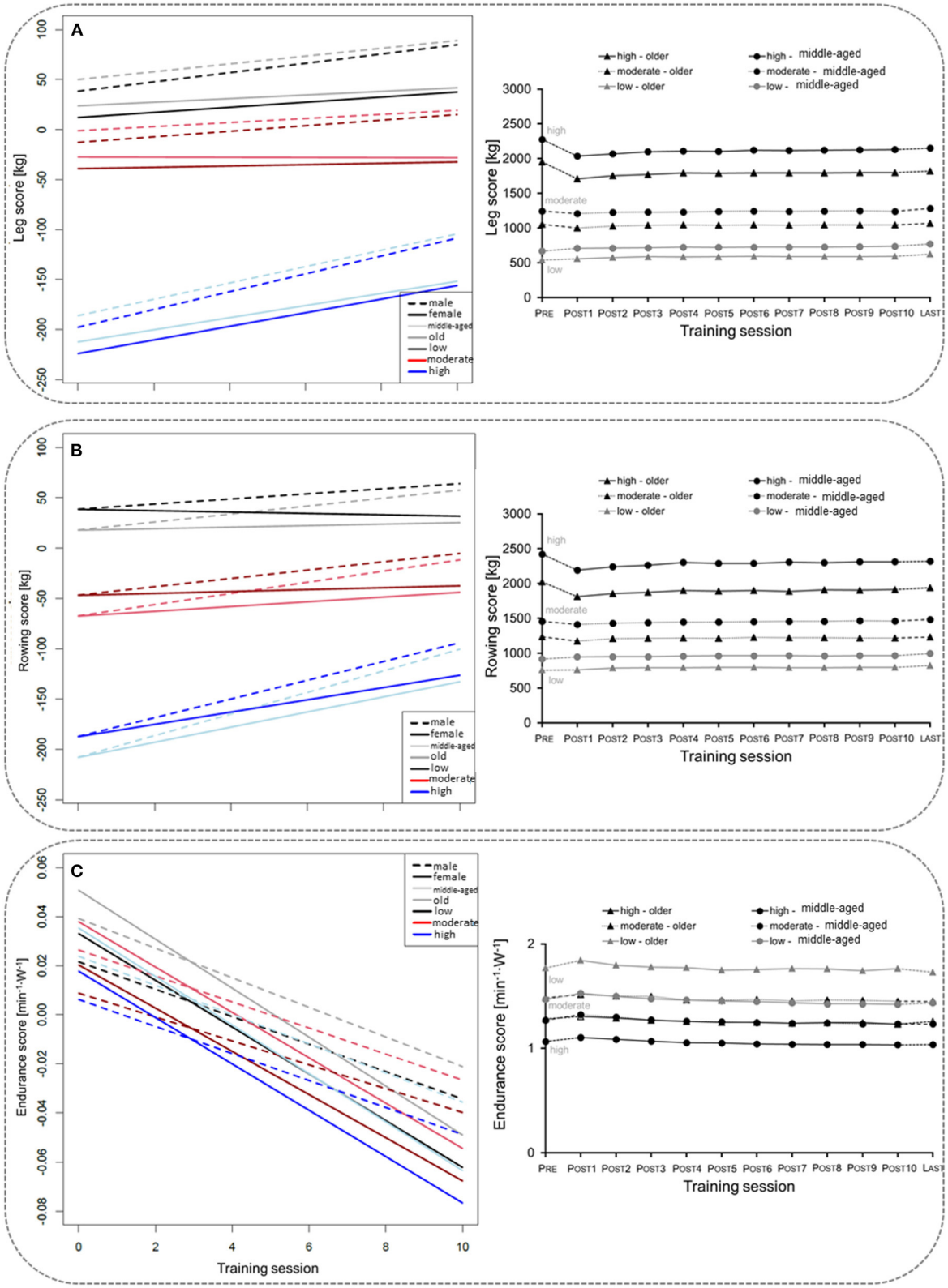

FIGURE 1
Left column: Course of changes in the for the leg score **(A)**, rowing score **(B)**, and endurance score **(C)** over the first ten training sessions after the lockdown. Negative values indicate losses in the leg and rowing score in comparison to the values before the lockdown, and lower heart rates per given work rate. Right column: Description of the mean for the leg score **(A)**, rowing score **(B)**, and endurance score **(C)** before (Pre), during the ten first sessions after the lockdown period 1(POST1–10), and for the last training session (LAST) before the second lockdown in Germany, considering age and training intensity groups (TIG; low, moderate, high) based on the leg score before the lockdown (pre-COVID-$19_{legscore}$). SE are too small to be presentable.

TABLE 2 Mixed regression analysis for the first 10 training session.

	Leg score			Rowing score			Endurance score		
	Estimate [kg]	SE	Sig.	Estimate [kg]	SE	Sig.	Estimate [min^{-1}.W^{-1}]	SE	Sig.
Intercept	22.1	11.379	0.052	17.8	12.5	0.157	0.051	0.008	<0.001
Gender (male)	36.6	11.1579	0.001	0.2	14.5	0.988	−0.011	0.009	0.210
Older adults	−12.8	12.2801	0.299	0.8	1.3	0.561	−0.010	0.001	<0.001
Training session	2.1	1.1181	0.057	20.7	13.9	0.136	−0.018	0.009	0.048
TIG moderate	−52.6	14.434	<0.001	−85.4	16.3	<0.001	−0.013	0.010	0.221
TIG high	−240.1	15.1022	<0.001	−225.8	17.1	<0.001	−0.015	0.011	0.167
Older adults training session	1.0	1.207	0.422	3.2	1.5	0.032	0.004	0.001	<0.001
TIG moderate training session	−1.6	1.4212	0.267	−1.4	1.4	0.319	0.000	0.001	0.656
TIG high training session	5.1	1.4296	<0.001	1.6	1.7	0.337	0.001	0.001	0.529

The intercept value describes the change after the lockdown for a middle-aged, female adult in the low training intensity group (TIG).

again performed with a stepwise backwards algorithm using the AIC. Further, we included pairwise interaction terms of average training weight and average number of repetitions with the number of completed trainings. All metric variables and interactions were modeled with the possibility for a flexible non-linear effect using a P-spline basis and a tensor product P-spline, respectively.

For all regression models, the regression coefficients with 95% confidence intervals are reported as well as the adjusted R^2. For the non-linear effects, the estimated centered effect curves are plotted and for the bivariate interaction terms the estimated effects are provided in heatmaps with contour lines. Calculations were performed using the software R 4.1.0 (22) with the package "mgcv" (23).

3. Results

3.1. Changes in exercise training performance after the lockdown

Overall, 17,450 participants (11,097 middle-aged, 6,353 older age group) with complete data sets (pre, post 1–10) were included in the mixed linear regression model. The participants' baseline performance and cut-off values between the low, the moderate, and the high TIG in each age group are shown in Table 1. The time courses of the leg, rowing, and endurance scores over the first wave of the COVD-19 pandemic are shown descriptively for each age group and TIG in Figure 1 (right column). In the left column of Figure 1 and in Table 2, the results of the mixed linear regression model to evaluate the influence of the factors gender, age, TIG and training session on the change in leg, rowing and endurance scores during the first 10 sessions after the lockdown are shown. A substantial decrease in the leg and rowing score is exclusively seen in the high TIG in both age groups. In both scores a complete recovery to the pre-lockdown performance was not reached throughout the first ten training sessions in the high TIG. As expected, performance was lower in the older age group (opaque lines).

In the regression models to model influencing training habits before the lockdown for respective losses in the leg and rowing scores after the lockdown, negative values (age, the average number of sets, and the duration of the training pause) imply higher losses from pre- to post-lockdown (Table 3). The applied training weight and number of repetitions appear to reduce losses, however, in the model this is only true for training at very low intensities. After passing a certain threshold, the equation is inversed with higher intensity training, as characterized by a high number of sets, resulting in higher losses compared to baseline. The endurance score is mainly unchanged (Table 3).

3.2. Prediction of training recovery

The generalized additive mixed regression model, predicting the increase of the leg score after individual training resumption post lockdown, reveals that the number of sets a participant carries out, and to a small degree also male gender, predict an accelerated increase of performance, e.g., two instead of one set of repetitions led to ∼100% more increase in the leg score (∼650 kg) (Table 3). Age had only a small negative effect (Table 3). The effects of different training regimens, that participants applied when they resumed training after the lockdown, on their individual progress in regaining training performance are shown in Figure 2. The contour lines and colors show the course of the increase or reduction in the leg score. The visualization with heat maps allows the identification of effective training strategies. To clarify, we give some examples of the information the heat maps contain: as indicated by the dashed green lines in Figure 2A, participants training with an average training weight of 75 kg (sum of lifting and lowering) require about 20 training sessions to regain their exercise performance before the lockdown, while someone training with ∼ 40 kg would need ∼60 sessions. On the leg extension device, at least 15–20 repetitions should be performed per set; the more repetitions, the greater the benefit (green line in Figure 2B). Figures 1, 2 consistently show, that participants with lower pre-COVID-$19_{legscores}$ needed fewer training sessions to regain their baseline levels (Figure 2C). Participants with pre-COVID-$19_{legscores}$

TABLE 3 Results of the linear regression models to predict losses in the leg, rowing, and endurance scores from pre- to post-lockdown and the generalized additive mixed regression model to predict the regain of the leg score after individual training resumption.

	Prediction of losses from pre- to post-lockdown							Prediction of increases after the lockdown		
	Leg score ($R^2 = 0.157$)		Rowing score ($R^2 = 0.167$)		Endurance score ($R^2 = 0.030$)			Post-lockdown increase leg score ($R^2 = 0.663$)		
$n = 23,299$	Estimate [kg]	CI 95% [kg]	Estimate [kg]	CI 95% [kg]	$n = 12,174$	Estimate [kg]	CI 95% [kg]	$n = 69,197$	Estimate [kg]	CI 95% [kg]
								Intercept [kg]	−598.1	−619.7–−576.5
Gender (male)	22.1	8.7–35.4	67.5	52.0–83.0	Gender (male)	−0.041	−0.056–−0.025	Gender (male)	0.5	−6.8–7.8
Age [years]	−3.2	−3.8–−2.6	−4.1	−4.7–−3.4	Age [decade]	0.007	−0.008–0.009	Age [years]	−0.8	−1.2–0.5
Avg training weight [kg]	5.6	5.0–6.1	5.1	4.5–5.7	Duration [minutes]	0.009	−0.011–0.011	Sets$^{\#}$ = 2 [number]	655.3	652.2–658.4
Avg repetitions [number]	13.0	11.4–14.5	14.8	13.0–16.6	Avg heart rate [min^{-1}]	0.000	−0.001–0.000	Sets$^{\#}$ = 3 [number]	1,244.9	1,240.5–1,249.3
Sets* = 2 [number]	−9.0	−26.3–8.2	−4.0	−23.5–15.5	Avg rpm [min^{-1}]	0.002	−0.003–−0.002	Sets$^{\#}$ = 4+ [number]	1,751.7	1741.7–1761.7
Sets* = 3 [number]	−93.3	−124.1–−62.5	−100.3	−136.6–−64.0	Sets [number]	−0.035	−0.079–0.008			
Sets* = 4 [number]	−219.9	−289.6–−150.2	−158.9	−223.2–−94.6						
Sets* = 5+ [number]	−273.4	−402.3–−144.6	−233.1	−366.4–−99.8						
Pre-COVID-$19_{legscore}$ [kg]	−0.3	−0.4–−0.3	0.0	0.0–0.0	Pre-COVID-$19_{legscore}$ [kg]	−0.002	−0.001–0.001			
Pre-COVID-$19_{rowscore}$ [kg]	0.0	−0.0–0.0	−0.4	−0.4–−0.3	Pre-COVID-$19_{endurancescore}$ [$min^{-1} \cdot W^{-1}$]	−0.101	−0.114–−0.088			
Training pause [days]	−0.8	−0.9–−0.7	−0.9	−1.1–−0.8						

Regression coefficients with 95% confidence intervals.

Avg, average over all sets of the last three training sessions; rpm, revolutions per minute; pre-COVID-$19_{legscore}$, pre-COVID-$19_{rowingscore}$, pre-COVID-$19_{endurancescore}$, average of the three last training sessions before the lock down for the leg extension device, the rowing exercise device, the cycle ergometer, respectively. Sets, the number of times a participant repeated an exercise. *Median number of sets from the last three training sessions before the lockdown, $^{\#}$number of sets per training session after the lockdown until October 31st 2020. Negative values indicate a higher loss in the particular score, positive values indicate a reduced loss.

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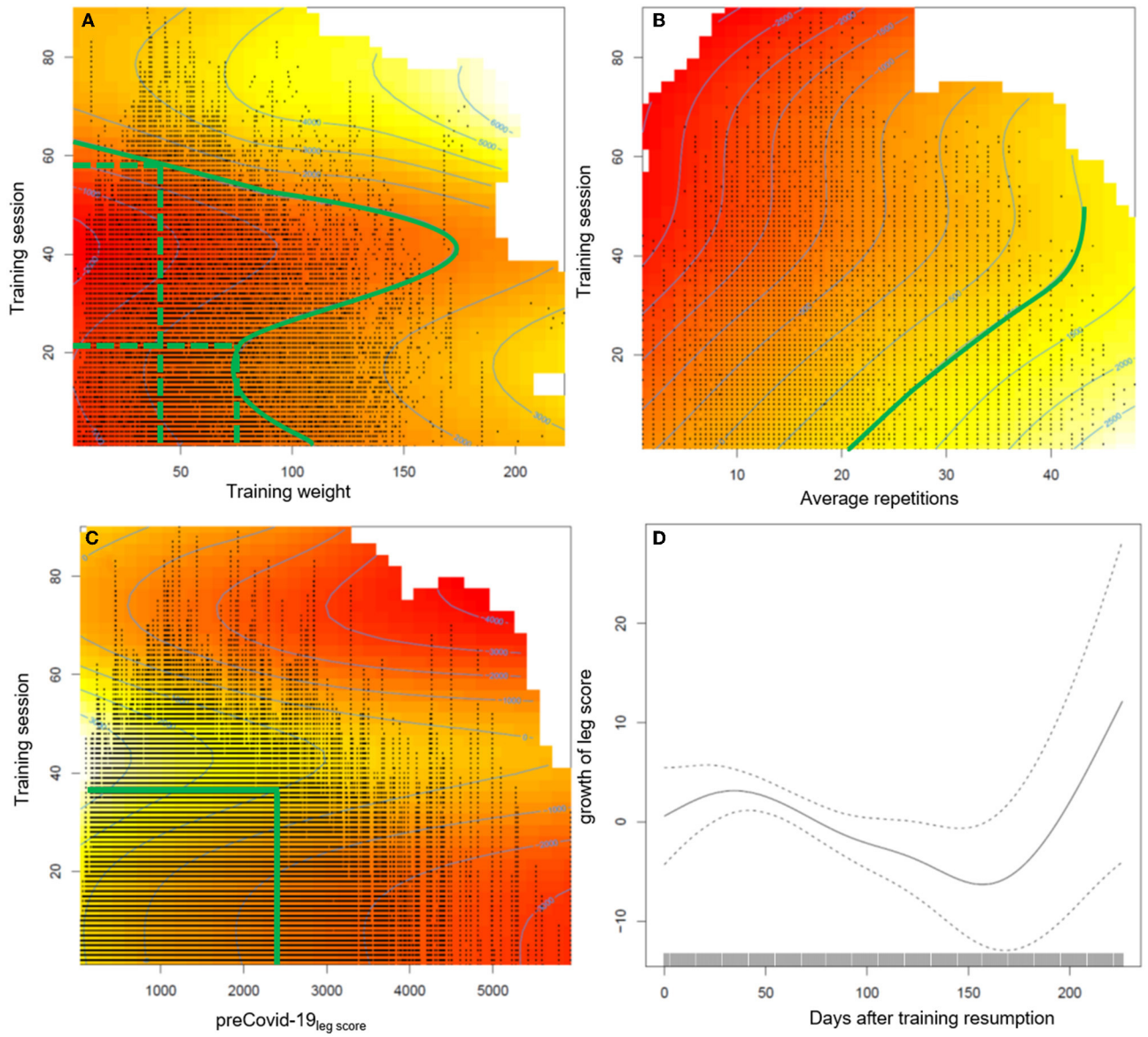

FIGURE 2
Presentation of the estimated effects on the increase of the leg score of **(A)** average training weight per repetition (sum of lifting and lowering the training weight), **(B)** average repetitions per set, **(C)** pre-COVID-19$_{legscore}$, and **(D)** the number of days after training resumption during the post lockdown training sessions. The heat maps include contour lines, which denote increase or loss in the leg score compared to the first training session after the lockdown. As the intercept of the model is −598.06 kg, the zero line still indicates a loss in training performance of at least ≈600 kg compared with baseline level, the difference will be larger depending on age and gender. Therefore, we marked the contour line 1,000 in **(A, B)** which indicates recovery of baseline values. The red color indicates a permanently reduced leg score until October 2020.

higher than ∼3,000 kg did not reach their baseline levels by the end of October 2020. The mere number of days after training resumption, irrespective of training sessions, did not predict the increase of the leg score (Figure 2D).

4. Discussion

The aim of this data analysis was to show, (i) how individual exercise training performance, which we interpret as a surrogate of physical fitness, changed due to the training interruption caused by the first COVID-19 lockdown in different age groups with different initial training intensities, and (ii) to identify training regimens beneficial for a fast recovery of the baseline training performance.

4.1. Exercise training performance after the lockdown

Interestingly, we see similar results for both age groups: Participants who trained with high intensity before the lockdown had pronounced and long-lasting reductions in training weights for lower (leg score, Figure 1A) and upper body (rowing score, Figure 1B) exercise. For cycle ergometer exercise, the most

pronounced increase in HR per given work rate was about 0.05 $min^{-1} \cdot W^{-1}$, thus 2.5 beats·min^{-1} for 50 W, in the middle-aged adults of the low TIG. Physiological and clinical relevance is questionable. For comparison, differences of about 10 beats·min^{-1} at a WR of ∼50 W after 60 d of bed rest were reported (24). The regression models confirmed the result showing a substantial reduction in performance in participants who trained with a higher number of sets before the lockdown (Table 3). Accordingly, Suzuki et al. (8) reported a greater decrease in self-reported physical activity in people who were highly active before the COVID-19 pandemic. This finding is of substantial relevance, as the main concern of health care professionals and politics was on the most vulnerable groups, the frail older population. However, adverse effects of the protective social distancing regulations appear to have affected the physical capacities of the fittest seniors the most.

The losses for the leg, and especially the rowing score were lower in male compared with female participants. In contrast, in a review no sex-dependent differences in submaximal strength after training cessations of up to 200 days were reported (18), and natural age-related loss in muscle power appears to be lower in women (−1.7 vs. −3% per year) (25). With no information about physical activity during the lockdown period, it can only be speculated, that male individuals integrated more upper body muscular exercise in their daily life.

The factor age had small influence on the losses in performance and only marginal impact during the recovery phase. Generally, longer recovery periods after phases of inactivity, due to bed rest or detraining phases have been reported for older people several times in the literature (15–19). In a recent review, analyzing short term (4–14 d) immobilization studies, comparing older and younger adults, greater muscle atrophy was not a consistent finding for older adults, and high-quality research on this topic is lacking (26). The individual level of physical activity might be more important for muscle atrophy than chronological age. Kirwan et al. (5) consider the "catabolic crisis" model, as proposed by English and Paddon-Jones (27), to facilitate sarcopenia during rather short phases of inactivity and not as a gradual process. Individual trajectories of declines in physical performance over the course of life seem to be variable and task specific (28–30). Considering the catabolic crisis model, the lockdown-induced training cessation might have long-lasting effects on the high intensity group, as sarcopenia is well-known as a main influencing factor on frailty (31). Furthermore, compared to values of the same time interval for 2019, an increased fall rate was reported for older adults after the lockdown period in 2020 (32). We conclude, that the increased offers for guidance on physical activity and online exercise classes (13) or the individual exercise routines, encompassing walking and cycling, seem to be sufficient to enable uptake of the pre-lockdown exercise training level after longer interruption for the low and moderate exercise groups, but not for the high intensity training group.

4.2. Prediction of training recovery

The semiparametric regression model revealed that to regain the pre-COVID-$19_{legscore}$, 20–60 sessions were necessary, with fewer sessions required when training with a higher weight on the leg extension training device. Further, at least 15–20 repetitions were beneficial to achieve baseline levels (green line in Figure 2B). Training effectiveness increased substantially with the number of sets. Participants with a pre-COVID-$19_{legscore}$ lower than ∼2,500 kg reached their baseline levels after training session number 40, individuals with higher leg scores from the high TIG did not reach their baseline exercise performance, and most likely physical capacity, over the ∼21 weeks until the second lockdown.

Regarding training intensity, it seems to be important to achieve momentary muscle fatigue during training by either a high number of repetitions or a higher training weight (33, 34), however, results are inconclusive. Based on the results of an umbrella review on the effectiveness of exercise interventions to increase muscle strength in the context of sarcopenia prevention, low-intensity resistance training [≤50% of the one repetition maximum (1RM)] may be sufficient to increase muscle strength, but high-intensity resistance training (∼80% of the one repetition maximum) is recommended to optimize effects on strength (33, 35). Beckwée et al. (35) recommend 1–4 sets of 8–15 repetitions on 1–3 days a week. Based on our data, we recommend the following strategy to recover the pre-lockdown training level: training should be performed with at least 50 kg (sum of lifting and lowering) and 20 repetitions. However, individual training preferences in terms of low and high training weights should be considered and adjusted accordingly.

4.3. Strengths and limitations

This is the first study, to our knowledge, to explore the effect of closure of sports facilities during the first wave of the COVID-19 pandemic on physical performance, based on objective training data. Furthermore, the sample size of 17,450 individuals is large enough for sub-group analyses, e.g., different age groups and training intensity. As a limitation, we can only hypothesize that training intensity is a marker of physical fitness as we have no data on maximal strength, whether the weights were changed by the trainer or participant, whether the training was pushing the limits or not. As our data strengthen the importance of resistance training at a high intensity level, participants should be assessed for maximal training data or fitness data on a regular basis. Technically this could be integrated in the circuit. An according entry in the data base would be helpful for training monitoring as well as the use of training data in research. No further information on the study population is available concerning health issues, including infection with SARS-CoV-2, or individual exercise routines during the lockdown periods. Personal interviews to assess individual physical activity habits would offer important information for training recommendations. The study population is not representative for the population as a whole, as it is a selection of adults who exercise regularly in a sports facility.

4.4. Conclusion

The presented results examine objective training data of persons regularly exercising in a chip-controlled fitness circuit in

Germany. In both, the middle-aged (45–64 yrs), and older age (≥65 yrs) groups, especially participants with vigorous training routines showed the greatest losses in exercise performance for upper and lower body muscle groups after the end of the first COVID-19-related lockdown, but no changes in endurance exercise performance. Endurance exercise, performed unrelated to the gym, seemed to have been effective in preserving individual training loads on the cycle ergometers. Independent of age, the high intensity training groups did not reach the pre-lockdown level, even after ∼5 months of training. We conclude that a high intensity resistance training cannot be compensated without explicit resistance exercise. For the recovery of prior fitness levels, a training regimen of at least two sets with a minimum of 15 repetitions each and a training weight of ∼50 kg was necessary in the analyzed study population. People, especially seniors, should be motivated to engage in more intense, but safe home-based resistance trainings to mitigate decreases in training loads, and eventually individual fitness, when sports facilities are not available, or individuals are hesitant to visit those facilities due to high incidences of infectious diseases. The use of health or fitness apps with focus on home-based resistance exercises may be a temporary alternative for training in gyms.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: anonymous training data from a chip controlled training cycle. Requests to access these datasets should be directed to geriatrie@uol.de.

Ethics statement

The study involving human participants were reviewed and approved by the Ethics Committee of the Medical Faculty of the University of Oldenburg. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

JK, SL, MH, and TZ developed the concept and design of the study. JK and TZ responsible for study management and prepared the manuscript. AS and FO-S conducted data clearance. FO-S conducted the statistical analysis. JK, TZ, and FO-S interpreted the data. All authors contributed to interpretation of data, drafting of the article, and final approval of the version to be published.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Recent advances in the identification of related factors and preventive strategies of hip fracture

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Hip fracture is the most devastating type of osteoporosis-related fracture, and is a major worldwide public health problem with a high socioeconomic burden, morbidity rate, and mortality rate. Thus, it is crucial to uncover the risk factors and protective factors to create a hip fracture prevention strategy. In addition to a briefly review of some well accepted risk and protective factors of hip fracture, this review mainly summarized the recent advances in the identification of emerging risk or protective factors for hip fracture, in terms of regional differences in medical services, diseases, drugs, mechanical load, neuromuscular mass, genes, blood types, cultural differences. This review provides a comprehensive review of the associated factors and effective prevention measures for hip fracture, and discusses issues that need further investigation. These issues include the determination of the influencing mechanism of risk factors triggering hip fracture and their interlinked correlation with other factors, as well as the confirmation or correction of emerging factors associated with hip fracture, particularly those that are still controversial. These recent findings will aid in optimizing the strategy for preventing hip fracture.

KEYWORDS

osteoporosis, hip fracture, risk factors, protective factors, prevention measures

1. Introduction

Hip fracture is a common injury among older adults, which are associated with potential loss of autonomy, long-term disability and increased risk of mortality, resulting in both significant personal and socioeconomic burden (1, 2). Therefore, comprehensive screening of risk factors of hip fracture and optimization of fracture risk prediction system are of great significance for early prevention of hip fracture.

Although low BMD is an accept sign to identify people with an elevated risk, it is not reasonable to screen out all people at imminent, intermediate, and long-term risk for hip fracture by measurement of BMD alone, because BMD measurement does not capture microstructural deterioration which increases fragility disproportionate to the bone loss, leading to the mild BMD defects in postmenopausal osteopenia or so-called "normal" BMD women (3). Therefore, BMD cannot completely help us predict the occurrence of fragility fracture.

At present, related studies have shown that the relationship between the risk factors of hip fracture is also complex, and is related to the causes of the risk factors of hip fracture. In addition to some genetical and immutable conditions like age, gender, ethnicity and family history of fracture, a series of modifiable unhealth behaviors, as well some diseases, particularly those affect bone metabolism and their treatment can also lead to risk factors

for hip fracture. For example, the natural deterioration of tissue structure and the decline in physiological function of various systems in the elderly are associated with an increased risk of hip fractures (4). In addition, several chronic health conditions and long-term use of a variety of medications are associated with both fall and bone health (5).

Based on numerous epidemiological data, this review focuses on the latest progress in identifying factors related to hip fracture and evaluating the correlations between hip fracture and other factors, which will help to modify behavior and identify high-risk groups, thereby developing a sound public health strategy to reduce the incidence of hip fracture.

2. Methods

2.1. Literature search

Five databases were searched by computer, including PubMed, Web of Science, Cochrane library database, Embase. At the same time, experts in the field of orthopeadic surgery were consulted to supplement and obtain relevant literature. The retrieval time limit is from the establishment of the database to December 31, 2021. Search terms were predefined to allow a comprehensive search strategy that included text fields within records, and the search strategy was based on a combination of "hip," "fracture," "cataclasis," "bone," "hip," "protective factor," "risk factor," "influencing factor," etc. We used Boolean operators (within each axis, we combined keywords with the "OR" operator to expand the search, and we then linked the search strategies for the two axes with the "AND" operator to narrow the search). For the first three databases, the retrieval strategy is shown in Appendix.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Types of studies: original cross-sectional studies, randomized controlled studies and case-control studies. (2) Types of participants: population with hip fracture. (3) The outcome of influencing factors: divided into the risk factors and protective ones.

Literature exclusion criteria: (1) Case report, review, systematic evaluation, and meta-analysis. (2) Repeated published and poor-quality literature. (3) The information is incomplete, and the relevant data cannot be obtained or missing (Figure 1). PICOS framework is presented in Table 1.

2.3. Data extraction and quality assessment

First, the title information of relevant literature was retrieved through the retrieval strategy, and Endnote X9 software was used for literature management. For the qualified literature finally selected, yaohui Yu and yudan Wang independently extracted the research information and then comprehensively evaluated the included references, thereafter independently evaluated the risk of bias included in the study and cross-checked the results. Xiaoli Hou decide the final conclusion by discussion (xiaoli Hou) when Yu and Wang got different opinions. The quality of the included articles were assessed by the Joanna Briggs Institute (JBI) quality assessment tool (6). The JBI offers a set of critical appraisal checklists for different study designs. The main focus of the appraisal checklist is on methodological rigor, avoidance of bias including selection bias, and information bias, appropriate use of statistics, and appropriate reporting, etc. Additionally, the risk of bias of the included studies was assessed using the 'risk of bias assessment tool for non-randomized studies' (RoBANS) (7). The RoBANS tool focused on six major domains to address selection bias, performance bias, detection bias, attrition bias, and reporting bias (Table 2).

3. Results

3.1. Well-accepted risk factors

The well-accepted risk factors for hip fracture are summarized based on the World Health Organization (WHO) fracture risk assessment tool FRAX (www.shef.ac.uk/FRAX) and the other two osteoporotic fracture risk assessment scales Garvan Fracture Risk Calculator (www.qfracture.org) and QFracture (www.qfracture.org). Risk factors positively correlated with hip fracture include age, women, Caucasian ethnicity, smoking, alcoholism, low body weight, living in nursing homes or long-term care institutions, past fracture, family history of fracture, osteoporosis, rheumatoid arthritis, cancer, asthma, chronic obstructive pulmonary disease (COPD), chronic liver disease, chronic kidney disease (stage 4 or 5), cardiovascular disease [(heart attack, angina, stroke or transient ischemic attack (TIA)], nervous system disease (epilepsy, dementia, and Parkinson's disease), malabsorption (Crohn's disease, ulcerative colitis, coeliac disease, steatorrhea, or blind loop syndrome), endocrine problems (diabetes, thyrotoxicosis, hyperparathyroidism, and Cushing's syndrome), use of steroid tablets regularly, use of estrogen only or Hormone replacement therapy (HRT), use of psychotropic drugs such as benzodiazepines and barbiturates and history of falls (Figure 2).

3.2. Recently confirmed risk factors

In addition to those above-mentioned well-accepted risk factors of hip fracture, recent studies have reported newly confirmed risk factors, including regional differences in medical services, some new diseases, drugs, and other variables that affect bone strength (Figure 3).

3.2.1. Regional differences in medical services

It is reported that the process of urbanization may be parallel to the increasing hip fracture rate in most areas. A nationwide data analysis in Norway showed that the highest tertile of urbanization degree (city), compared to the lowest (rural), was related to a 23 and 24% increase in hip fracture risk in men and women, respectively

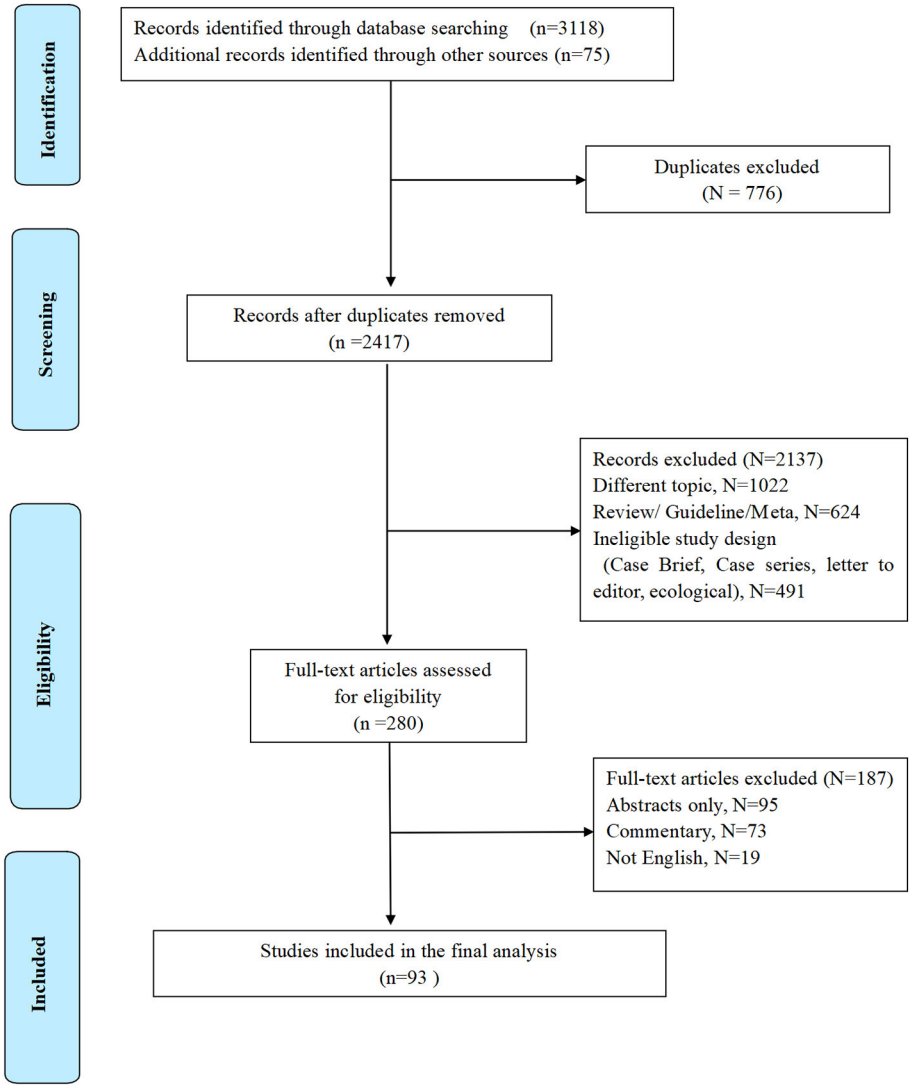

FIGURE 1
Flow diagram of study selection.

(13). In a systematic review included 14 cohort studies and 1 case-control study, identified moderate evidence for rural residents have lower risk of hip fracture compared to urban residents (14, 15).

The reasons for such a phenomenon remain poorly understood, but may include decreased physical activity, soil sealing, calcium and vitamin D deficiencies, less sun exposure, and changes in BMD (16–18).

However, on the contrast, a series of studies support a beneficial effect of urbanizationon bone. Rural to urban migration as an adult is associated with higher BMD and greater predicted hip strength (19).

Compared with rural areas, the social level in urban areas is higher. It is reported that low socio-economic status has been confirmed as a risk factor for hip fracture (20). The results of a Chinese study show that income level is positively correlated with awareness of the perceived risk of osteoporosis (21). This suggests that people with higher incomes are more likely to be aware of hip fractures and maintain a healthy lifestyle and diet, which will be beneficial to the prevention of hip fractures. Further, urbanization is most often equal to higher levels of healthcare services. A recent study reported that regional differences in healthcare services are closely related to the risk of hip fracture, which may be due to the

TABLE 1 PICOS framework of the study for the identification of related factors of hip fracture.

Parameter	Description
Population	Healthy population, population with hip fracture
Intervention/ exposure	A series of risk or protective factors of hip fracture
Comparison	Patients in hip fracture and healthy control population
Outcome	The occurrence of hip fracture
Study design	Cross-sectional studies, randomized controlled studies and case-control studies

TABLE 2 Characteristics of included representative articles, summary of the main findings, and their quality assessment.

References	Region; country	Study design; sample size	Study population (gender and age)	Study period (year)	Main findings related to factors causing hip fracture	Quality assessment scores
Mayhew et al. (8)	Canada	Cross-sectional study	77 total population Age: Female 68.5 (41.0–75.0) Age: Male 70.0 (44.0–76.5)	1.00	Mechanical load and bone geometric parameters (femoral neck cortical stability)	9
Dargent-Molina et al. (9)	France	Cohort study	7,575 total population Female 77.8 (78.8–79.8)	1.94	Neuromuscular and visual impairments	8
Puttnam et al. (10)	America	Cohort study	22,180 total population Age: [mean (SD) 70.4 (6.7)]	8.00	Antihypertensive Medications	10
Kiel et al. (11)	America	Cohort study	1,042 total population Age: [mean (SD) 85.0 (7.0)]	1.60	Hip protector	9
Follis et al. (12)	America	Cohort study	11,020 postmenopausal women Age: [mean (SD) 62 (7.0)]	8.00	Psychosocial stress	10

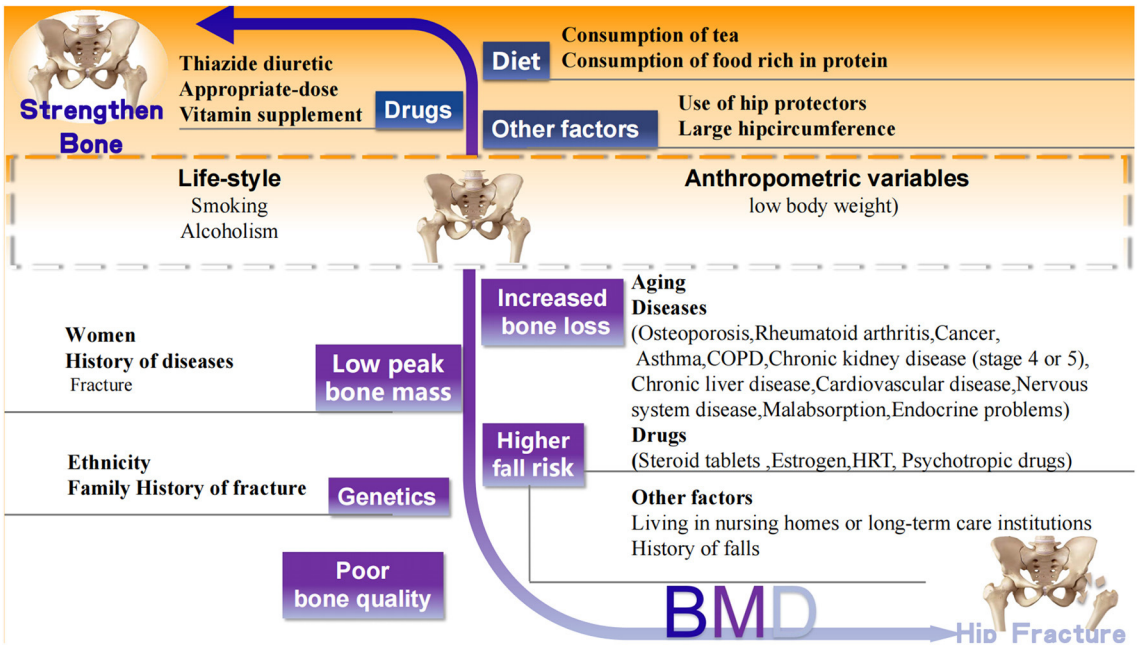

FIGURE 2
Well-accepted factors associated with hip fracture. Black words: well accepted risk (white background) and protective (orange background) factors related to hip fracture. CODP, chronic obstructive pulmonary disease; HRT, Hormone replacement therapy.

relative improvement of healthcare service in urban areas with a prosperous social economy (22). In this context, narrowing the gap of healthcare services level between rural and urban areas should be encouraged to reduce the fracture risk in rural areas.

Therefore, process of urbanization is a double-edged sword for the occurrence of hip fracture. It is important to recognize the factors influencing hip fracture and improve the awareness of preventive strategies to enhance the strengths and avoid the weaknesses of urbanization.

3.2.2. Diseases

It is well established that BMD and other risk factors can be used to predict fracture risk (23). Recent research has found that diseases and drugs are also closely related to changes in BMD and the risk of hip fracture.

3.2.2.1. Anorexia nervosa

A recent study found that anorexia nervosa (AN) is closely related to low BMD and an increased risk of hip fracture

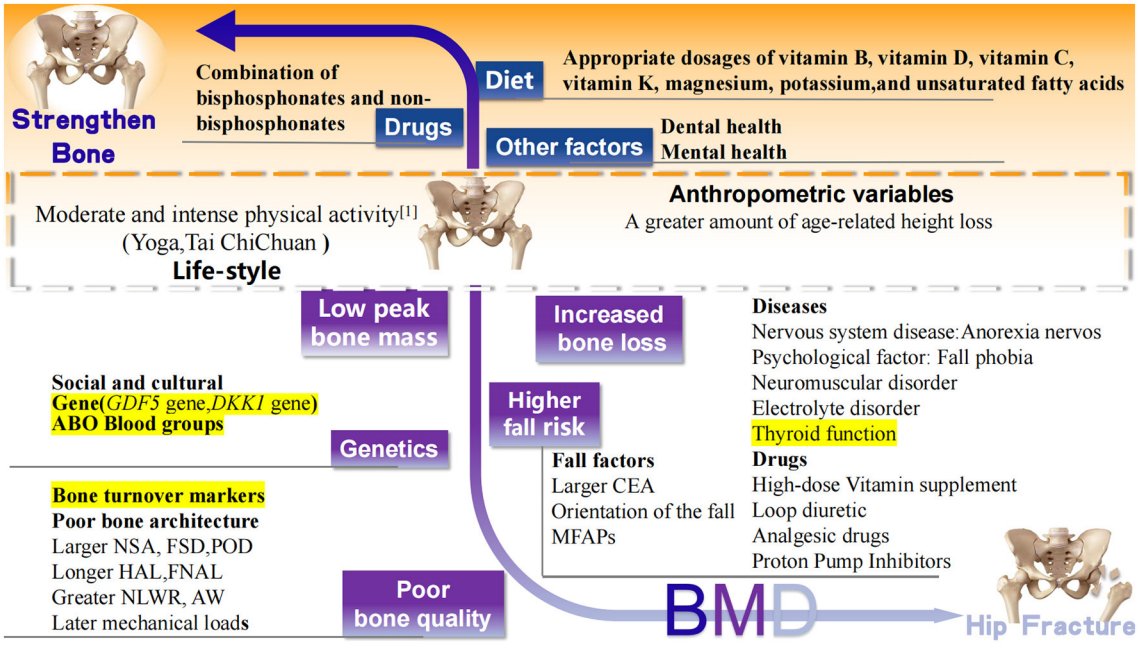

FIGURE 3
Recently confirmed factors associated with hip fracture. Black words: well accepted risk (white background), protective (orange background) factors, and controversial (yellow background) factors related to hip fracture. BMD, bone mineral density; MFAPs, meteorological factors and air pollutants; GDF5, Growth differentiation factor 5; DKK1, Dickkopf 1 gene; CEA, central edge angle; NSK, neck shaft angle; FSD, femoral shaft diameter; POR, pelvic outer diameter; HAL, length of hip axis; FNAL, femoral neck axial length; NLWR, neck length-width ratio; AW, acetabular width.

(24). Studies have shown that the bone loss rate of the hip joint of amenorrhea women with anorexia nervosa is 2.4% per year (25, 26). AN is a mental illness, long-term malnutrition is accompanied by severe bone loss, followed by hypogonadism and growth hormone resistance, which becomes an important intermediary factor for bone loss in patients with AN (27, 28). The lack of soft tissue around the trochanter of the femur due to insufficient calorie intake and the inability of individuals to maintain normal weight increases the risk of hip fracture in patients with AN (29). In addition, 50–60% of women with the disease do not recover until more than 20 years after initial diagnosis (30). In view of the long-term nature of the disease and the lack of approved treatment for bone loss in this population, future studies are necessary to optimize treatment strategies for osteopenia and increased risk of fracture in anorexia nervosa.

3.2.2.2. Electrolyte disorders

With the advent of the "aging world", an increasing number of studies have confirmed that electrolyte disorders affect the occurrence of fracture. Among these electrolyte disorders, hypokalemia is most frequently discussed. Hypokalemia may damage bone health by affecting bone turnover and low BMD, thus increasing the risk of fracture (31). An experimental study found that the decrease of bone trabecula and cortical bone led to abnormal bone histomorphology. This study found that hyponatremia could stimulate osteoclast formation and increase absorptive activity. This may be due to the increased level of circulating arginine-vasopressin hormone released from the posterior pituitary. The chronic increase of this hormone can also stimulate osteoclast activity and lead to bone resorption (32). A meta-analysis showed that hyponatremia is significantly correlated with fracture, osteoporosis, and higher mortality (33). Furthermore, patients with hyponatremia are more likely to fall than the general population, and the incidence of hyponatremia is increased in the older adult population, which strengthens the connection between hyponatremia and fracture (34). Chronic hyponatremia is also a risk factor for hip fracture in patients with chronic kidney disease who are older than 60 years (35). However, the risk of hip fracture in patients with chronic kidney disease is closely related to high levels of thyroid hormones (36). This suggests that doctors should be aware of the risk of hyponatremia. Further studies are needed to assess the risk of osteoporosis or fracture after hyponatremia treatment.

Although the mechanism of the effect of the above-mentioned diseases on hip fracture is complex and difficult to control, it helps to identify people at high risk of hip fracture to promote the prevention of hip fracture in patients with AN, hyponatremia, and hyponatremia.

3.2.3. Drugs

A popular current research topic is the effect of drugs on the individual bone mass and the risk of hip fracture.

3.2.3.1. Antihypertensive drugs

A large randomized clinical trial provided evidence of a beneficial effect of thiazide-type diuretic therapy in reducing hip and pelvic fracture risk compared with treatment with other antihypertensive medications (9). The latest study found that

the use of thiazides (hydrochlorothiazide, bendroflumethiazide, or fixed drug combinations containing a thiazide) is effective in reducing the risk of hip fracture, while treatment with loop diuretics can increase the risk of fracture (37). Long-term administration of medullary loop diuretics leads to urinary calcium loss and/or PTH-driven bone turnover. Ultimately leading to a decrease in hip BMD in older men (38, 39). In addition, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and beta-adrenergic blockers are risk factors for falls in the older adult population (40). There is evidence that different classes of medications might contribute to falls in older adults *via* orthostatic hypotension. Diuretics are associated with hypovolemia and orthostatic hypotension (41–43), which is a risk factor for both falls and syncope (44, 45). Clinicians should carefully consider the risk of falls in their selection of drugs for hypertension and the clinical use of hypertensive drugs. This should be monitored in older adults initiating antihypertensive therapy particularly among those with a prior history or other risk factors of falls to prevent the occurrence of hip fracture.

3.2.3.2. Analgesic drugs

Hip fracture causes a massive amount of pain that is controlled with opioids in most cases (46). However, recent studies have found that opioids may increase the incidence of secondary hip fracture; a meta-analysis confirmed this finding and suggested that this may be related to the cognitive impairment, lethargy, and sedation caused by opioids (47). Thus, the use of opioids increases the likelihood of falls and leads to fracture (48). Among patients on hemodialysis in the United States, opioid use increases the risk of hip fracture regardless of the duration of intake (49). Weak opioids also affect the occurrence of hip fracture. Tramadol is an analgesic that is a weak opioid receptor. Although the risks of tramadol addiction and dependence are very small compared with commonly used weak opioid drugs (such as codeine) or commonly used non-steroidal anti-inflammatory drugs (such as naproxen, ibuprofen, celecoxib, and etoricoxib), tramadol is more likely to cause hip fracture (50). Overall, opioids and other analgesics should be used cautiously to control the pain associated with hip fracture to avoid the occurrence of secondary hip fracture.

3.2.3.3. Vitamin supplements

Vitamin supplements are very popular among the general population, but dose control is important. Patients who receive high doses of vitamin B6 (≥35 mg/d) and vitamin B12 (≥20 μg/d) have a higher risk of hip fracture than those who receive appropriate doses of these vitamins (51). Similarly, the biological explanation for the effect on bone strength caused by higher and lower intake of nicotinic acid (a B3 vitamin) is unclear. High doses of vitamin B6 supplementation can cause neuromuscular damage and increase the risk of falls. Moreover, vitamin B6 may invalidate the regulatory effect of estrogen on steroid receptors, accelerate bone loss, and even cause damage (52). Vitamin D and calcium play important roles in bone development and are essential and necessary for bone health. Low levels of serum 25(OH)D may be associated with bone loss, lower bone mineral density (BMD) and higher bone turnover (53). A study containing 400 hip fractures found a dose-related increase in hip fracture risk for lower serum 25 (OH) D levels [OR = 1.33 (95%CI, 1.06–1.68) for each 25 nmol/l decrease] (54), while another study concluded that there was a significantly reduced risk of hip fracture in those with 25(OH)D levels ≥62.5 nmol/L compared to levels below this [RR = 0.64 (95%CI, 0.48–0.89)] (55). However, high doses bolus vitamin D supplements of 100,000 IU (2.5 mg) monthly over 2.5–4.2 years do not prevent falls and hip fracture, but rather increase the risk of falls (56–58). Therefore, vitamin intake and supplement should be based on their own needs and scientific advice to prevent the occurrence of the hip fracture, a recent meta-analysis suggested daily vitamin D dose of 800–1,000 IU was the most probable way to reduce the fracture and fall risk (59).

3.2.3.4. Proton pump inhibitors

Proton pump inhibitors (PPIs) are widely used in several acid-related gastrointestinal disorders. *In vivo* studies have suggested that gastric suppression by PPIs could result in decreased intestinal calcium absorption. Subsequently, there have been concerns that the chronic use of a PPIs is associated with an increased risk of fracture, Previous studies on hip fracture risk associated with the use of PPIs have been inconsistent (60, 61). However, recent studies have agreed that the use of PPIs increases the risk of hip fractures. The impairment of bone health has been shown in both Caucasian (62) and Asian cohorts (63, 64). In particular, Lee et al. described the increase risk of hip fractures in PPIs users/BP non-users in comparison with PPIs/BP non-users in a large cohort of Korean subjects (OR: 1.34, 95% CI 1.24–1.44) (65). This was also confirmed by a meta-analysis and quantifying the magnitude of the association between PPIs and the risk of hip fracture. Patients with PPIs had a greater risk of hip fracture than those without PPI therapy (RR 1.20, 95% CI 1.14–1.28, $p < 0.0001$), with a positive relationship between hip fracture risk and doses of PPI taken (66). A recent meta-analysis has explained, the possible mechanisms of fractures induced by PPIs including hypersecretion of histamine and hyperparathyroidism due to hypergastrinemia, as well as mineral and vitamin B malabsorption due to hypochlorhydria (67). Therefore, physicians and patients themselves should be cautious of a higher risk of hip fracture of long-term PPI treatment, it should be encouraged to consider alternative treatment strategies, especially when PPI efficacy is suboptimal.

3.2.4. Mechanical load and bone geometric parameters

The risk of hip fracture is largely dependent on the condition of the bones, with bone structure playing the most important role. Extensive studies have investigated the influence of hip geometric parameters on the risk of hip fracture, especially focusing on the length of the hip axis (HAL), followed by the geometric parameters of the proximal femur, including the femoral neck axial length (FNAL), neck shaft angle (NSA), central edge angle (CEA), femoral neck width, femoral shaft diameter, cortical thickness, cross-sectional area, and cross-sectional modulus. Differences in proximal femur geometry leads to different types of hip fracture. Femoral neck fracture is related to a larger NSA, larger femoral shaft diameter (FSD), larger pelvic outer diameter (POD), longer HAL, longer FNAL, greater neck length-width ratio (NLWR), and larger acetabular width (AW) (68). Recent research based on these findings has shown that compared with patients with femoral neck

fracture, patients with intertrochanteric fracture often have a larger CEA because they have longer osteophytes and narrower joint spaces. This makes the impact point between the posterior edge of the acetabulum and the posterior edge of the femoral neck closer to the intertrochanteric region of the femur when they fall (69).

Early mechanical loads also affect the hip joint. The age at which an individual starts walking in infancy may change the shape of their hips, and some characteristics of babies who start walking earlier may reduce the risk of hip fracture. This may be because infancy is the key stage of hip development, and the bone load caused by early walking makes the femoral head and neck larger, the neck shaft angle smaller, and may result in the optimal hip joint configuration (70). Conversely, mechanical unloading decreases bone volume and strength. For instance, being excessively sedentary may negatively affect bone health by disrupting the bone formation-resorption balance, as occurs in immobilized individuals (71), a study performed in 11- to 13-year old boys have shown that changes in sedentary time were negatively related to changes in whole-body bone mineral density (BMD), lumbar spine bone mineral content (BMC), lumbar spine bone area (BA), femoral neck (FN) BMD, and FN BMC ($r > -0.157$; $p < 0.05$) (72). In addition, a cohort study showed that the cortical thickness of 60-year-old women decreased by 6.4% (SD1.1) per decade ($p < 0.0001$), due to atrophic thinning caused by underloading of the upper lateral cortex. Therefore, it is very necessary to do more targeted exercise for people of different ages in order to strengthen fragile bones (8).

Genetic factors (height) play an important role in bone development (33), as height is positively associated with an increased risk of hip fracture (73). In contrast, a recent study showed that a greater amount of age-related height loss is associated with a higher risk of hip fracture in men (74). On the other side, genetic variability affects the skeletal response to unloading, an animal study with different strains of mice proved magnitude of bone loss from immobilization is heritable, and bone transcriptomic response to immobilization is influenced by genetic variation. Thus, genetic factors not only play a major role in the accrual and maintenance of bone mass, but also influence the skeletal response to mechanical unloading. Future studies are suggested to identify genes that are responsible for unloading-induced bone changes thereby to uncovering novel genes responsible for protecting bone from unloading.

3.2.5. Neuromuscular function

A cohort study showed that bone microstructure changes are affected by neuromuscular function. In men, poor physical fitness and lower limb relative appendicular lean mass accelerate cortical bone loss and increase the risk of falls, leading to hip fracture (75). In addition, recent research suggests that people with a fall phobia are more likely to fall in the first 12 weeks after a hip fracture because of their high degree of neuroticism (76). A cross-sectional study reported that the combination of sarcopenia and osteoporosis potentially increases the risk of hip fracture (77). Another established fall factor that should be corrected is a decline in muscle quality in certain areas. The fall risk is related to the mass of the psoas major muscle and the extensor muscle of the spine, and weak psoas and spine extensors may increase the risk of fracture (78). In addition, a cohort study involving 7,575 women aged 75 or older showed that neuromuscular injury (gait speed and tandem walk) and poor vision were important and independent predictors of hip fracture risk (9).

3.2.6. Social and cultural

Though ethnic differences have a well-known effect on the risk of hip fracture, the underlying mechanism has not been identified. One potential factor affecting the ethnic differences in hip fracture risk is interracial differences in social and cultural concepts. People in Asia have a conservative way of thinking, which limits their opportunities to participate in certain activities (79). Similarly, compared with white, low fall rates evident in Chinese cohorts result from greater levels of concern about falling. These findings suggest that the interracial difference in hip fracture incidence may be caused by the different frequency of falls (80). However, a recent study focused on the race-specific association of social environmental factors with hip fracture incidence proved that a greater social stress is associated with a greater hip fracture incidence, with a lower hazard ratio (HR) value in white women [HR 1.04, 95% confidence interval (CI) 1.01–1.08] than Asian women (HR 1.37, 95% CI 1.01–1.86) and native American women (HR 1.84, 95% CI 1.10–3.10) (81). A cohort study from the United States based on data from 11,020 postmenopausal women confirmed this result. After adjustment for confounders, each point higher in social strain was associated with 0.082% greater loss of femoral neck BMD, 0.108% greater loss of total hip BMD and 0.069% greater loss of lumbar spine BMD ($p < 0.05$) (82).

3.3. Well-accepted protective factors

Previous studies have confirmed that the protective factors negatively correlated with the risk of hip fracture include hormone replacement therapy, the use of thiazide diuretics, consumption of tea, weight-bearing exercises of relatively low intensity, consumption of food rich in protein, increased calcium and vitamin D intake, and the use of hip protectors (10, 12, 83, 84) (Figure 1).

3.4. Recently confirmed protective factors

Diet, nutrition, and physical activity are inextricably linked to hip fracture. Recent studies confirm that the risk of hip fracture can be reduced by the intake of essential nutrients (vitamin C, vitamin K, magnesium, potassium, and unsaturated fatty acids) (Figure 2).

3.4.1. Vitamins

A meta-analysis showed that dietary vitamin C intake reduces the risk of hip fracture, with every 50 mg increase in daily vitamin C intake reducing the risk of hip fracture by 5% (85). According to another meta-analysis, increasing the vitamin C intake reduces the risk of osteoporosis by 33% and increases the BMD of the hip (86),

which is further confirmed in a latest study that dietary vitamin C-targeted food intake is negatively associated with the risk of fracture and a decrease in BMD (87).

Vitamin K causes blood coagulation and may greatly affect bone metabolism. The effect of vitamin K on the incidence of hip fracture is controversial. Previous studies have shown that dietary vitamin K intake does not affect the risk of hip fracture (88, 89), However, other studies have shown that every 50-mg increase in vitamin K in the diet reduces the risk of fracture by 3%. Overall, a higher dietary intake of vitamin K reduced the risk of fracture by 22%, and suggest that the protective effect of vitamin K on bone health depend on its effect on bone transport and BMD (90).

3.4.2. Magnesium and potassium

Most epidemiological studies have shown that magnesium intake is associated with higher BMD, although the appropriate doses of calcium and magnesium remain unclarified (91). A meta-analysis has shown that a high-dose magnesium intake does not affect the risk of hip fracture, but that there is a slight correlation between magnesium intake and hip BMD (pooled $r = 0.14$) (92). In addition, a cross-sectional study of 4,000 people in Europe showed that a low dietary intake of magnesium and potassium reduces the BMD of the whole hip (93). A recent South Korean study found that higher levels of potassium in food (3,600–3,800 mg per day) are good for the heart and bones of older women (94). Alkaline potassium salts are thought to prevent the pH homeostasis of bone resorption. Therefore, dietary potassium may prevent bone loss by affecting the acid-base mechanism (95). There is no doubt that nutritional elements are important for bone health protection. While little is known about the influence of trace elements on hip fracture, a study proposed that many trace elements affect bone metabolism. Zinc and copper affect bone turnover and increase bone strength, while magnesium, iron, manganese, boron, and fluoride protect bones. However, excessive intake of protective elements (zinc, fluorine, magnesium, and iron) can also have an adverse effect on bones (96).

3.4.3. Unsaturated fatty acids

A prospective cohort study suggested that low fish intake may increase the risk of hip fracture, and that this association is stronger in men (HR 1.84, 95% CI 1.10–3.08). Fish are rich in nutrients, including high-quality protein, large amounts of unsaturated fatty acids, and phospholipids. Among these nutrients, unsaturated fatty acids play a protective role in hip fracture (97). Although previous studies reported differences in the associations between unsaturated fatty acids and hip fracture, a recent review determined the protective effects of unsaturated fatty acids based on more than a dozen dose-response relationships and showed that dietary n-3PUFA intake is negatively correlated with fracture risk (98). Furthermore, saturated fatty acids are associated with a lower risk of cognitive impairment (99). This effect may be indirectly associated with reduced risks of falls and hip fracture.

3.5. Controversial factors

Some factors with no consistent results with respect to the association between them and hip fracture risk, are considered as controversial factors.

3.6. Thyroid function

Some recent studies on thyroid function contradict the previous conclusions. Most studies have found that in normal subjects with thyroid function, a decrease in the levels of thyroid stimulating hormone and an increase in the level of free thyroxine are associated with an increased risk of hip fracture (100). In contrast, Siru et al. reported that thyroid stimulating hormone and free thyroxine levels are not associated with incident hip fracture. However, their data supports the hypothesis that older men are less susceptible to elevated levels of thyroid hormones than older women, and identifies sex differences in the associated fracture risk (101). However, a recent study reported that for both men and women, patients with hip fractures whose plasma TSH levels were higher than the median (1.41 mIU/L) at admission after surgery had an increase in mortality at 30 days after operation (102). Therefore, future studies should consider potential sex differences in thyroid function related to the risk of fracture.

3.7. Bone turnover markers

Bone turnover markers (BTMs) are a group of proteins and peptides released during bone remodeling that can be found in serum or urine. It was suggested that higher serum levels of procollagen type I N propeptide (PINP) and C-terminal crosslinking telopeptide of type I (CTX-I) were associated with an increased risk of hip fracture (103, 104). However, in a case-control study, S-CTX, and S-PINP did not differ between groups (105). Another study from Marques et al. (106) do not support the routine use of BTM to assess fracture risk in older men and women. However, these studies only assessed those BTMs at single time point, and given the known variability of BTMs, multiple measurements may drive to more substantial evidence of their associations with bone loss and fracture (107). Furthermore, a study has found that higher levels of BTMs were associated with higher cortical porosity and thinner cortices, which may lead to a higher incidence of fracture (108). The relationship between bone turnover markers and fractures and the underlying mechanism needs to be verified by more standardized studies in the future.

3.8. Genetics

The mechanism that affects the risk of hip fracture is complex, part of which is attributed to heredity. Studies have shown that genetic factors are mainly focused on gene polymorphisms that affect BMD, turnover, architecture and size. To date, although researchers have determined that vitamin D receptor (VDR) gene, collagen I-α-1 (COLIA1) gene, and estrogen receptor (ER) gene

are associated with the risk of osteoporosis (109). However, it is still controversial whether these genes are associated with BMD. The results of a prospective cohort study showed that VDR CC genotype and COLIA1 TT genotype were associated with increased hip fracture risk in Caucasian women, and this association was independent of BMD and age (110). ER gene are not associated with osteoporotic fractures, bone mass, or bone turnover (111). In addition, Studies show that the hip axis length is affected by both the GDF5 gene (112) and the DKK1 gene (113) and whether both genes will increase the hip fracture risk is further confirmed by future studies. In general, individual studies lack sufficient power to identify genetic associations with fracture that are independent of BMD.

In addition to the above referred genes associated with hip fracture. Recent studies have shown that the ABO blood group system may also have effects on bones. However, the influence of the ABO blood group system on hip fracture remains controversial. A recent study suggested that the ABO blood group affects the risk of proximal femoral fracture, as patients with A blood group are more likely to incur intracapsular fractures than those with other blood types (114). In contrast, Toro et al. found that the ABO blood group system does not influence hip fracture pattern, but that patients with A blood group are more prone to fracture than those with type O blood (115). The mechanism by which the ABO blood group system affects hip fracture is unclear. A study showed that Blood type O was associated with higher BMD (116). Contrarily, a cross-sectional study showed that postmenopausal women in North India who do not have O blood group have a higher BMD than those with type O blood. It has been reported that ABO antigen may exist in bone tissue, suggesting a biological relationship between ABO blood group and fracture (117). In addition, the ABO blood group is related to the incidences of cardiovascular diseases and cancer (118, 119), which are considered risk factors for hip fracture. Therefore, further work is needed to assess the association between ABO blood group and risk of hip fracture, as well the underly mechanism whereby blood group affect fracture risk.

3.9. Concrete preventive measures

Based on the above-mentioned influencing factors, we suggest the following intervention measures and discuss the problems involved in optimizing the strategies for preventing bone loss and hip fracture.

3.9.1. Fall prevention

Falls are the main cause of hip fracture in the older adult population. It is estimated that 30% of people older than 65 years fall each year and 87% of fractures are caused by falls; therefore, the prevention of falls is an important means to reduce the incidence of hip fracture (120). The external environmental factors contributing to falls include balustrade stairs, loose carpets, poor lighting, and potholed floors, landing on or near the hip, orientation of the fall (backward or to the side), greater potential energy of the faller, reduced soft-tissue padding over the hip. Individuals should avoid walking in these places or walk carefully. Slowing down also greatly reduces the incidence of falls (121, 122). In recent years, the global climate environment has deteriorated sharply, and the impact of meteorological factors and air pollutants (MFAPs) on hip fracture is becoming increasingly obvious. Different MFAPs (average temperature, day rainfall, wind speed, daily snowfall, and particulate matter 2.5) are positively correlated with the risks of falling and hip fracture. Therefore, it is necessary to focus on the protection of the environment and strengthen the public's cognition of MFAPs to reduce the occurrence of hip fractures (123). It is also important to identify high-risk groups that are prone to falls and have an increased risk of hip fracture, such as older adults, women, patients with a history of falls, lower limb dysfunction, neuromuscular injuries, less physical activity, visual impairment, stroke, neurodegenerative diseases (Parkinson's and Alzheimer's disease), and mental disorders (depression) (124, 125). Patients at high risk of falls should wear a hip protector (126). However, the use of physical restraint increases the incidence of falls and because some people do not have good compliance, the hip protector can't play a full role (11, 127). Therefore, it is necessary to further improve the comfort of protective tools to improve the protection against hip fracture.

Internal mental health is also an issue that requires attention. Patients with a fall phobia are more likely to fall in the first 12 weeks after hip fracture because of their neuroticism (76). Therefore, it is essential to provide all-round psychological counseling to people who have fallen.

3.9.2. Selection and use of medicines

The administration of estrogen, glucocorticoids, aromatase inhibitors, and psychotropic drugs (such as benzodiazepines and barbiturates) is associated with decreased BMD of the hip and an increased risk of falling. In addition, recent studies have found that the choice of anti-osteoporotic drugs is important. Anti-osteoporotic drugs are generally divided into three categories: calcium supplements, bone resorption inhibitors, and bone-forming agents. Bisphosphonates [alendronate (ALN), risedronate, ibandronate, etidronate and zoledronic acid], non-bisphosphonates [denosumab (DEN) and raloxifene], and bone-forming agents (teriparatide and romosozumab) have protective effects against hip fracture (128). However, questions have recently been raised about the efficacy of bisphosphonates in preventing hip fracture, as frail older adults who use bisphosphonates still reportedly develop fractures (129).

Numerous recent studies show that non-bisphosphonates have a more obvious protective effect than bisphosphonates. Bisphosphonates mainly work in women, especially postmenopausal women, and the protective effects of bisphosphonates on hips vary with the type of drugs. ALN may be more effective in the secondary prevention of hip fracture (130). Compared with ALN alone, romosozumab followed by ALN was associated with lower incidences of hip fractures among East Asian patients (131). The Postmenopausal women can safely transition from a bisphosphonate to DEN, which is more effective at improving BMD than continuing with a bisphosphonate (132). DEN is more effective than bisphosphonates in the treatment of total hip

BMD in patients with glucocorticoid-induced osteoporosis (133, 134). Teriparatide is more effective than risedronate in increasing the BMD of the femoral neck and total hip (135). Furthermore, long-term bisphosphonate treatment should be converted to teriparatide in high-risk patients with hip fracture (136).

In summary, the selection and use of medicines have important implications regarding hip fracture, and high-risk groups should use drugs that have a protective effect against hip fracture; such drugs include thiazide diuretics (hydrochlorothiazide, bendroflumethiazide, or fixed drug combinations containing a thiazide) and sequentially bisphosphonates and non-bisphosphonates s treatment for osteoporosis should be suggested.

3.9.3. Formulation of the dietary treasure book of professionals

A moderate dietary intake of vitamin C, vitamin K, magnesium, and potassium is good for hip bone health, while an excessive intake of protective elements (vitamin D, zinc, fluorine, magnesium, and iron) has an adverse effect on bone health. Therefore, the control of nutrient intake is very important. Interestingly, nutrients play an important role in dental health, and a decrease in the number of natural teeth is associated with low BMD and hip fracture, with a relative risk of hip fracture of 12% (137). In addition, a retrospective cohort study showed that eating highly nutritious foods (fruits, vegetables, and whole grains) reduces the risk of traumatic fracture, while eating high-energy foods (soft drinks, potato chips, French fries, meat, and desserts) and a high total energy intake are not associated with fracture (138). However, specific studies on how dietary patterns affect hip bone health are very limited; future studies should develop a dietary guide for people at high risk of hip fracture.

Low body weight is an important factor in hip fracture, and it is well known that low body weight may be caused by malnutrition, intentional weight loss, poor appetite, and small body size. Most studies have focused on the simple measurement of body weight, while few studies have evaluated lean body weight or fat content. One study showed that fat content in patients with gestational diabetes mellitus is related to bone health, but not to body mass index (139). Therefore, future research on fat content is very important to reduce hip fractures. For underweight people, poor appetite, lack of nutrition, and intention to lose weight can all be subjectively corrected to achieve a normal weight and promote health. The latest data show that weight gain is a protective factor for hip fracture (140). However, excessive weight gain may lead to abdominal obesity and general obesity, which increase the risk of hip fracture (141). In addition, in the middle-aged and older adult population, a larger hip circumference has a protective effect against hip fracture, which may be related to better muscle strength and internal factors affecting bone strength (142). Therefore, further studies are needed to identify easily measurable factors influencing hip fracture.

3.9.4. Reasonable adjustment of exercise intensity and lighting time

Appropriate physical activity effectively helps older adults improve their physical function and reduce the risk of fall-related injuries. Among the mechanisms related to hip fracture, many studies have emphasized the importance of physical activity. A case-control study showed that quality of life is closely related to hip fracture. Furthermore, long-term exercise and physical intervention can improve physical fitness (143). However, the prevention of hip fracture by exercise has not been confirmed. A randomized controlled trial showed that exercise self-intervention had no significant effect on action-related disability and falls (144). However, another study showed that walking for an hour a day and participating in yoga and physical activity reduced the risk of hip fracture by 15–20% (145). Regular Tai Chi Chuan would appear to be of benefit (146). Outdoor sports increase the time spent in the sun, which is good for bone health, but prolonged exposure to sunlight can lead to photochemical damage (147). In addition, a combination of moderate and intense physical activity may improve bone mass and reduce the risk of hip fracture (148, 149). A cohort study found that farmers who engaged in higher levels of physical activity are less likely to incur hip fractures (150). In addition to the amount of activity, changes in regular physical activity status are associated with the risk of hip fracture; those who became active and those who were always active exhibited a 0.24/1,000 person-years reduction in incidence rate and a 0.39/1,000 person-years reduction in incidence rate, respectively (151). Therefore, regular physical activity at an appropriate intensity is beneficial for skeletal health and is a preventive factor for hip fracture.

4. Discussion

This review summarizes the recently identified risk factors that are positively correlated with the risk of hip fracture, including AN, hyponatremia, hypokalemia, loop diuretics, analgesics, high doses of vitamin B and vitamin D supplements, Proton pump inhibitors, early mechanical loads, larger NSA, CEA, FSD, POD, longer HAL, FNAL, greater NLWR and AW, neuromuscular damage, climate deterioration, adventure way of thinking, and high social stress.

Newly identified protective factors associated with a reduction in the risk of hip fracture include a moderate dietary intake of vitamin C, vitamin K, magnesium, potassium, and unsaturated fatty acids, dental health, large hip circumference, and moderate or high-intensity physical exercise (yoga, Tai Chi Chuan) and regular physical activity, sequentially using of bisphosphonates and non-bisphosphonates, the use of thiazide diuretics. In addition, there has been recent controversy about the associations of thyroid function, bone turnover markers and genetics with hip fractures, which needs to be verified by more standardized studies.

In summary, maintaining the normal physiological structure of hip bones, controlling infant walking time, improve the exercise time of the elderly, monitoring height, neuromuscular quality are key measures to prevent or delay the onset of hip fracture, while the use of antihypertensive drugs with different sites of action, analgesics of different strengths, PPIs and psychotropic drugs in clinical practice should be given reasonable doses according to

pharmacokinetics and overall individual metabolism, and closely monitored for drug side effects to meet the safety standards of these drugs for hip patients.

In addition, in daily life and physical examination, attention should be paid to the effects of trace elements, unsaturated fatty acid intake and related ion concentration on bone health. At the same time, with the improvement of economic level and health awareness, the elderly and teenagers often take certain vitamins to maintain the balance of energy metabolism. However, due to the lack of safety awareness and scientific advice, people recognize that non-toxic, non-dose and unlimited "health products", such as vitamin supplements, may cause some diseases after long-term use. Therefore, vitamin intake and supplement should be based on their own needs and scientific advice to prevent the occurrence of fractures.

5. Conclusion

Hip fractures constitute one of the most important causes of morbidity and mortality among the elderly, and are associated with considerable and increasing economic burden. Given the increasing per capita life expectancy and the progressive increase in the tendency to aging, it is foreseeable that hip fractures will be one of the major challenges facing the global public health in the coming years.

This review provided a systematic description of the influencing factors and preventive measures of hip fracture, which summarizes the recently identified diseases related to the risk of hip fracture, including disease, medication, mechanical load, neuromuscular mass, ions related to energy metabolism, abnormalities of vitamins and unsaturated fatty acids, and the influence of social background.

Future research should optimize intervention strategies by improving the comfort of protective tools and providing guidance on psychological counseling after falls, appropriate selection of therapeutic drugs and appropriate doses of therapeutic drugs and more targeted and reasonable exercise for people of different ages to optimize the intervention strategy. It is also important to further develop reasonable dietary guidelines and to strengthen the identification of easily measurable risk factors for hip fractures.

Author contributions

YY and YW drafted the manuscript. XH assisted in the writing. FT edited the manuscript to its final version. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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The influence of natural environment in residential areas on subjective well-being of the elderly

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Objectives: The aim of this study is to explore the relationship between the natural environment of residential areas and the subjective wellbeing of the elderly and the role of elderly's evaluation of the government's environmental protection work in both.

Methods: Based on the China Social Survey Database in 2013, 2015, 2017, 2019, Stata were used to process the data screened according to the restricted conditions. Ordered Probit Model and Sobel were used to test the effect relationship among the variables.

Results: The subjective wellbeing of the elderly is roughly increasing. The natural environment of the living area has a significant positive effect on the subjective wellbeing of the elderly. The evaluation of the elderly on the government's environmental protection work has a positive impact on the elderly's subjective wellbeing similarly and plays an increasingly important intermediary role in the impact of the natural environment in the residential area on the elderly's subjective wellbeing.

Conclusion: To improve the subjective wellbeing of the elderly, the government should continue to play a leading role in coordinating environmental protection and pollution control, strengthen publicity of environmental protection work. Moreover, improve the residential environment governance and protection system oriented by the elderly's evaluation of the government's environmental protection work.

KEYWORDS

natural environment in residential areas, subjective wellbeing of the elderly, mediation effect, elderly's evaluation of the government's environmental protection work, Sobel test

1. Introduction

Subjective wellbeing (Abbreviated as SWB) results from evaluating one's quality of life according to the standards set by oneself (1). The SWB of the elderly reflects the overall spiritual life of the elderly and is one of the important indicators for measuring the physical and mental health and quality of life of the elderly (2). With the increasing proportion of the elderly population in China, the wellbeing of the elderly has become a more critical livelihood issue. The 14th Five-Year Plan for the Development of the National Aging Cause and the Elderly Care Service System points out that the whole society should actively cope with the aging population pattern as it initially takes shape, and the elderly's sense of gain, happiness and security should be significantly improved.

At present, academics are focused on the definition and characteristics (3), the current situation and influencing factors (4–6), and practical research tools (7, 8) relating to the SWB of the elderly. Among them, the influencing factors are divided into subjective factors, such as personality traits and cognitive patterns, and objective factors, such as demographic factors, economic conditions, health conditions, and family life (7). However, the relationship between the natural environment and the SWB of the elderly is less discussed. China's environmental pollution has become a nuisance to residents' healthy lives, and the physical and psychological damage to residents cannot be ignored (9). According to the World Health Organization report, China ranked second worldwide in 2016 for the number of deaths caused by environmental pollution (10). Meanwhile, as people grow older, their bodily functions decline, as do their immunity and resistance. They are more vulnerable to be affected by external environmental pollution, thus inducing various diseases, and their SWB is more likely to be affected (11).

Second, most studies measure the quality of the natural environment in residential areas based on objective measurement data. For example, air pollution is calculated using the total amount of soot and dust emissions, nitrogen oxide emissions, and industrial waste gas in the past 12 months (12) or represented using the PM10 (Refers to particulate matter with particle size below 10 microns) level (13); the total amount of wastewater emissions from the whole society over the past 12 months is used to estimate water pollution (12); domestic waste pollution is estimated from the total amount of domestic waste collected and transported to disposal plants or sites in the past 12 months (12); the sound level of wind turbine noise in wind power generation is used to study its influence on residents' happiness (14). Few studies have been conducted from the perspective of the elderly's subjective cognition of the natural environment in the living area. In addition, the mediation effect of the elderly's evaluation of the government's environmental protection work on the living natural environment and the SWB of the elderly remains to be further studied in China. Based on the literature and social reality, this study speculated that elderly people had slightly different effects on their SWB from the living natural environment conditions depending on their evaluation of the government's environmental protection work.

Because of this, in combination with the China Social Survey (Abbreviated as CSS) database, this study uses Stata to try to explore the relationship between the living natural environment conditions of the elderly, their evaluation of the government's environmental protection work and their SWB, so as to provide a specific mechanism to formulate more targeted environmental governance policies for relevant government departments and provide theoretical support and policy ideas for helping "active aging."

Abbreviations: SWB, Subjective wellbeing; CSS, China Social Survey database; CFPS, China Family Panel Studies database; LS, Life satisfaction; ES, Satisfaction with living natural environment; GV, Evaluation of government environmental protection work.

2. Literature review

2.1. The natural environment of the living area and the SWB of the elderly

In the 1980's, Tao's "human settlement theory" was translated by Wu Liangyong, a famous Chinese scholar, and developed into a new disciplinary system of human settlement science (15), which focuses on the coordination between man and nature and focuses on the living environment. The five principles of human settlement environment construction indicate that we should face the ecological dilemma squarely and improve our ecological consciousness, care for all people, and attach importance to the overall interests of social development. In recent years, China has made active efforts to control environmental pollution, but environmental pollution is still a major threat to the construction of a better living environment and has become an important reason for the deterioration of Chinese people's wellbeing (16).

The natural environment of residential areas includes various elements, such as air and water, and research (12) has depicted that public awareness is strongest around the three environmental pollution problems of water pollution, air pollution, and household waste pollution. Many scholars have discussed the impact of air pollution on SWB. According to the 2005–2018 Gallup World Poll of 151 countries, better subjective cognition of air quality is associated with higher personal happiness (17). Subjective cognition of air pollution has a more serious impact on happiness than Objective cognition of air pollution (17). Air pollution has a more significant negative impact on the wellbeing of unhealthy and elderly people than healthy people and young people (18). In addition, studies have found that air pollution negatively correlates with people's ethical behavior and that air pollution exacerbates anxiety, which in turn may increase unethical behavior (19). This means that the interactions between air pollution and SWB need to be further studied, and certain moderating and mediating variables may explain the relationship between air pollution and SWB. Like air, water quality is closely related to the SWB of the elderly. Studies (20) have demonstrated a correlation between residents' mental health and perceived water pollution in China, Japan, and South Korea. Furthermore, psychological and mental health issues like anxiety and depression are also related with exposure to noise pollution (21). Due to the influence of airport noise, the happiness of residents living within 50 km of Amsterdam Airport is significantly lower than that of those living over 50 km away (22). In addition, other environmental pollution (such as land pollution and electromagnetic ionizing radiation pollution) is strongly correlated with the SWB of the elderly (23). According to a report from the World Health Organization, electromagnetic radiation pollution has become the fourth major environmental pollution after air, water, and noise pollution. Residents exposed to soil pollution have poorer psychosocial health than those who are not exposed, with higher levels of anxiety and depression (24). Based on this, the following hypothesis is put forward:

Hypothesis 1: The natural environment of the residential area has a positive impact on the SWB of the elderly. The better the natural environment of the residential area, the higher the

SWB of the elderly. On the contrary, the worse the natural environment of the residential area, the lower the SWB of the elderly.

2.2. The intermediary role of the elderly in the evaluation of the government's environmental protection work

On the one hand, both objective environmental quality and residents' subjective perception of environmental quality will impact the government's environmental protection work evaluation. Studies (25) have depicted that the improvement of objective environmental quality does not necessarily improve residents' evaluation of the government's environmental work, on the contrary, it may reduce the correlation positive evaluation. However, the public's subjective perception of environmental pollution has a significant direct impact on the assessment of the government's environmental work. The more serious the perceived pollution, the lower the rating of the government's environmental work. On the other hand, uncertainty about the health effects of exposure to chronic and invisible pollutants can lead to distrust of policymakers by victims and conflict within communities (26). In environmental risk perception, the government's environmental behavior positively impacts residents' perception of the risks to their quality of life and mental health. For example, Song et al. (27) used panel data composed of microscopic data from China Family Panel Studies database (CFPS) 2012, 2014, and 2016 to conduct an empirical test and found that residents' SWB continuously improved with the enhancement of environmental regulations. And the enhancement of environmental regulations can indirectly improve the SWB of residents by improving residents' health status.

Hypothesis 2: The elderly's evaluation of the government's environmental protection work plays an intermediary role in the impact of natural environmental pollution on the elderly's SWB.

As mentioned above, this study attempts to incorporate the natural environment in the residential area, elderly's assessment of the government's environmental protection work, and the elderly's SWB into the same analysis framework demonstrated in Figure 1.

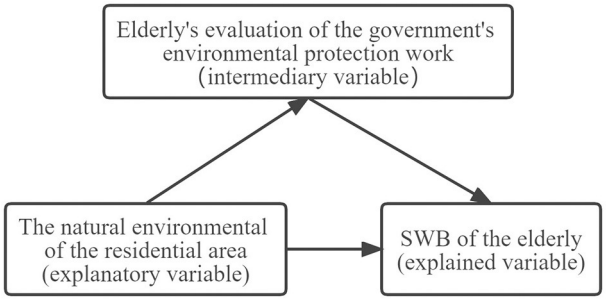

FIGURE 1
Theoretical model of the influence of natural environment in residential area on subjective well-being of the elderly.

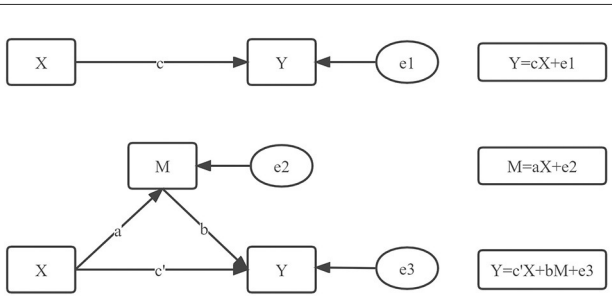

FIGURE 2
Regression equation and path diagram.

3. Data source and methods

3.1. Data source

The data used in this study are from the CSS conducted by the Institute of Sociology of the Chinese Academy of Social Sciences. CSS is a biennial longitudinal survey that adopts the method of probability sampling. The survey area covers 31 provinces (autonomous regions/municipalities) directly under the central government, including 151 counties (districts) and 604 villages (neighborhood committees). Each survey visits more than 10,000 urban and rural families. The research results can infer the country's household population aged 18–69. In this study, owing to CSS is a biennial longitudinal survey, so samples respondents with age characteristics over 60 years old in CSS2013, CSS2015, CSS2017 and CSS2019 were selected from the CSS database, and the number of valid samples respondents was 1,801, 2,005, 2,248, and 1,049, respectively after eliminating the missing values.

3.2. Variable selection

The Explained variable in this study was the SWB of the elderly. In Economics of Happiness, Life satisfaction (LS) can be a proxy variable of happiness (28). Deaton and Stone (29) proposed that SWB is a cognitive process, which is related to an individual's overall evaluation of life, or the overall memory of an individual's living conditions for a period of time. The measurement method is based on Cantrell Ladder Method, which divides life satisfaction into 10 grades, representing satisfaction levels of different quality of life from low to high. In this study, the corresponding question in the CSS2013, CSS2015, CSS2017 and CSS2019 questionnaires "Please use 1–10 points to express your satisfaction with life, 1 point to express very dissatisfied, 10 points to express very satisfied" to express the SWB of the respondents. The higher the number, the higher the satisfaction with life. Studies have revealed that although this measurement method is simple, it also has high reliability and validity (30).

The explanatory variable was satisfaction with the environmental conditions of the residence (ES). In this study, the corresponding question in the CSS2013, CSS2015, CSS2017 and

TABLE 1 Descriptive statistics of main variables.

Variables	Option	2013 ($N = 1,801$)		2015 ($N = 2,005$)		2017 ($N = 2,248$)		2019 ($N = 1,049$)	
		Frequency	Percentage (%)	Frequency	Percentage (%)	Frequency	Percentage (%)	Frequency	Percentage (%)
LS	1	19	1.1	33	1.7	53	2.4	24	3.0
	2	22	1.2	34	1.7	45	2.0	19	1.8
	3	36	2.0	77	3.8	88	3.9	27	2.6
	4	77	4.3	109	5.4	105	4.7	26	2.5
	5	248	13.8	396	19.8	387	17.2	128	12.2
	6	266	14.8	336	16.8	305	13.6	119	11.3
	7	308	17.1	313	15.6	282	12.5	120	11.4
	8	461	25.6	393	19.6	494	22.0	213	20.3
	9	175	9.7	161	8.0	168	7.5	87	8.3
	10	189	10.5	153	7.6	321	14.3	286	27.3
ES	1	38	2.1	87	4.3	135	6.0	46	4.4
	2	28	1.6	72	3.6	83	3.7	10	1.0
	3	57	3.2	111	5.5	136	6.1	31	3.0
	4	71	3.9	162	8.1	109	4.9	33	3.2
	5	215	11.9	369	18.4	391	17.4	178	17.0
	6	279	15.5	294	14.7	238	10.6	96	9.15
	7	313	17.4	271	13.5	269	12.0	129	12.3
	8	479	26.6	376	18.8	423	18.8	230	22.0
	9	164	9.1	118	5.9	157	7.0	64	6.1
	10	157	8.7	145	7.2	307	13.7	232	22.1
GV	Excellent	160	8.9	254	12.7	467	20.8	294	28.0
	Relatively good	999	55.5	1,063	53.0	1,120	49.8	554	52.8
	Not so well	522	29.0	528	26.3	468	20.8	152	14.5
	Terrible	120	6.7	160	8.0	193	8.6	49	4.7
Gender	Male	870	48.3	1,027	51.2	1,145	50.9	492	46.9
	Female	931	51.7	978	48.8	1,103	49.1	557	53.1
Education	Not in school	422	23.4	470	23.4	515	22.9	227	21.7

(Continued)

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TABLE 1 (Continued)

Variables	Option	2013 ($N = 1,801$)		2015 ($N = 2,005$)		2017 ($N = 2,248$)		2019 ($N = 1,049$)	
		Frequency	Percentage (%)	Frequency	Percentage (%)	Frequency	Percentage (%)	Frequency	Percentage (%)
	Primary school	754	41.9	761	38.0	837	37.2	326	31.1
	Junior high school	398	22.1	476	23.7	561	25.0	290	27.7
	High school	157	8.7	217	10.8	254	11.3	169	16.1
	Junior college	52	2.9	50	2.5	50	2.2	30	2.9
	Bachelor degree	15	0.8	26	1.3	26	1.2	4	0.4
	Graduate students and above	3	0.2	5	0.3	5	0.2	3	0.3
Marital	Unmarried	25	1.4	23	1.2	32	1.4	16	1.5
	Married	1,751	97.2	1,955	97.5	2,186	97.2	1,017	97.0
	Divorced	25	1.4	27	1.4	30	1.3	16	1.5
Political	Party member	1,544	85.7	272	13.6	303	13.5	164	15.6
	Non-party people	257	14.3	1,733	86.4	1,945	86.5	885	84.4
Nature of household registration	Agricultural household	1,252	69.5	1,346	67.1	1,554	69.1	707	67.4
	Non-agricultural household	549	30.5	659	32.9	694	30.9	342	32.6
Job	Have a job	809	44.9	946	47.2	1,164	51.8	540	51.5
	No job	992	55.1	1,059	52.8	1,084	48.2	509	48.5
Annual income	-	8.8 (*m*)	3.0 (*SD*)	8.5 (*m*)	2.4 (*SD*)	8.0 (*m*)	3.1 (*SD*)	8.3 (*m*)	2.9 (*SD*)

N, sample size; m, mean; SD, standard deviation; Annual income: total personal income of the previous year after logarithm.

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TABLE 2 Correlation analysis of main variables.

Variables	2013 (N =1,801)			2015 (N = 2,005)			2017 (N = 2,248)			2019 (N = 1,049)		
	LS	ES	GV	LS	ES	GV	LS	ES	GV	LS	ES	GV
LS	1.0			1.0			1.0			1.0		
ES	0.3***	1.0		0.5***	1.0		0.6***	1.0		0.3***	1.0	
GV	−0.1***	−0.4***	1.0	−0.1***	−0.3***	1.0	−0.1***	−0.2***	1.0	−0.2***	−0.4***	1.0

N, sample size; LS, Life satisfaction; ES, Satisfaction with living natural environment; GV, Evaluation of government environmental protection work; *P < 0.05, **P < 0.01, ***P < 0.001.

CSS2019 questionnaires, "Please use 1–10 points to express your satisfaction with the environmental conditions of your residence. 1 point means very dissatisfied, and 10 points means very satisfied" to express the respondents' satisfaction with the environmental conditions of their residence. The higher the number, the higher the respondents' satisfaction with the environmental conditions of their residence.

This study took the evaluation of the elderly on the government's environmental protection work (GV) as an intermediary variable. The corresponding question in the CSS2013, CSS2015, CSS2017 and CSS2019 questionnaires, "Is the government doing a good job in environmental protection and pollution control?" Eliminate the "not clear" option, and the alternative answers were "excellent," "relatively good," "not so well," "terrible."

Apart from the living environment's influence on SWB in older adults, personal characteristics are highly correlated with SWB. For example, social comparison theory reveals that happiness is influenced by comparing one's income or status with the average level of the whole society. In addition, other personal characteristics, such as education level and work status, similarly affect the subjective assessment by the elderly of their external living conditions and wellbeing (31). Therefore, demographic factors such as gender, education level, marital status, working status, political status, nature of household registration and personal annual income, which are control variables, were included in the study.

3.3. Methods

The life satisfaction of the elderly, the evaluation of the elderly on the government's environmental protection work, and satisfaction with the environmental conditions of the residence did not conform to the expected data. So Spearman correlation analysis and Ordered Probit Model were used to test the correlation and interaction of the main variables. The difference was statistically significant with $P < 0.05$. The intermediary effect test model of Wen and Ye (32) was used to examine the intermediary effect of the elderly on evaluating the government's environmental protection work. As shown in Figure 2, coefficient c represented the total effect obtained through the regression analysis of the independent variable X and the dependent variable Y; Coefficients a and b represented intermediate effect process values. a was obtained by regression analysis of independent variable X and intermediary variable M. b was obtained by regression analysis of intermediary variable M and dependent variable Y after controlling the influence of independent variable X. The coefficient c' represented the direct effect value. After controlling the influence of the intermediary variable M, it was obtained through the regression analysis of the independent variable X on the dependent variable Y. $e1$, $e2$, and $e3$ represented the regression residual.

4. Results

4.1. Descriptive statistical analysis

As shown in Table 1, from 2013 to 2019, almost 90% of the sample respondents' life satisfaction was "5" and above in each year, indicating that the respondents were relatively satisfied with their lives. The sample respondents' satisfaction with the living natural environment was "8," which accounted for the largest proportion in each year. The proportion of the sample respondents who thought that the government's environmental protection work was "Not so well" and dissatisfied with the government's environmental protection work fell from 35.7% in 2013 to 19.2% in 2019.

4.2. Spearman correlation analysis

It can be seen from Table 2 that the correlation coefficients between residents' satisfaction with environmental conditions and their life satisfaction of the sample respondents from 2013 to 2019 were 0.3, 0.5, 0.6 and 0.3, respectively, indicating that they were positively correlated and had statistical significance ($P < 0.001$), which was consistent with the research conclusions of Huang and He (33); In addition, the correlation coefficients between the evaluation of the sample respondents on the government's environmental protection work and their life satisfaction were −0.1 ($P < 0.001$), −0.1 ($P < 0.001$), −0.1 ($P < 0.001$), −0.2 ($P < 0.001$), respectively from 2013 to 2019, indicating that the two were negatively correlated; the correlation coefficients of the sample respondents' satisfaction with environmental conditions and their evaluation of the government's environmental protection work were −0.4 ($P < 0.001$), −0.3 ($P < 0.001$), −0.2 ($P < 0.001$), −0.4 ($P < 0.001$), respectively, indicating that they were also negatively correlated. In this study, owing to the indicators of the elderly's evaluation of the government's environmental protection work were reverse values, the larger the value, the lower the respondents' evaluation of the government's environmental protection work. Therefore, the sample respondents' evaluation of government environmental protection work was negatively related to their life satisfaction and their satisfaction with natural environmental conditions.

4.3. Regression analysis

To further investigate the impact of the quality of the natural environment in residential areas on the SWB of elderly, this study adopted Ordered Probit Model, including three models. It can be seen from Table 3 that in the 4 years, the satisfaction of the sample respondents with the living natural environment has been positively and significantly influencing their life satisfaction ($P < 0.001$). Moreover, the R value of the model 1 in 2013 was 0.09, which means that the satisfaction of the residential environment can explain the 9% change of the life satisfaction. For model 2, after adding control variables on the basis of model 1, the F value changes significantly ($P < 0.05$), which means that the control variables has explanatory significance for the model after adding. For model 3, after adding the evaluation of the samples respondents on the government's environmental protection work on the basis of model 2, its impact on life satisfaction was not significant ($P > 0.05$), as was the case in 2015. The evaluation of the samples respondents on the government's environmental protection work was added on the basis of model 2 in 2017, and we found that it had a negative impact on life satisfaction, with a regression coefficient of −0.09 ($P < 0.05$). In 2019, the regression coefficient was −0.26 ($P < 0.01$), which was also statistically significant.

4.4. Robustness check

In order to verify the robustness of the results, we used the ordinary least squares (OLS) Model to estimate. The results are shown in Table 4. The probability of "very satisfied" life satisfaction of the samples respondents increased by 31.6, 48.3, 48, and 25.9%, respectively when their satisfaction with the living natural environment increased by one level in 2013, 2015, 2017 and 2019. In addition, the *D-W* value was close to 2, indicating that there is no autocorrelation in the model and no correlation between sample data, the model is good. The above regression results showed that whether demographic variables were controlled or different measurement methods were used, the satisfaction of the elderly's living environment had a significant positive impact on their SWB. Hypothesis 1 is valid.

4.5. Intermediary effect test

According to the Ordered Probit Model analysis results, the evaluation of the samples respondents on the government's environmental protection work had a significant negative impact on their SWB in 2017 and 2019. This provided conditions for the next step to test whether the evaluation of the elderly on the government's environmental protection work had an intermediary effect. We used Sobel test (32) by Stata and found that the mediating effect of it in 2017 accounted for 1.19% ($P < 0.05$), and in 2019 rose to 11.12% ($P < 0.05$) (Table 5), indicating that it plays an increasingly important intermediary role in the impact of living natural

TABLE 3 Regression analysis of main variables.

LS	2013 ($N = 1,801$)			2015 ($N = 2,005$)			2017 ($N = 2,248$)			2019 ($N = 1,049$)		
	M 1	M 2	M 3	M 1	M 2	M 3	M 1	M 2	M 3	M 1	M 2	M 3
ES	0.29*** (0.02)	0.31*** (0.02)	0.32*** (0.02)	0.48*** (0.02)	0.48*** (0.02)	0.48*** (0.02)	0.49*** (0.02)	0.49*** (0.02)	0.48*** (0.02)	0.28*** (0.03)	0.29*** (0.03)	0.26*** (0.03)
GV	-	-	−0.04 (0.06)	-	-	−0.04 (0.05)	-	-	−0.09* (0.05)	-	-	−0.26** (0.09)
Control	-	YES	YES	-	YES	YES	-	YES	YES	-	YES	YES
F	186.31	34.87	31.03	852.36	121.60	108.13	1,029.71	137.72	123.04	96.92	17.13	16.15
Prob > F	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
R	0.09	0.14	0.14	0.30	0.33	0.33	0.31	0.33	0.33	0.08	0.12	0.12

N, sample size; M, Model; LS, Life satisfaction; ES, Satisfaction with living natural environment; GV, Evaluation of government environmental protection work; Standard error in brackets; *P < 0.05, **P < 0.01, ***P < 0.001.

environment conditions on the SWB of the elderly. Hypothesis 2 is verified.

5. Discussion

The natural environment of the living area has a significant positive effect on the SWB of the elderly. It is consistent with the conclusions of previous studies (34). The elderly's evaluation of the government's environmental protection work similarly has a significant positive impact on their SWB. The reason may be that environmental pollution has a direct and long-term harmful impact on human life and health, and the elderly worries about their health and panic about the living environment will stimulate their identification and discussion of the responsibility for environmental protection. According to principal-agent theory, the relationship between citizens and the government can be regarded as a principal-agent relationship (35). The government, as the trustee of public fiduciary social responsibility, should properly manage environmental and other public resources on behalf of citizens after obtaining public power. Although the government has actively taken many measures to improve environmental quality, the above results depicted that 19.4% of sample respondents were still unsatisfied with the government's environmental protection work. Environmental pollution has gradually surpassed itself and become a political and social issue. Therefore, the elderly's evaluation of the government's environmental protection work may profoundly impact the SWB of elderly people (36). In addition, the more serious elderly's subjective perception of the living environment pollution, the more frequently they discuss the environmental pollution with their families and friends, thus becoming suspicious and dissatisfied with the government's environmental protection work. Such social interactions often lead to the spread of negative emotions and further reduce the SWB of the elderly (37).

The elderly's evaluation of the government's environmental protection work plays an increasingly important intermediary role in the impact of living natural environment conditions on the SWB of the elderly. Satisfaction with the government's investment in environmental protection is the primary source of the elderly's subjective happiness perception of the living environment (38). The mechanism is that the government effectively solves the air, water, soil, and other pollution problems. On the one hand, this reduces the health problems caused by environmental pollution and the treatment costs of related diseases, healthy body and reduced spending significantly improve the SWB of the elderly. On the other hand, the government's environmental protection work improves the environmental quality, and the elderly experience the improvement of life quality through factors such as blue skies, white clouds, and clean water, which not only reduces their psychological pressure but also helps to enhance their trust in the government, thus enhancing their own SWB (39).

TABLE 4 OLS regression analysis.

Variables	2013 (N = 1,801)	2015 (N = 2,005)	2017 (N = 2,248)	2019 (N = 1,049)
ES	0.316** (11.646)	0.483** (23.388)	0.480** (26.050)	0.259** (7.037)
GV	−0.042 (−0.631)	−0.037 (−0.682)	−0.094 (−1.786)	−0.258* (−2.514)
Gender	0.157 (1.693)	0.220** (2.654)	−0.049 (−0.581)	0.121 (0.806)
Education	0.058** (4.700)	0.031** (2.780)	0.012 (1.008)	0.019 (1.018)
Marital	−0.403 (−1.384)	0.385 (1.634)	−0.176 (−0.715)	−0.916* (−2.311)
Political	0.280* (2.364)	0.189 (1.907)	0.269** (2.634)	0.476** (3.314)
Nature of household registration	0.404** (3.649)	0.400** (3.841)	0.381** (3.505)	0.207 (1.166)
Job	0.051 (0.491)	0.124 (1.310)	0.020 (0.217)	−0.094 (−0.574)
Annual income	−0.002 (−0.120)	0.048* (2.486)	0.024 (1.664)	0.074** (2.790)
R-Square	0.135	0.328	0.331	0.123
Adjusted R-Square	0.131	0.325	0.328	0.115
F	F (9, 1, 791) = 24.050, P = 0.000	F (9, 1,995) = 83.543, P = 0.000	F (9, 2,238) = 93.559, P = 0.000	F (9, 1, 039) = 14.814, P = 0.000
D-W	1.733	1.905	1.954	2.012

N, Sample size; Explained variable: LS; *P < 0.05 **P < 0.01; t value in parentheses.

TABLE 5 Mediating effect test.

	2017				2019			
	Coef	SE	Z	$P>\|Z\|$	Coef	SE	Z	$P>\|Z\|$
a	−0.062	0.007	−8.945	0	−0.126	0.009	−13.620	0
b	−0.094	0.046	−2.030	0.042	−0.258	0.094	−2.731	0.006
Indirect effect	0.006	0.003	1.98	0.048	0.032	0.012	2.677	0.007
Direct effect	0.480	0.015	31.273	0	0.259	0.031	8.491	0
Total effect	0.486	0.015	32.189	0	0.291	0.281	10.338	0
Proportion of total effect that is mediated	0.0119				0.1112			

6. Conclusion

Based on the above discussions, we can see: The better the natural environment of the living area, the higher the SWB of the elderly; The better the evaluation of the government's environmental protection work by the elderly, the higher the SWB of the elderly; In addition, the natural environment of the living area gradually affects the SWB of the elderly by influencing their evaluation of the government's environmental protection work. Therefore, the corresponding conclusions are drawn: First, to improve the SWB of older people, the government should continue to coordinate environmental protection and pollution control. Such as taking "improving residents' perceived environmental quality" as part of its policy objectives, implement an environmental protection target responsibility system and strengthen the quantitative assessment of comprehensive remediation of the urban environment. Second, the government should increase the publicization of its environmental protection work in various ways so that the elderly can see the government's efforts to improve the quality of the living environment, which would improve the elderly's assessment of the government's environmental protection activities. For example, establish an open and transparent environmental information disclosure system, regularly publicize pollution level measurements, publish environmental quality improvement results in the media, and inform the public of progress toward achieving targets. Third, the government should strengthen communication with residents so that they can understand the residents' subjective perception of the living natural environment and demands in a timely manner and carry out the necessary follow-up work.

There are still deficiencies in the study. This study only verifies the impact of the single intermediary role of the elderly in evaluating government environmental protection work on the SWB of the elderly. Whether the SWB of the elderly will be affected by other intermediary variables needs to be further studied.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found at: http://csqr.cass.cn/DataExplore/?ProjectID=20180619094632459272610663 14. Repository: CSS2013, CSS2015, CSS2017, and CSS2019. Accession number: 18383022018.

Author contributions

Methodology, data collection, and analysis were performed by ZL. The first draft of the manuscript was written by ZL, ZJ, and YJ. All authors commented on the previous versions of the manuscript, contributed to the study conception and design, read, and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Sensory impairments and subjective well-being status in middle-aged and older Chinese population: Cross-sectional and longitudinal analyses of a nationally representative survey

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Purpose: To investigate the impacts of sensory impairments (SIs) including single vision impairment (SVI), single hearing impairment (SHI) and dual sensory impairment (DSI) on subjective wellbeing measurements including life expectancy (LE), life satisfaction (LS) and self-rated health (SRH) in middle-aged and older Chinese population.

Methods: We obtained data from the China Health and Retirement Longitudinal Survey (CHARLS). In total, 9,293 Chinese middle-aged and older adults aging over 45 were included at baseline 2011 in this study, and 3,932 participants who accomplished all 4 interviews from 2011 to 2018 were adapted for longitudinal analyses. Sensory status and subjective wellbeing measurements were collected. Other covariates included socio-demographic characteristics, medical condition and lifestyle-related factors. The impacts of baseline sensory status on LE, LS and SRH were assessed using univariate and multivariate logistic regression analyses. A linear regression analysis with generalized estimating equations (GEE) was used to assess the association between time-varying sensory statuses with LE, LS and SRH over 8 years after being adjusted with multi-confounding factors.

Results: Participants with SIs had significantly lower level of LE, LS, and SRH, compared to those who were free of SI. All kinds of SIs were significantly associated with LE, LS, and SRH according to cross-sectional data. The correlations between SIs and LE or SRH over 8 years were also noticed. However, only SHI and DSI were found to be significantly associated with LS according to longitudinal data (all p values < 0.05).

Conclusion: Sensory impairments had explicitly detrimental effects on subjective wellbeing status over time among middle-aged and older Chinese population.

KEYWORDS

China health and retirement longitudinal study, life expectancy, life satisfaction, self-rated health, sensory impairment

1. Introduction

The wellbeing status of aging population is one major challenge for both developed and developing countries all over the world (1). Substantial increase in the number of middle-aged and older people in our society generates an urgent requirement of attaining a successful aging life, which fosters daunting challenges for biological, social and medical science. Over the past decades, although the clear definition and scope of a successful aging have not reached a consensus, many researchers have emphasized the subjective nature of this concept and suggested that to define a successful aging, the self-perception of elderly individuals should be well considered (2).

Subjective life expectancy (LE), also known as perceived life expectancy or perception of future time (PFT), represents an individual's expectation or subjective probability of survival to a certain age, which has been considered as a pivotal predictor of one' s economic, health, and mental status and a direct benchmark survival indicator (3). On the other hand, the adage: "happy person lives longer" appears to be common knowledge. Life satisfaction (LS), defined as the perception of a person's overall quality of life, has also been regarded as an essential representative that reflects individual's overall subjective life evaluation (4). Also increasingly, self-rated health (SRH) has been used as a succinct way to approximate diverse objective components of health status, such as physical, psychological and behavioral health factors (5), which indicates the continuum of a person's perceived health by eliciting perspective of the individual on previous, current, and future health (6). These subjective wellbeing measurements have gained certain attention from the academic for evaluation of a successful aging, which have been widely adapted in studies on health and wellbeing status in recent years.

The judgements of subjective perceptions are usually based on personal criteria, which could be affected by situational factors under many circumstances (7). Therefore, identification of the affecting factors, especially modifiable risk factors of subjective wellbeing status may not only help revealing the inherent mechanisms of subjective elements of health and wellbeing status, but also provide supports of specific interventions to promote self-perception of a better living status. To date, multiple factors have been noticed to have certain impacts on subjective wellbeing status. For instance, individuals with higher age (8), pain and limitation of physical function (9) would be more likely to report poorer health status. Lower educational level, financial strain and lower depressive symptoms were reported to have strong associations with higher life satisfaction (10). And Personal socioeconomic status could greatly affect one's perception of future time (11). However, to the best of our knowledge, the effects of a common chronic physical dysfunction among middle-aged and older population, sensory impairment, have not been well explored (8).

With the increasing trend in life expectancy, sensory impairments (SIs), including hearing impairment (HI), vision impairment (VI), and dual sensory impairment (DSI) which refers to the simultaneous presence of VI and HI, are common age-related conditions. SIs have wide ranging implications for health and general wellbeing in elderly population (12), whose impacts on various adverse events in aging life including psychological distress (13), jeopardized quality of life (14), and even all-cause mortality (15–17) have been widely investigated. However, there is a paucity of literature on the associations between SI with subjective wellbeing measurements including LE, LS, and SRH in aing life, especially from developing countries (8, 18, 19).

China is the most populous developing country, which also faces severe aging society problems. More importantly, elderly Chinese are likely to neglect SIs and consequent problems owing to the traditional attitudes regarding SIs as normal parts of aging life, which might further contribute to the higher prevalence of SIs in China than in some western countries (20). SIs have been noticed to have certain influences on adverse health consequences in middle-aged and older Chinese population (21–23). Allowing for the specific cultural background, social institution, and health system in mainland China, the aim of the present study is to address the research gap of the associations between SIs with LE/LS/SRH among middle-aged and older Chinese population using cross-sectional and longitudinal data over 8 years of observation.

2. Methods

2.1. Participants and public involvement

Data was obtained from the China Health and Retirement Longitudinal Study (CHARLS). CHARLS is a longitudinal survey that aims to be representative of the residents in mainland China aged 45 and older. It attempts to set up a high quality public micro-database, which can provide a wide range of information from socioeconomic status to health conditions, to serve the needs of scientific research on the elderly. To ensure the adoption of best practices and international comparability or results, CHARLS is harmonized with leading international research studies in the Health and Retirement Study (HRS) model. The national baseline survey was conducted in 2011–12, with wave 2 in 2013, wave 3 in 2015, and wave 4 in 2018. In order to ensure

sample representativeness, the CHARLS baseline survey covered 150 countries/districts, 450 villages/urban communities, across 28 provinces over the country, involving 17,708 individuals in 10,257 households, reflecting the mid-aged and older Chinese population collectively. With response rates over 80%, CHARLS provides the most up-to-date longitudinal data for investigation of the health status and wellbeing of middle-aged and elderly population in China. CHARLS enrolled 17,708 participants at baseline (Wave 1), 18,254 participants at Wave 2 (2013), 20,273 participants at Wave 3 (2015), and 19,816 participants at Wave 4 (2018). For respondents surveyed in the baseline wave, more than 90% of them were re-contacted in each of the follow-up waves, and the response rate of the tracked sample (panel sample) remains at higher than 86% in any of the follow-up waves. Therefore, the success follow-up rates of CHARLS are high compared to many HRS-type surveys.

3. Measures

3.1. Main outcome

3.1.1. Life expectancy

In CHARLS, life expectancy was assessed according to the respondent's response to a series of stratified questions: "On what step ("Almost impossible", "Not very likely", "Maybe", "Very likely", "Almost certain") do you think is your chance that you will live to be [75 (if respondent's current age is 64 or less)/80 (if age is between 65 and 69)/85 (if age is between 70 and 74)/90 (if age is between 75 and 79)/95 (if age is between 80 and 84)/100 (if age is between 85 and 89)/105 (if age is between 90 and 94)/110 (if age is between 95 and 99)/115 (if age is 100 or more)]?". The 5-point Likert scale responses range from 1 (almost impossible) to 5 (almost certain). Higher SLE scores indicate longer lifespan anticipation. In this study, we defined SLE scores of 1–3 as lower life expectancy and considered SLE scores of 4–5 as higher life expectancy."

3.1.2. Life satisfaction

Life satisfaction was measured according to the respondent's response to the question "Please think about your life as a whole. Are you completely satisfied, very satisfied, somewhat satisfied, not very satisfied, or not at all satisfied with it?" Satisfaction is defined by answers including "completely satisfied", "very satisfied" and "somewhat satisfied", while dissatisfaction is defined by answers including "not very satisfied" and "not at all satisfied".

3.1.3. Self-rated health

Self-rated health status was acquired by the question: "Would you say your health is very good, good, fair, poor or very poor". In our study, we defined SRH by dichotomizing answers into "very good to fair" vs. "poor to very poor" for subsequent analysis.

3.1.4. Exposures

The main exposure in this present study is sensory status including no sensory impairment (NSI), single vision impairment (SVI), single hearing impairment (SHI) and dual sensory impairments (DSI). In CHARLS, VI consists of distal and near ones. Distal VI and near VI were evaluated by asking participants whether their eyesight was excellent, very good, good, fair, or poor when seeing things at a distance or up close, respectively. Reporting of fair or poor eyesight was classified as VI. Similarly, for HI assessment, the question was: "Is your hearing excellent, very good, good, fair or poor." A response of fair or poor hearing was identified as HI. Such assessment of SI has been widely used in previous CHARLS-related studies (22). DSI refers to participants with both VI and HI, and single SI refers to sole VI or HI without the other one.

SI in aging population could be amended by medical supports such as cataract surgery and hearing aids, or vice versa, get worse due to aging or pathologic progressions. Thus, along with baseline sensory status, we also investigated the impacts of time-varying SI statuses during 8 years of follow-up on the outcomes to further explore the longitudinal effects on subjective wellbeing status.

3.2. Other variates

3.2.1. Socio-demographic characteristics

Gender was a binary variable: male and female. Age was treated as a categorical variable including 3 groups (45–59, 60–74, and ≥75 years). Marital status indicated whether the respondent lived alone or got accompanied. Participants who were separated, divorced, widowed or never married were coded as "living alone', while those who were married or partnered were coded as "living with partner". Living area referred to urban or rural places where participants lived. Educational attainment represents one's social economic status, which could probably affect people's access to health supports and other socio-economic resources. Educational status was categorized into 5 groups: illiterate, less than elementary school, elementary school, middle school, and high school or above.

3.2.2. Medical condition

Data on the medical condition were collected with the following question: "Have you ever been diagnosed by a doctor as having the following diseases: hypertension, dyslipidemia, diabetes, cancer, chronic lung diseases, liver diseases, heart disease, stroke, kidney diseases, memory-related diseases, digestive diseases, arthritis, and asthma?". Suffering from more than 2 diseases were defined as multi-morbidities. Insurance covering referred to coverage of one kind of health insurance or more.

3.2.3. Lifestyle-related factors

The lifestyle variables included smoking and drinking status. Smoking is categorized as current/former smoker or never smoked. Drinking is a 3-category variable which indicates the frequency of drinking: none, less than once a month or more than once a month.

3.4. Statistical analysis

Statistical analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC, US). In this study, the primary exposures of

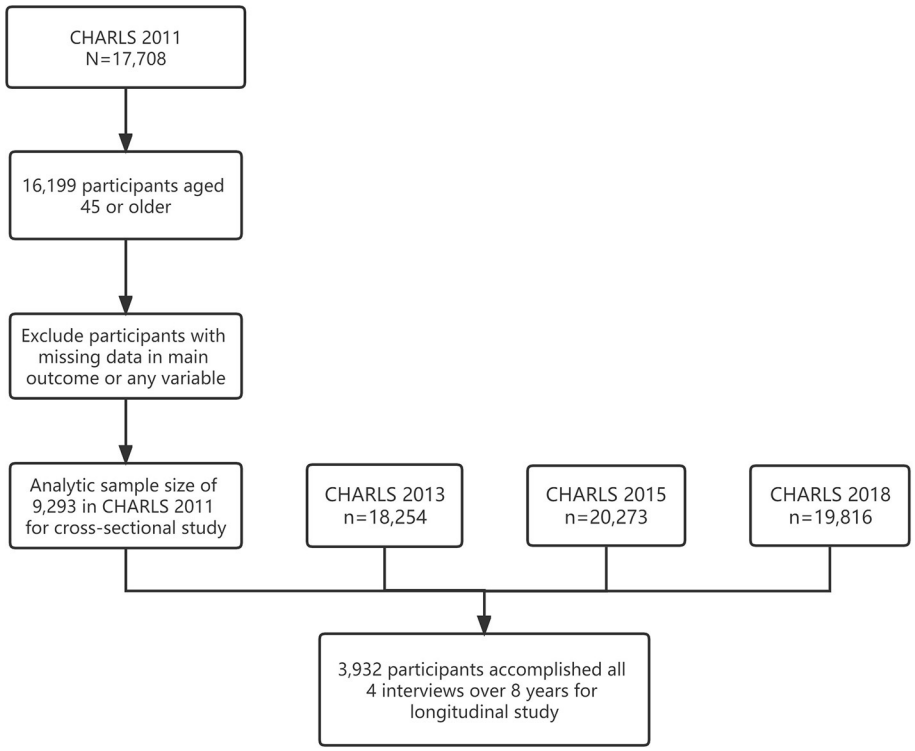

FIGURE 1
Graphic abstract of sample screening of the present study.

interest were SIs, while the other independent variables served as control variables. Baseline characteristics were compared among participants according to SI statuses (4 groups) using the Chi-square test analysis. Logistic regression analyses were conducted to assess the associations between SIs, multiple covariates and subjective wellbeing measurements at baseline for cross-sectional analyses. Associations between time-variant SIs and all three subjective wellbeing measurements changes over time (across 4 interviews over 8 years) were assessed using logistic regression analysis with generalized estimating equations (GEE), controlling for the intraindividual correlation between repeated measurements using an exchangeable correlation structure as previously described (24). To examine whether LE, LS, and SRH were dependent on the status of sensory impairments, models that adjusted for potential confounders as mentioned above were employed, and their parameter estimates were shown with 95% confidence intervals.

4. Results

In total, 9,293 participants over 45 years old from baseline CHARLS 2011 were deemed eligible for the current study, among which 3,932 accomplished all 4 interviews from 2011 to 2018 and were adapted in the longitudinal analyses (Figure 1). The baseline socio-demographic characteristics, medical conditions, lifestyle-related factors and subjective wellbeing measurements of the study sample were grouped by sensory statuses and shown in Table 1. Participants who were free from any kind of sensory impairment appeared to have explicitly higher LE, LS, and SRH. Changes of LE, LS, and SRH over 8 years were performed in Figure 2.

Before multivariate regression analysis, we first runed an univariate logistic regression which indicated certain covariables, including gender, age, marital status, educational level, living area, alcohol consumption and multi-morbidities, that could probably confound the relationship between SIs and subjective wellbeing status (Supplementary Table 1). To clarify the cross-sectional association between SIs and LE/LS/SRH, we analyzed their relevance by controlling for the covariates (Table 2). At baseline, all kinds of SIs showed profound and detrimental impacts on all three subjective wellbeing measurements after being adjusted for various confounders in all 4 Models (all p-values < 0.05). Compared to single SI, DSI had higher odds ratios, which suggests a potentially greater impact on subjective well-being status. The results shows that DSI is associated with lower LE (OR: 1.969, 95% CI 1.779–2.179, $p < 0.001$), lower LS (OR: 1.422, 95% CI 1.224–1.652, $p < 0.001$) and poorer SRH (OR: 2.018, 95% CI 1.833–2.223, $p < 0.001$).

In longitudinal analyses, associations between time-variant SIs and subjective wellbeing status over time were assessed using linear regression analysis with generalized estimating equations, which could provide longitudinal observation of intraindividual correlations between repeated measurements. Consistent with cross-sectional analyses, we found that all kinds of SIs were significantly associated with LE and SRH, even after receiving adjustments of various confounders (Table 3, all p-values < 0.001). As for SI-LS correlations, only SHI and DSI remained to be

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TABLE 1 Characteristics of 9,293 participants of the present study sample from CHARLS 2011.

Variables	Total	NSI	SVI	SHI	DSI	*P*-value
Gender						<0.0001
Male	4,630 (49.82%)	1,600 (52.44)	577 (46.12)	867 (53.09)	1,586 (47.23)	
Female	4,663 (50.18)	1,451 (47.56)	674 (53.88)	766 (46.91)	1,772 (52.77)	
Age						<0.0001
45–59	5,202 (55.98)	2,010 (65.88)	699 (55.88)	889 (54.44)	1,604 (47.77)	
60–74	3,415 (36.75)	908 (29.76)	469 (37.89)	613 (37.54)	1,425 (42.44)	
75–	676 (7.27)	133 (4.36)	83 (6.63)	131 (8.02)	329 (9.80)	
Marital status						0.0051
Live with partner	7,807 (84.01)	2,614 (85.68)	1,053 (84.17)	1,373 (84.08)	2,767 (82.40)	
Live alone	1,486 (15.99)	437 (14.32)	198 (15.83)	260 (15.92)	591 (17.60)	
Education						<0.0001
Illiterate	2,244 (24.15)	606 (19.86)	329 (26.30)	363 (22.23)	946 (28.17)	
Less than elementary school	1,621 (17.44)	442 (14.49)	224 (17.91)	292 (17.88)	663 (19.74)	
Elementary school	2,053 (22.09)	617 (20.22)	276 (22.06)	383 (23.45)	777 (23.14)	
Middle school or vocational school	2,062 (22.19)	773 (25.34)	260 (20.78)	371 (22.72)	658 (19.59)	
High school and above	1,313 (14.13)	613 (20.09)	162 (12.95)	224 (13.72)	314 (9.35)	
Living area						<0.0001
Urban area	3,865 (41.59)	1,447 (47.43)	530 (42.37)	640 (39.19)	1,248 (37.16)	
Rural area	5,428 (58.41)	1,604 (52.57)	721 (57.63)	993 (60.81)	2,110 (62.84)	
Smoke						0.0369
Yes	3,800 (40.89)	1,243 (40.74)	486 (38.85)	716 (43.85)	1,355 (40.35)	
No	5,493 (59.11)	1,808 (59.26)	765 (61.15)	917 (59.65)	2,003 (59.65)	
Drinking status						0.0009
Drink more than once a month	2,422 (26.06)	835 (27.37)	314 (25.10)	456 (27.92)	817 (24.33)	
Drink but less than once a month	727 (7.82)	269 (8.82)	80 (6.39)	128 (7.84)	250 (7.44)	
No drink	6,144 (66.11)	1,947 (63.82)	857 (68.51)	1,049 (64.24)	2,291 (68.23)	
Multi-morbidities						<0.0001
Yes	1,803 (19.40)	374 (12.26)	235 (18.78)	319 (19.53)	875 (26.06)	
No	7,490 (80.60)	2,677 (87.74)	1,016 (81.22)	1,314 (80.47)	2,483 (73.94)	
Insurance covering						0.4308
Yes	8,714 (93.77)	2,873 (94.17)	1,162 (92.89)	1,535 (94.00)	3,144 (93.63)	
No	579 (6.23)	178 (5.83)	89 (7.11)	98 (6.00)	214 (6.37)	
Life expectancy						<0.0001
Higher	6,720 (72.31)	2,524 (82.73)	900 (71.94)	1,204 (73.73)	2,092 (62.30)	
Lower	2,573 (27.69)	527 (17.27)	351 (28.06)	429 (26.27)	1,266 (37.70)	
Life satisfaction						<0.0001
Satisfaction	7,876 (84.75)	2,689 (88.14)	1,056 (84.41)	1,394 (85.36)	2,737 (81.51)	
Dissatisfaction	1,417 (15.25)	362 (11.86)	195 (15.59)	239 (14.64)	621 (18.49)	
Self-rated health						<0.0001
Healthy	4,480 (48.21)	1,934 (63.39)	566 (45.24)	806 (49.36)	1,174 (34.96)	
Unhealthy	4,813 (51.79)	1,117 (36.61)	685 (54.76)	827 (50.64)	2,184 (65.04)	

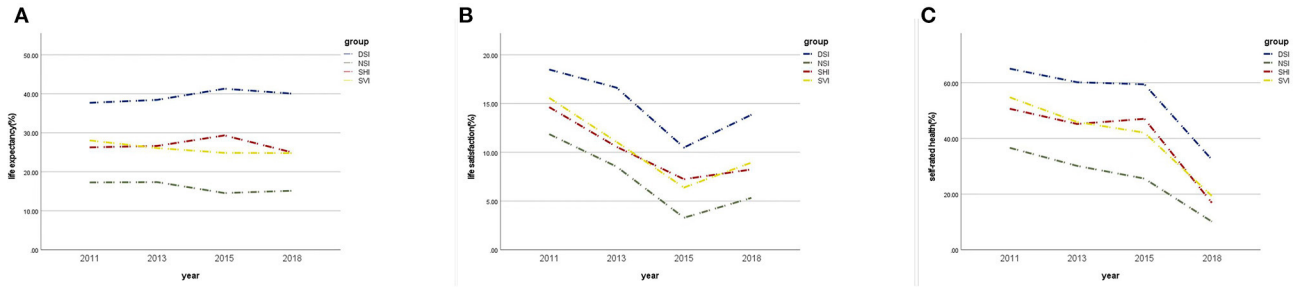

FIGURE 2
Changes of subjective wellbeing measurements over time, 2011–2018. **(A)** Changes in life expectancy by sensory impairment status; **(B)** Changes in life by satisfaction by sensory impairment status; **(C)** Changes in self-rated by sensory impairment status.

TABLE 2 Cross-sectional logistic regression analyses of sensory impairments and subjective wellbeing measurements.

Sensory status	Model 1		Model 2		Model 3		Model 4	
Ref: NSI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Life expectancy								
SHI	1.707***	(1.477, 1.972)	1.631***	(1.410, 1.887)	1.534***	(1.322, 1.780)	1.458***	(1.255, 1.695)
SVI	1.868***	(1.600, 2.181)	1.781***	(1.953, 2.733)	1.676***	(1.429, 1.965)	1.612***	(1.372, 1.893)
DSI	2.898***	(2.578, 3.258)	2.682***	(2.382, 3.019)	2.447***	(2.168, 2.762)	2.240***	(1.982, 2.533)
Life satisfaction								
SHI	1.273**	(1.112, 1.583)	1.327**	(1.112, 1.583)	1.275**	(1.067, 1.523)	1.241*	(1.038, 1.483)
SVI	1.371**	(1.136, 1.655)	1.413***	(1.169, 1.706)	1.354**	(1.120, 1.638)	1.319**	(1.089, 1.596)
DSI	1.685***	(1.465, 1.938)	1.791***	(1.553, 2.064)	1.675***	(1.451, 1.934)	1.599***	(1.382, 1.849)
Self-rated health								
SHI	1.776***	(1.573, 2.007)	1.741***	(1.541, 1.958)	1.701***	(1.504, 1.925)	1.611***	(1.420, 1.828)
SVI	2.095***	(1.834, 2.395)	2.028***	(1.773, 2.319)	1.983***	(1.732, 2.270)	1.916***	(1.669, 2.199)
DSI	3.221***	(2.908, 3.568)	3.078***	(2.775, 3.414)	2.972***	(2.676, 3.300)	2.722***	(2.445, 3.029)

The results of the logistic regression models were expressed as odds ratios (OR) and 95% confidence intervals (CI). The analytic sample size was 9,293.
Model 1: adjusted for demographic factors including age and gender; Model 2: adjusted for factors in Model 1, as well as social-economic including marital status, educational level and living area; Model 3: adjusted for factors in Model 2, as well as life-style factors including smoking status and alcohol consumption; Model 4: adjusted for factors in Model 3, as well as medical condition including multi-morbidities and insurance covering.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
NSI, No sensory impairment; SVI, Single vision impairment; SHI, Single hearing impairment; DSI, Dual sensory impairment.

significantly associated with LS. Participants with SHI (odds ratio [OR] 1.461, 95% CI 1.185–1.801; $p < 0.001$) or DSI (odds ratio [OR] 1.422, 95% CI 1.224–1.652; $p < 0.001$) were more likely to have lower LS compared with participants without SIs after adjustments. But we failed to find any profound correlation between SVI and LS in any of the 4 models.

5. Discussion

To date, few studies have examined the associations between sensory impairments and subjective wellbeing status among middle-aged and older population. To our knowledge, the present study provides explicit evidences on such associations from a national level survey among Chinese population for the first time, which extends current knowledge regarding this issue.

5.1. Life expectancy

LE has been conceived as a mental model of one's remaining lifetime, and the length of LE is related to physical conditions and mortality in later life (25). On the other hand, people form LE based on the rational expectations of remaining years, which could be possibly influenced by life experiences and perceptions of being (26). Thus, it is essential to investigate affecting factors of LE for prevention of inappropriate estimation of remaining life among aging population. To date, very few studies have mentioned the potential effects of some unmodifiable factors such as demographic characteristics including age and gender (27, 28), while the present study might be one of the very first studies that focused on the impacts of one common, modifiable and age-related physical disorder: sensory impairments, on the subjective life expectancy among middle-aged and older population.

TABLE 3 Longitudinal logistic regression analyses of time-varying sensory impairment statuses and subjective wellbeing measurements, 2011–2018.

Sensory status	Model 1		Model 2		Model 3		Model 4	
Ref: NSI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Life expectancy								
SHI	1.402***	(1.235, 1.592)	1.387***	(1.217, 1.580)	1.201***	(1.201, 1.577)	1.365* * *	(1.188, 1.567)
SVI	1.363***	(1.237, 1.5020	1.358***	(1.227, 1.502)	1.222***	(1.222, 1.512)	1.360***	(1.220, 1.516)
DSI	2.022***	(1.844, 2.217)	1.998***	(1.817, 2.198)	1.799***	(1.799, 2.195)	1.969***	(1.779, 2.179)
Life satisfaction								
SHI	1.462***	(1.196, 1.787)	1.486***	(1.212, 1.823)	1.472***	(1.196, 1.811)	1.461***	(1.185, 1.801)
SVI	1.099	(0.930, 1.297)	1.087	(0.920, 1.284)	1.078	(0.910, 1.277)	1.074	(0.905, 1.274)
DSI	1.476***	(1.277, 1.706)	1.472***	(1.272, 1.704)	1.441***	(1.242, 1.672)	1.422***	(1.224, 1.652)
Self-rated health								
SHI	1.757***	(1.542, 2.002)	1.747***	(1.531, 1.992)	1.724***	(1.508, 1.970)	1.715***	(1.496, 1.965)
SVI	1.265***	(1.265, 1.555)	1.391***	91.253, 1.544)	1.387***	(1.247, 1.542)	1.401***	(1.258, 1.560)
DSL	1.927***	(1.927, 2.321)	2.077***	(1.891, 2.281)	2.035***	(1.849, 2.239)	2.018***	(1.833, 2.223)

The results of the logistic regression models were expressed as odds ratios (OR) and 95% confidence intervals (CI). The analytic sample size was 3,932.
Model 1: adjusted for demographic factors including age and gender; Model 2: adjusted for factors in Model 1, as well as social-economic including marital status, educational level and living area; Model 3: adjusted for factors in Model 2, as well as life-style factors including smoking status and alcohol consumption; Model 4: adjusted for factors in Model 3, as well as medical condition including multi-morbidities and insurance covering.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.
NSI, No sensory impairment; SVI, Single vision impairment; SHI, Single hearing impairment; DSI, Dual sensory impairment.

Although SIs have been commonly considered to have strong associations with physical and mental health statuses in elderly people, which could possibly contribute to jeopardized life expectancy and increased mortality (29, 30), researches on the associations between SIs and LE have yielded mixed results over the past decades. Jagger et al. pointed out that both VI and HI reduced disability-free life expectancy (DFLE) among a sample of English population over 65 years old (31). However, total life expectancy (TLE) was not associated with HI, and VI-TLE associations was not observed in male population from that study (31). Another study based on the Australian Longitudinal Study of Aging (ALSA) and the Blue Mountains Eye Study (BMES) indicated that SIs greatly reduced TLE in Australian people over 65 years old (32). As for Chinese population, according to the present study, for the first time, we revealed that all kinds of SIs were significantly associated with LE in univariate logistic analysis. And after adjustment of multiple confounders in all 4 models, SVI, SHI and DSI were also significantly and independently associated with LE in both cross-sectional and longitudinal analyses. Thus, the present study showed light to the direct associations between SI and LE among Chinese population. We also propose future studies on underlying mechanisms of SI-LE associations and specific interventions.

5.2. Life satisfaction

According to our cross-sectional analyses, all SIs were found to be significantly associated with LS in univariate logistic regression. Such associations remained even after receiving adjustment of various confounders. These findings were consistent to two cross-sectional-designed studies among German people and French-speaking adults in eastern Canada (33, 34). We also noticed another relating study which reported cross-sectional SVI-LS association among very old Chinese population (over 95 years of age) (35). However, when we further tried to verify SIs-LS correlations in the longitudinal analyses, we failed to find any significant result of SVI-LS correlations in any of the 4 models. Our results provide important evidences that HI, especially along with concurrent VI, have significant impacts on LS, which would decline as a consequence of sensory deficits among middle-aged and older population.

Several hypotheses may explain why SI and life satisfaction are consistently associated. First of all, SI is associated with consequently decreased functional abilities (36). The mediating role of functional ability between SIs, especially visual deficit, and life satisfaction has been described in a previous study (35). Another reason that could underlie the link between SIs and life satisfaction might be negative health comparisons. That means individuals with SIs may compare their health status (especially sensory functions) with other individuals who are presumably free of SIs. Appearance of SIs may lead to conclusion of poorer health conditions compared to others. A previous study demonstrated that negative health comparisons could markedly reduce subjective wellbeing (37). Also, senior adults with SIs commonly need assistance from others to deal with daily activities (36, 38). It may seem impossible to repay the person whom they receive assistance from, which could have consequences for social relationships (39–41). People with SIs may perceive their relationships as unidirectional rather than bidirectional, and this feeling on dependency has been demonstrated to be associated with lower autonomy (41, 42).

The present study further indicated more profound longitudinal SHI-LS association than SVI-LS association, which was not consistent to the comparisons of OR values according to logistic regressions. One possible explanation for such situation might lay in the fact that there is less feasibility and probability in amelioration of SHL status than SVL status over time among aging Chinese. Assistive devices such as glasses and portable magnifiers are relatively efficient, economic and easy-to-carry interventions for quite a lot people who suffer reversible SVI (43). On the other hand, interventions like wearing hearing aids for improvement of hearing status would more likely confront financial constraints, unfamiliarity with hearing aids, and difficulties during manipulating, which might all contribute to the fact that application level of hearing aids is far less than expected among Chinese population (44). Besides amplifying desired sounds, hearing aids would amplify noises as well, thus making users feel too loud and noisy. Such muffled effect also jeopardizes peoples' belief in hearing aids (44). Some authors argued that, even when listening aids are used, the promotion of LS might be limited in people with HI (34, 45). Therefore, untreated HI and the subsequent sustaining hearing deficit might exert more explicitly longitudinal effects on LS among our population over time.

5.3. Self-rated health

Self-rated health is one of the various health concepts that have been developed from the definition of health according to the WHO statement in 1948 (46). Although the assessment of SRH is usually summarized into one general question, it has been broadly adapted as an indicator to monitor the health status of individuals (47), and it is often used as a screening tool in epidemiological surveys or for identifying persons at risk of diseases (47, 48).

In the present study, we provide explicit evidences of profound correlations between SIs and SRH, according to both cross-sectional and longitudinal analyses among middle-aged and older Chinese population. Similarly, the Cache County Investigators also reported that, among various health measurements, sensory impairment, including vision and hearing could be regarded as predictors of SRH (49). Longitudinal evidences were also raised from the Second Supplement on Aging (SOA-II) Study among American population (50). On the other hand, Harada et al. reported that self-perceived poor health only showed an association with VI but not with HI in rural Japanese people with older age (51). Astrid et al. also failed to identify SIs as risk factors among a Norwegian population of older people participating in a preventive home visit program, which is partly owing to selection bias and the vague definition of SIs in their study (9).

Factors that might increase the one's perceptions of good health appear to be broadly related to social participation. Studies have also shown that social factors, including social support, household composition, contact with family members and attending educational or training courses, are positively associated with better SRH (52, 53). Preserved hearing and visual functions facilitate social participation, which further improve social functioning and relationships. Old people who see their friends and relatives as often as they like are also more likely to rate their overall health positively (49, 50). On the other hand, SIs, including VI and HI, and more severe condition of DSI, have already been considered to have correlations with various adverse events in aging life, such as multiple chronic medical conditions (54), reduced physical activities (28), increased fall risk (22) and poorer mental health status (21). Each of these events, if sustained for extended periods, could adversely shape health outcomes, and eventually influence personal perception on health status.

Our findings clearly demonstrated the detrimental effects of vision and hearing impairments on SRH, a holistic subjective measure of individual health among middle-aged and older Chinese population. Due to the central role of SRH in age-related challenges and risks, we anticipate that new knowledge of SI-SRH association could facilitate the improvement of health status in aging life.

5.4. Strengths and limitations

CHARLS is a national study with a large sample size, indicating that the findings from the current study could be generalized to the entire country. to our knowledge, the current study is the first nation-wide study based on middle-aged and older Chinese population to verify the associations between SIs and subjective wellbeing status according to both cross-sectional study and longitudinal observation over 8 years. Results in our study could be used as a reference to promote living status among aging population in China. Lastly, multiple associated factors were included and adjusted in analyses, which could otherwise potentially confound the relationship between SIs and outcomes.

Meanwhile, we acknowledge some limitations. First, self-reports provide information about subjective perception, and therefore, are clinically highly relevant and suitable for studies on subjective wellbeing status like ours. Although this method has also been used in quite a few well-known population-based studies such as NHANES and NHIS, we still need to notice the potential bias owing to the nature of self-reported data. On the other hand, exclusion criteria of the present study might lead to selection bias. Second, although we tried best to adjust for as many covariates as possible, still other covariates that may affect subjective perceptions of wellbeing might not have been included in the present study. Future researches may consider more robust study designs such as randomized controlled trials for more reliable results.

6. Conclusion

In summary, the present study provides explicit evidences that sensory impairments including vision impairment, hearing impairment and dual sensory impairment are negatively associated with life expectancy, life satisfaction and self-rated health among middle-aged and older Chinese population.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: The original dataset of CHARLS is accessible on http://charls.pku.edu.cn/.

Ethics statement

The studies involving human participants were reviewed and approved by Institutional Review Board at Peking University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

QP and JL designed the research. KA, XQ, and YeL analyzed the data. YZ drafted the manuscript. YanL, MX, and YH revised the manuscript. YZ, YanL, and YeL contributed equally to this research and should be considered as equivalent authors. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1099754/full#supplementary-material

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The impact of grandchild care on depressive symptoms of grandparents in China: The mediating effects of generational support from children

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Objectives: Despite extensive studies about the direct effect of grandchild care on caregiver depression in China, understanding of its internal influencing mechanism has been limited. After controlling for socioeconomic factors, this study investigated whether the experience of caring for grandchildren had a long-term impact on the depression levels of grandparents, either directly or indirectly through generational support from adult children.

Methods: The subjects of this study were a total of 9,219 adults over 45 who participated in the China Health and Retirement Longitudinal Surveys in 2015 and 2018. We adopted a lag-behind variable to examine the impact of grandchild care on depressive symptoms of grandparents. The proposed mediation model was analyzed using bootstrap modeling, and the KHB method was conducted further to examine differences in the effects of generational support.

Results: The experience of caring for grandchildren had a significant negative correlation with the depression level of Chinese grandparents. Moreover, children's support significantly mediated the impact of parenting experience on grandparents' depression. Significantly, instrumental support mediated the effect to the greatest extent, while emotional support from children contributed the least. The intermediary effect has urban–rural heterogeneity.

Conclusion: These findings indicated that grandchild care significantly inhibited the depression level of Chinese grandparents through increased intergenerational support from adult children. The implications of the study's findings were discussed.

KEYWORDS

grandchild care, depression, financial support, emotional support, instrumental support

1. Introduction

Grandchild care is relatively widespread in China. Approximately 50% of middle-aged and elderly couples care for their grandchildren as families or individuals (1). With increasing life expectancy, more Chinese older adults can take care of their grandchildren (2), sharing time pressure and living costs with adult children's families (3). Chinese grandparents play an increasingly important role in caring for their grandchildren.

However, care activities could be associated with grandparents' mental health. Some studies found that grandchild care could limit grandparents' time and opportunities to care for themselves and bring physical burden and emotional pressure (4), while other studies

came to a different conclusion that grandparenting may help the elderly gain respect from family members and derive emotional wellbeing through generational interaction (5, 6). In addition, empirical research results presented transnational differences and the influence of specific cultural contexts on caregivers' mental health. Due to young couples' poverty, AIDS, imprisonment, unmarried pregnancy, unemployment, and illegal drug use, grandparents in the U.S. especially African American grandparents may suffer from being forced to care for their grandchildren (7, 8). However, Chinese grandparents generally do not regard care as a burden (9). Responsibility ethics with Chinese characteristics and intergenerational reciprocity can alleviate grand-parenting pressure (10, 11). For Chinese grandparents, care is a family obligation conducive to intergenerational relations and family unity (12).

Among the elderly in China, ∼ 30% of men and 43% of women suffer from depression (13). The existing epidemiological literature shows that depression can reduce physical function, daily living ability, and cognitive ability (14); it is also the most critical factor leading to suicide in the elderly (15). In the context of healthy aging, it is necessary to explore the influencing mechanism of depression outcomes to help grandparents avoid health risks. Researchers have argued that social support plays an important role in improving the mental health of older people (16). Characterized as the care and support that members of society receive from others, social support includes formal support (e.g., government, institutions) and informal support (e.g., family, friends) (17, 18), the latter of which is likely to be affected by grandchild care (19).

Previous research has indicated the protective effects of informal social support in the relationship between caregiving and depression (20, 21), while investigating the mediating effects of different functional aspects of children's support is still lacking, which is particularly important in Chinese traditions of filial piety (22). In fact, receiving financial support from adult children in the form of rewards is associated with a reduction in the psychological stress of raising grandchildren (23). Thus, the present study aimed to explore the effects of caring for grandchildren on the depressive symptoms of Chinese grandparents, as well as the intermediary mechanism of adult children's support. Such efforts can present practical and policy suggestions to manage depression in elderly individuals.

1.1. Grandchild care and depressive symptoms

Caring for grandchildren can have positive or negative effects on older adults' depression (24). This controversy may be based on two different points: Role Accumulation Theory and Role Tension Theory. Role Accumulation Theory holds that multiple social roles can enable individuals to achieve social integration and self-satisfaction in different areas of social participation, eventually benefiting mental health (25, 26). With aging, retirement and the reduction of the degree of social integration, it may be more necessary to strengthen the social role than ever before (27). Caring for grandchildren enables grandparents to assume more social roles, which not only meets their intergenerational emotional needs (28) but also promotes their social integration (29) and can bring higher life satisfaction and self-efficacy (30). On the other hand, Role Tension Theory suggests that individuals may face different types of role conflicts when required to perform specific obligations (31). When such role strain exceeds the individual's physical and mental abilities, it causes role pressure, which is harmful to health (32). Providing grandchild care may limit grandparents' time and opportunities to care for themselves (33), maintain personal social activities (34) and assume the role of marriage (8), making them more vulnerable to emotional stress.

1.2. Generational support from children as a potential mediator

Social Exchange Theory provides a theoretical possibility for exploring the intermediary role of children's support. According to Social Exchange Theory and Equity Theory, individuals seek equal exchange relationships in interpersonal communication, and unequal exchange may adversely affect mental health (35, 36). It is also applicable in the family field in China.

Grandparenting could strengthen intergenerational relationships and bring rewards from adult children (37). First, based on the principle of reciprocity in intergenerational exchange, providing care for grandchildren reinforces adult children's willingness to return. Second, as a form of social participation, parenting grandchildren makes it more likely for grandparents to receive adult children's support by increasing the intensity and frequency of intergenerational contact (38). Third, sharing the labor cost of parenting also strengthens adult children' capacity to reciprocate in remittances (39). The data of Class2012 confirmed that helping to care for grandchildren can significantly increase the amount of financial support and the frequency of adult children's housework and visits (40).

Financial, emotional and instrumental support have been partially verified as protective factors against depression (41). Due to the acceleration of population migration and the inadequacy of the elderly pension and medical security system, the primary source of livelihood for elderly parents, especially in rural areas of China, comes from their children (42). Additionally, money remittance reflects the return of contribution to adult children, and as a psychological reward, it helps to protect the self-esteem and self-efficacy of the elderly (43).

Chinese adult children are mainly responsible for providing emotional support for the elderly as well (44). Data from China and South Korea support that for parents who do not live together, face-to-face contact and online contact can protect the depression level of elderly parents (45, 46). It also confirms the effectiveness of online contact as a form of emotional contact to protect mental health, especially in the context of China's rapid and extensive urbanization.

Some studies have not verified the mediating effect of instrumental support (19). However, elderly individuals with physical limitations were excluded. Those without physical limitations may experience a sense of incompetence when they are offered instrumental support (47). This may cause sample selection error, and we tried to keep samples with physical limitations.

However, grandparents who receive instrumental support from their adult children are associated with poorer physical health and are therefore more likely to provide lower intensity grandchild care than those who are healthier. Considering that those respondents might gain more health benefits with less intensive grandchild care (24), we controlled for respondents' self-rated health status to lessen endogenetic problems.

1.3. Differences between urban and rural areas

The literature has mainly discussed the psychological impacts of a reciprocal pattern of behavior. Intergenerational time-for-money exchanges (39) or financial exchange (48) could reduce the depressive symptoms of older grandparents. However, the lack of view of grandparents' support and offspring's feedback as separate but related behaviors hinders further understanding of older grandparents' psychological expectations of generational relationships. We assumed that the result of social transformation brought about by modernization had changed the expectations of the elderly on generational relations. Therefore, the intermediary effect of generational support has urban–rural heterogeneity. Urban areas are characterized by a higher degree of modernization and economic wealth but a stronger emotional connection (49). Moreover, the proportion of urban elderly receiving pension is higher than that of rural elderly (22). Thus, compared with urban residents who are more financially independent, the economic support of adult children of rural residents is a stronger predictor of higher life satisfaction and happiness (41, 50), while emotional support can reduce the risk of depression in urban residents (49). We investigated how parents' expectations of children's support in return would influence whether the mental benefits of grandchild care functioned. This paper adopted a "space for time" analysis strategy, that is, through a comparative study between urban and rural areas, to describe the changes in family support relations in the process of changing from traditional society to modern society (51).

1.4. The present study

This study contributes to the literature in three ways. First, we used longitudinal and large-scale national data from China to study the impact of caring for grandchildren on Chinese grandparents' depression and therefore alleviated the deviation caused by the endogeneity of reverse causality to some extent, expanding previous studies that focused on cross-sectional (38) or specific region observation windows (19). Second, we discussed the mechanism of adult children's support in the relationship between grandchild care and caregivers' depression. Previous studies have researched the mediating effect of social participation outside the family (52), as well as the psychological effects of grandparenting, child support, and intergenerational reciprocity patterns (41, 48), and have not adequately explained the context of the relationship between caring for grandchildren and grandparents' depressive symptoms within the family field. In particular, different types of generational support rather than a specific type were incorporated into the mediating model for a more detailed explanation. Finally, by investigating how the mediating effect of children's support changes in different areas of residence, we further explored older people's psychological expectations of intergenerational relationships and the potential realization path of the mental impact of intergenerational exchange. Based on the current evidence, we expect that the depression level of grandparents 2 years later with grandchild care experience will be significantly lower than that of non-caregivers (Hypothesis 1). Additionally, caring for grandchildren will be associated with the level of depression of grandparents 2 years later, directly or indirectly, through changes in economic, emotional and instrumental support from their adult children (Hypothesis 2). Finally, among the three types of generational support, financial support contributes most in rural areas, while emotional support contributes most in urban areas (Hypothesis 3).

2. Methods

2.1. Data and sample

The data came from the two China Health and Retirement Longitudinal Surveys (CHARLS) hosted by the National Development Research Institute of Peking University. CHARLS adopted probability proportional to size sampling to collect a nationally representative sample of Chinese residents aged 45 and above. CHARLS's follow-up survey covered 450 villages in 150 counties and districts across China. We obtained national tracking survey data in 2015 and 2018 from the official website (http://CHARLS.pseeku.edu.cn). Our analysis was limited to respondents above 45 in 2015 ($n = 20{,}085$)[1] who reported having at least one grandchild under 16 at baseline ($n = 13{,}949$), provided complete answers to the independent variable ($n = 13{,}882$), demographics and family characteristics ($n = 13{,}585$), health status ($n = 12{,}970$), children's support ($n = 12{,}806$), household per capita expenditure ($n = 11{,}073$), follow-ups ($n = 9{,}944$) and at least 8 indicators (53) in the depression level measurement in 2018 ($n = 9{,}219$).[2]

2.2. Measures

2.2.1. Depression

The dependent variable was the level of depression in 2018. According to the epidemiology research center Depression Scale (CESD), respondents were asked to assess their psychological and emotional states within a week. The scale included ten subitems. The 4-point responses were rescaled from little or no (0) to most of the time (3). The total score was between 0 and 30. The higher the score, the more serious the depression. In this study, Cronbach's α was 0.80.

1 We limited the sample to people above 45. Due to the intergenerational difference in the age of first marriage, there are sufficiently young grandparents. We believe that the age limit of 45 maximizes the sample utilization rate as much as possible.

2 Due to missing values in weight variables, the final sample size of descriptive analysis was 9134.

2.2.2. Grandchild care

The independent variable was grandchild care, measured by asking the respondent "Did you spend any time taking care of your grandchildren last year" in the 2015 baseline data. If the respondent answered "Yes", the variable was assigned 1. If the answer was "No", the variable was assigned 0. The answer to this question distinguished between "caregivers" and "non-caregivers".

2.2.3. Generational support from children

Support from children includes financial, emotional, and instrumental support (50, 54, 55) respondents received in the last 12 months. Financial support was measured by the total amount of money and in-kind support respondents received from their children in the past year. We took the logarithm to realize the normal distribution. Because there are no direct measures of emotional intimacy with children in the CHARLS questionnaires, seeing children is considered a form of emotional support (22). In addition, considering the importance of telephone, SMS, and other network contact methods in daily life, we also viewed online contact as an important part of emotional support. Therefore, emotional support was measured by the frequency of respondents' offline meeting and online contact with their children in the past year, and the maximum of the two was taken as emotional support. The 9-point responses were rescaled from almost never (0) to almost every day (8), and the contact frequencies of all children were summed. It should be added that since CHARLS 2015 did not ask these questions to respondents living with their children, the emotional support of these samples was assigned the maximum value of 8. Instrumental support was measured by whether respondents would get help from their children if they needed help with basic daily activities such as eating or dressing at the time of the interview or in the future (56). The answer was a binary variable.

2.2.4. Control variables

The control variables at baseline included gender (female = 0); location (rural = 0); education level (illiterate = 0; primary school and below = 1; secondary school graduation = 2; high school graduation = 3; university and above = 4); marital status (married people living together or in different places due to different jobs were assigned as 0; separation, divorce, widowhood, never married = 1); self-rated health status (poor = 0; general = 1; good = 2); age; whether to live with children (not with children = 0); number of grandchildren under the age of 16; number of surviving children; and household per capita expenditure (logarithmic conversion).

2.3. Data analysis

In this study, the Ordinary Least Squares (OLS) model was used to determine whether there was a significant correlation between caring for grandchildren and respondents' depressive symptoms 2 years later. To avoid the endogenous problem caused by mutual cause and effect, the result that the dependent variable lagged behind one period was adopted (57, 58). To study the mediation effects of children's support, we used the bootstrap method to test the direct and indirect effects of generational support from children at baseline, which also reduced potential endogeneity. Since this paper tested several intermediary variables, to explore which intermediary variable contributes the most to the indirect effect, we used the KHB[3] method (59). Moreover, we performed a robust analysis of the mediating effect grouped according to residence. To take into account the complex sample designs, descriptive statistics used the appropriate design weights provided by the CHARLS teams. Since CHARLS data collected after 2013 only offer cross-sectional weight, weight cannot be used in regression analysis in this study. The outcomes are still acceptable, because there is literature indicating that model analysis is less susceptible to weighting whereas descriptive statistical analysis is more sensitive (60). All statistical analyses were performed with Stata 17.

3. Results

3.1. Descriptive statistics

The total depression score of Chinese grandparents with grandchildren over 45 years old was 8.513, which is close to mild depression according to the standard (61). Table 1 describes the weighted data and shows that there is a significant correlation between grandchild care and respondents' depressive symptoms 2 years later. In the sample, 58.3% of people (or spouses) provided grandchild care. In demographic and social characteristics, 49% of the samples were male, 68.2% lived in rural areas, more than 90% were married or cohabiting, and the average model education level was primary school or above. The respondents' self-rated health was close to the general level, with a mean age of 60. From family information, 36.5% of respondents lived with their children, and the average number of children and grandchildren was more than 2.

3.2. Regression analysis

Table 2 shows the linear regression results of the impact. Model 1 included all control variables and showed that grandchild care reduced grandparents' depression. H1 was verified. Additionally, rural women with a low level of education, poor health, single status at a young age, and having a larger number of grandchildren or children were associated with higher depression levels.

Next, according to the stepwise regression model, the provision of grandchild care positively impacted generational support (Model 2, Model 4, and Model 6). The impact factors of grandchild care decreased after adding generational support from adult children (Model 3, Model 5, and Model 7), which preliminarily showed that generational support could have a mediating effect.

3 KHB model is a model that calculates the total effect, direct effect and indirect effect by Logit or Probit method. This model was created and developed by Karlson, Holm and Breen. Its main idea is that the total effect can be decomposed into direct effect and indirect effect by direct comparison of coefficients in the linear model.

TABLE 1 Descriptive statistics (with weights) and correlation coefficient matrix.

Variables	Mean	SD	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Depression	8.513	0.179	1														
2. Grandchild care	0.583	0.010	−0.054***	1													
3. Gender	0.490	0.004	−0.185***	−0.009	1												
4. Location	0.318	0.027	−0.106***	0.059***	0.004	1											
5. Education	1.284	0.039	−0.205***	0.066***	0.309***	0.252***	1										
6. Marry	0.096	0.005	0.087***	−0.089***	−0.094***	0.0120	−0.106***	1									
7. Health	0.995	0.015	−0.302***	0.035***	0.094***	0.067***	0.119***	−0.045***	1								
8. Age	60.68	0.197	0.005	−0.156***	0.090***	0.025**	−0.155***	0.226***	−0.084***	1							
9. Co-residence	0.365	0.014	−0.002	0.124***	−0.010	0.039***	−0.003	0.021**	0.004	−0.126***	1						
10. Grandchildren	2.490	0.085	0.084***	0.067***	0.008	−0.158***	−0.149***	−0.005	−0.062***	0.153***	−0.006	1					
11. Children	2.686	0.057	0.104***	−0.171***	−0.019*	−0.155***	−0.201***	0.125***	−0.095***	0.419***	−0.007	0.486***	1				
12. Expenditure	8.947	0.042	−0.051***	0.042***	0.019*	0.191***	0.178***	−0.032***	0.038***	−0.078***	−0.333***	−0.097***	−0.109***	1			
13. Financial support	6.743	0.095	−0.008	0.028***	−0.020*	−0.056***	−0.057***	0.017	−0.019*	0.126***	−0.063***	0.123***	0.214***	0.050***	1		
14. Emotional support	18.42	0.354	0.032***	−0.038***	−0.023**	−0.069***	−0.119***	0.058***	−0.021**	0.227***	0.358***	0.360***	0.692***	−0.175***	0.164***	1	
15. Instrumental support	0.610	0.012	−0.096***	0.059***	−0.022**	−0.044***	−0.024**	0.0160	0.100***	−0.006	0.091***	0.038***	0.026**	0.004	0.063***	0.117***	1

***$p < 0.01$, **$p < 0.05$, *$p < 0.1$.

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TABLE 2 Regression analysis.

Variables	Model 1 Depression Coef (SE)	Model 2 Financial support Coef (SE)	Model 3 Depression Coef (SE)	Model 4 Emotional support Coef (SE)	Model 5 Depression Coef (SE)	Model 6 Instrumental support Coef (SE)	Model 7 Depression Coef (SE)
Gender	−1.482*** (−10.91)	−0.137** (−1.98)	−1.491*** (−10.98)	−0.291** (−2.31)	−1.495*** (−11.01)	−0.025** (−2.34)	−1.509*** (−11.15)
Location	−0.648*** (−4.06)	−0.275*** (−3.39)	−0.666*** (−4.17)	0.460*** (3.10)	−0.628*** (−3.93)	−0.067*** (−5.33)	−0.720*** (−4.52)
Education	−0.800*** (−10.50)	−0.035 (−0.90)	−0.802*** (−10.53)	0.131* (1.86)	−0.794*** (−10.43)	−0.008 (−1.24)	−0.808*** (−10.64)
Marry	1.377*** (6.14)	−0.143 (−1.26)	1.367*** (6.10)	−0.962*** (−4.62)	1.334*** (5.94)	0.028 (1.58)	1.407*** (6.29)
Health	−2.539*** (−27.51)	0.027 (0.57)	−2.537*** (−27.50)	0.536*** (6.26)	−2.515*** (−27.21)	0.077*** (10.50)	−2.457*** (−26.56)
Age	−0.057*** (−6.18)	0.023*** (4.89)	−0.055*** (−6.01)	−0.008 (−0.93)	−0.057*** (−6.22)	0.001 (1.20)	−0.056*** (−6.10)
Co−residence	−0.105 (−0.73)	−0.265*** (−3.63)	−0.122 (−0.85)	6.850*** (51.41)	0.201 (1.23)	0.106*** (9.35)	0.009 (0.06)
Grandchildren	0.122*** (3.05)	0.021 (1.05)	0.123*** (3.08)	0.153*** (4.15)	0.128*** (3.22)	0.006** (1.98)	0.128*** (3.23)
Children	0.233*** (3.70)	0.488*** (15.27)	0.265*** (4.16)	4.913*** (84.15)	0.453*** (5.41)	0.008 (1.52)	0.241*** (3.85)
Expenditure	−0.034 (−0.51)	0.209*** (6.28)	−0.020 (−0.30)	0.142** (2.34)	−0.027 (−0.42)	0.024*** (4.71)	−0.007 (−0.11)
Grandchild care	−0.442*** (−3.31)	0.487*** (7.19)	−0.410*** (−3.06)	0.467*** (3.77)	−0.421*** (−3.15)	0.051*** (4.85)	−0.387*** (−2.90)
Financial support			−0.066*** (−3.21)				
Emotional support					−0.045*** (−3.98)		
Instrumental support							−1.068*** (−8.15)
Constant	15.970*** (19.02)	2.142*** (5.02)	16.111*** (19.17)	0.667 (0.86)	16.000*** (19.07)	0.202*** (3.03)	16.185*** (19.34)
Observations	9,219	9,219	9,219	9,219	9,219	9,219	9,219
R^2	0.145	0.062	0.146	0.615	0.146	0.029	0.151
F	141.96***	55.76***	131.11***	1336.95***	131.65***	25.09***	136.58***

***$p < 0.01$, **$p < 0.05$, *$p < 0.1$.

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TABLE 3 Intermediary effect analysis.

Mediator effect	β (95%CI)	SE	Z	*P*
Financial support				
Indirect effect	−0.032*** (−0.055, −0.014)	0.011	−2.98	0.003
Direct effect	−0.410*** (−0.692, −0.146)	0.136	−3.00	0.003
Emotional support				
Indirect effect	−0.021*** (−0.039, −0.008)	0.008	−2.67	0.008
Direct effect	−0.421*** (−0.663, −0.146)	0.130	−3.23	0.001
Instrumental support				
Indirect effect	−0.055*** (−0.086, −0.032)	0.014	−3.97	0.000
Direct effect	−0.387*** (−0.652, −0.118)	0.139	−2.79	0.005

Control variables: Gender, Location, Education, Marital status, Health, Age, Whether parents live with their children, Number of grandchildren, Number of children, Household per capita consumption expenditure.
*$p < 0.1$, **$p < 0.05$, ***$p < 0.01$.

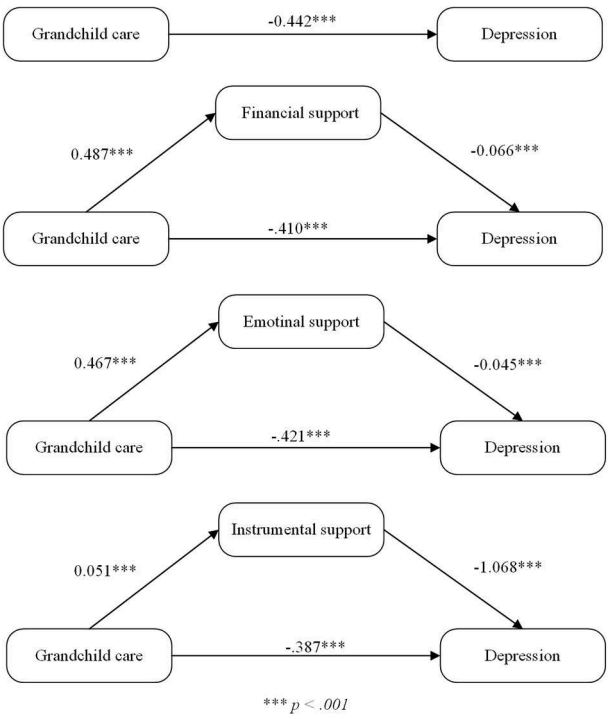

FIGURE 1
The influence of generational support from children on depression.

3.3. Mediating effect test

This study used the bootstrap method to repeatedly sample 1,000 times to test the mediating effect of adult children's economic, emotional, and instrumental support. It can be seen from Table 3 that the confidence intervals for the indirect effects of children's support all did not include 0, and there were intermediary effects.

Figure 1 illustrates the impact path. When the control variable was included in the model, the negative predictive effect of grandchild care on depressive symptoms was significant ($\beta = -0.442$, $p < 0.001$). When economic, emotional and instrumental support from adult children was included in the model as an intermediary variable, grandchild care still had a significant negative predictive effect on depression ($\beta = -0.410$, $p < 0.001$; $\beta = -0.421$, $p < 0.001$; $\beta = -0.387$, $p < 0.001$). Meanwhile, grandchild care had a significant positive effect on adult children's support ($\beta = 0.487$, $p < 0.001$; $\beta = 0.467$, $p < 0.001$; $\beta = 0.051$, $p < 0.001$), and the latter was associated with lower risk of depressive symptoms ($\beta = -0.066$, $p < 0.001$; $\beta = -0.045$, $p < 0.001$; $\beta = -1.068$, $p < 0.001$). H2 was verified.

TABLE 4 A comparative analysis of mediation effect based on the KHB method.

Mediating variable	*β*	SE	*P*-diff	*P*-reduced
Financial support	−0.026	0.011	27.53	5.84
Emotional support	−0.016	0.007	17.21	3.65
Instrumental support	−0.052	0.013	55.25	11.73

3.4. Comparison of intermediary effects

According to Table 4, generational support mediated 9.38% of the impact. Among them, instrumental support contributed 55.25% to the indirect effect, which was the largest; economic support contributed 27.53%; and emotional support contributed 17.21%.

The results of grouping regression of urban and rural samples are shown briefly as follows, and the omitted analysis procedure is described in the Supplementary material. Generational support mediated 6.98% in rural samples ($n = 7{,}053$). Instrumental support contributed 77.07% to the indirect effect, and emotional support contributed 22.93%. The bootstrap model indicated that economic aid was not a mediator. In urban samples ($n = 2{,}166$), generational support mediated 14.56 percent of grandchild care's depression effect. Instrumental support contributed 32.46 percent; financial support contributed 67.54 percent. Emotional support did not mediate this relationship. H3 was not verified.

4. Discussion

This paper suggested that the experience of caring for grandchildren significantly inhibited grandparents' depression using a nationally representative sample. We further tested whether caring for grandchildren weakened the depression level of the grandparents by increasing their adult children's support. Moreover, the data analysis showed that instrumental support mediated the impact to the greatest extent, followed by financial and emotional support. Considering potential differences in the expectations of intergenerational relationships between urban and rural elderly people, this study further compared the intermediary effects of children's support based on residence.

First, caring for grandchildren had a significant negative correlation with the depression level of Chinese grandparents. The results of this study supported the Role Accumulation Theory that caregivers feel they are valuable and experience positive care feelings in intergenerational interaction. It also provided a robust example for discussing the impact of raising grandchildren on caregivers in the Chinese context. In Confucian filial piety culture, grandparents regard caring for grandchildren as a productive role. Similar results have been found in studies of older Chinese Americans and Taiwanese adults under cultural norms that regard care as an obligation; grandparents can give more favorable meaning to the activity of caring for grandchildren and are more willing to care for grandchildren (62, 63). In addition, the role of such cultural norms has also been verified in European countries. In a social and cultural environment where grandparents are expected to provide care, grandparents who do not care for their grandchildren may have negative emotions and experience low life satisfaction (64) and subjective wellbeing (65).

Second, raising grandchildren had a significant positive effect on the economic support, emotional support, and instrumental support from adult children, while the increase in generational support was associated with lower depression levels of grandparents. The research results are consistent with the previous cross-sectional data analysis results (38). On the one hand, the experience of raising grandchildren has a direct protective effect on Chinese grandparents' mental health. The mainstream view is that, out of responsibility and obligation, Chinese parents will raise their offspring (including grandchildren) without any condition (66). On the other hand, the experience of grandchild care can also positively impact the psychological status of grandparents by increasing support from their adult children. Caring for grandchildren can significantly improve the frequency and opportunities for Chinese grandparents to obtain financial support, visit and help with housework (40, 67). In this case, intergenerational resource exchange constitutes a reciprocal state from which the elderly can feel satisfied and happy (68). It can be said that Social Exchange Theory and intergenerational reciprocity are essential mechanisms to explain the mental benefit of grandchild care. It further shows that Social Exchange Theory and the principle of reciprocity also apply to modern Chinese families affected by Confucian culture. As Yan Yunxiang, an anthropologist, observed in the last century, Chinese society, impacted by the new morality prevailing in the market economy, has more intergenerational relations transforming into rational and balanced exchange relations than being unconditionally given by any party (69). It should be noted that this does not mean that grandparents care for grandchildren for the purpose of obtaining adult children's resources. However, the timely feedback of children on care activities, undoubtedly plays an essential role in protecting the mental health of Chinese elderly people to a large extent.

Third, instrumental support mediated the impact of caring for grandchildren on grandparents' depression to the greatest extent, while emotional support from adult children contributed the least. The data from CHARLS2011 and 2013 also support similar results that only the exchange of instrumental support between generations can significantly improve the life satisfaction of grandparents in urban and rural China (22). We also speculated that instrumental support required children to devote higher time and energy costs when compared with offline visits, online contacts, or remittances; thus, it represented a closer intergenerational bond. In addition, a literature review on social support and depression levels also shows that only a small number of research results confirm that children's emotional support is related to the prevention of depression (70). This may be because the primary source of emotional support for the elderly is their spouse, followed by their friends, and finally, their children (70). It should also be noted that, under the current background of large-scale population mobility in China, it is more difficult for elderly parents to have face-to-face contact with their children (45), which may further weaken the emotional dependence of elderly parents on their children. In other words, we can speculate that under the background of modernity, China's intergenerational relations, on the one hand, maintain a certain degree of emotional intimacy and, on the other hand, gradually have the characteristics of rationality and independence.

Finally, urban areas were more inclined to show "time-money" exchange between generations, while rural samples were more inclined to "time–time" exchange of the same type, which was different from what we assumed. The differences between urban and rural areas reflect the transformation in the expectations of the elderly for intergenerational relations in the process of changing from traditional society to modern society. Specifically, the urban elderly put more emphasis on rational logic, while the rural elderly put more emphasis on emotional sense. On the one hand, as the old-age security and social support system in rural areas is more imperfect, elderly people must rely more on their children for daily care in old age (71). On the other hand, caring for grandchild may not raise expectations for monetary compensation because such care usually occurs in three generations of families without financial separation, and people share and coordinate their labor (72). For urban areas, the concept of filial piety has lost its cultural and social foundation, and the popular new morality in the market economy makes the relationship between the two generations more rational and balanced (69).

In conclusion, there are still the following limitations. First, although the inclusion of dependent variables with a lag of one period could alleviate the resulting bias caused by the endogeneity related to reverse causality to a certain extent, we could not confirm whether there were other missing variables in the data that affect the model. Therefore, the results of this study should not be interpreted as a strict causal relationship but only a causal inference under the social science paradigm. Second, in addition to children's support, there might be other relevant factors, such as feelings of care (73), participation in social activities (29), stress, and sleep quality (74), that regulate the relationship between care experience and caregivers. As a result, the data analysis results only reflected the partial impact of care experience. Third, future studies should use more detailed measurements of instrumental support, such as frequency and intensity, and dependent variables, such as care intensities, where data permit. Although we have tried to avoid the selection bias associated with deleting samples with physical limitations occurring in previous literature, there could still be some endogenetic problems. For example, grandparents who received instrumental support provided less intensive care, which resulted in more health benefits for them than those who did not. Fourth, this paper set the intermediary variable as generational

support in the baseline data, while generational support in the 2018 data corresponded to a delayed intergenerational reciprocity model. However, Chinese parents' upbringing and adult children's support are not only a kind of immediate feedback model (66). We can try to understand and compare whether there are differences in the impact of immediate and delayed generational support on grandparents' mental health. Fifth, this paper adopted a "space for time" analysis strategy rather than tracking data to explore the influence of modernity on expectations of generational relationships. However, the differences between urban and rural areas also affect the patterns of the family division of labor and the social security system. Therefore, there may be more detailed interpretation work to be done for the conclusions found in this paper. Despite these limitations, our findings still have theoretical and practical significance. Our study supported Role Accumulation Theory and emphasized the protective effect of social integration in the family domain on the mental health of elderly individuals. Specifically, by increasing their adult children's economic support, emotional support and instrumental support, caring for grandchildren achieved intergenerational reciprocity and therefore helped grandparents weaken their negative psychological feelings. Additionally, urban areas were more inclined to "time-money" exchange, while rural samples were more inclined to "time–time" exchange. It may show a trend of rational and independent intergenerational relations in China. With the further deepening of China's aging and the continuous advancement of the active aging process, we can actively advocate for elderly individuals to participate in family care and household activities. Meanwhile, for the elderly who take care of their grandchildren, adult children should pay attention to financial support for grandparents living in urban areas and instrumental support for them in rural areas to protect their psychological state to the greatest extent. Additionally, there is a need for deeper and more comprehensive state pension coverage as well as for affordable, high-quality healthcare, particularly in rural areas where the daily care of the elderly is still largely a family responsibility and grandparents may be compelled to look after their grandchildren in order to guarantee their future care from adult children.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: http://charls.pku.edu.cn.

Ethics statement

The CHARLS was approved by the Institutional Review Board at Peking University. Ethics Approval No. IRB00001052-11015. All participants provided informed consent.

Author contributions

WX and YH designed the study. YH contributed to the collection of literature, data processing, and result analysis and drafted the manuscript. LZ contributed to the data processing, result analysis and review, of the manuscript. All authors approved the current version of this manuscript for publication. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1043969/full#supplementary-material

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Impact of socioeconomic position on the utilization of rehabilitation services among the Chinese older adults disabled by injury

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Aim: This study aimed to explore the utilization of rehabilitation services and associated socioeconomic position (SEP) factors among Chinese older adults disabled by injury.

Methods: Data from the second China National Sample Survey on Disability (CSSD) were used in this study. Chi-square test was used to analyze the significant differences between groups, and binary logistic regression model was used to calculate the odds ratios and 95% confidence intervals for socioeconomic factors associated with utilization of rehabilitation services among Chinese older adults disabled by injury.

Results: Among the older adults disabled by injury in the CSSD, the gap between demand and utilization of medical treatment, assistive devices and rehabilitation training were around 38, 75, and 64%, respectively. This study revealed two relationship patterns ("high-low-high" and "low-high-low") among SEP, prevalence of injury-caused disability and odds of utilization of rehabilitation services among the Chinese older adults disabled by injury, that is, the older adult with higher SEP have a lower prevalence of injury-caused disability, but a higher odds of utilization of rehabilitation services; conversely, the older adults with lower SEP have a relatively higher prevalence but a lower odds of utilization of rehabilitation services.

Conclusion: There is a large gap between the high demand and low utilization of rehabilitation services among the Chinese older adults disabled by injury, especially for those living in the central or western regions or rural areas, without insurance or disability certificate, having the annual household per capita income lower than the national average or lower educational level. Strategies to improve the disability manage system, to strengthen the chain of "information discovery-information transmission-rehabilitation services supply-continuous health monitoring and management" for the older adults disabled by injury are warranted. In view of the poor and illiterate groups among the disabled older adults, to enhance medical aids and popularize the scientific information to compensate for the lack of affordability and awareness of rehabilitation services utilization is essential. In addition, it is necessary to further expand the coverage and improve the payment system of medical insurance for rehabilitation services.

KEYWORDS

aging, disability, rehabilitation service, socioeconomic position, injury

Introduction

Injury has become the main cause of death and disability in most countries (1), accounting for 8% of the global causes of death (2). Temporary or permanent disability by injury contributes to an even greater disease burden (3). In China, injury has exceeded infectious diseases and ranked the second cause of the disease burden. Every year, there are 700,000–800,000 deaths and 62 million emergency visits due to injury (4). With the growth of population life expectancy in China, the percentage of life expectancy with disability is also continuously expanding, and is expected to increase from 9.60% in 2015 to 14.54% in 2050 (5). The problem of "disability expansion" is more severe among the older adults in China, which is estimated to experience 5.78 years lived with disability in 2015, and this number is expected to increase to 11.45 in 2050 (5). The years lived with disability (YLD) caused by injury among the older adults over 70 years old has increased year by year since 2005 (6).

Rehabilitation service needs are universal, a conclusion confirmed by a study based on the Global Burden of Disease (GBD) 2019, which estimates that in 2019, 2.41 billion individuals had conditions that would benefit from rehabilitation, that is, at least one in every three people in the world needs rehabilitation at some point in the course of their illness or injury (7). However, the utilization of rehabilitation services is disproportionately insufficient (8, 9). As for the injury-caused disabled, a Chinese study revealed the challenge of significant under-utilization of rehabilitation services (10).

Based on this, some studies have explored more possible strategies to remove the barriers to the utilization of rehabilitation services for the disabled from the perspective of the socioeconomic position (SEP). And yet, to the best of our knowledge, there may be few studies on rehabilitation services and associated SEP factors for the Chinese older adults disabled by injury. Taken all these into consideration, this article analyzes the utilization of rehabilitation services and related SEP factors for the Chinese older adults with injury-caused disability. In this way, it aims to supplement the research in this field and provide empirical data in making rehabilitation policies for the older adults disabled by injury in China.

Methods

Data source

In this study, the Second National Sampling Survey on Disability in China in 2006 (CSSD) database was used to extract samples of the older adults aged 60 and above who were disabled by injury. It adopts the stratified, multi-stage and cluster probability proportional sampling method. It covers a total of 2,526,145 people from 771,797 households in 31 provinces, autonomous regions, and cities, with a sampling ratio of 1.93‰. The survey data is authentic (11).

Core concepts

Disability

Disability refers to the abnormality or the loss of anatomical structure and physiological function caused by various physical and mental diseases, or injuries, or congenital abnormalities, which results in long-term, continuous or permanent dysfunction of the body that cannot be cured (12).

Injury

Injury is defined as tissue damage or hypoxia by asphyxia that affect individual activities and need treatment or rehabilitation, resulting from energy transfer or interference exceeding the limits of biological endurance (13).

Injury-caused disability

Injury-caused disability is defined as a person who completely or partially loses the ability to engage in certain activities normally due to the loss or abnormality of certain organization or function in physiology and psychology caused by injury (10).

Medical rehabilitation

As an important part of rehabilitation, medical rehabilitation is the application of rehabilitation concept in the medical field. It refers to healing the dysfunction of the sick, the injured, and the disabled through medical means (14). The rehabilitation referred to in CSSD is medical rehabilitation, including medical treatment, assistive devices and rehabilitation training.

Socioeconomic position

Socioeconomic position (SEP) is an economic and sociological combined total measure of an individual's or family's economic access to resources and social position in relation to others (15, 16). When analyzing SEP, three variables, namely, income, education, and occupation are examined (17).

Study design and subjects

This research aims to study the demand and utilization of rehabilitation services in the Chinese older adults aged 60 and above who are disabled by injury, and the correlation between the utilization of rehabilitation services and individual's SEP. In the CSSD, it lists only organic and non-organic mental disorders as the causes of mental disability based on ICD-10 diagnostic criteria, failing to examine the injury-related causes (18, 19). Therefore, this research focuses on the older adults with vision, hearing, speech, physical, and intellectual disabilities. Following the existing research (20, 21), this paper extracts the injury-related causes of disability from the CSSD as follows (Table 1):

In this study, the dependent variable is "the usage of rehabilitation services", that is, as long as any one of "medical services and assistance, assistive devices, rehabilitation training

and services" is used, the participant is considered to have used rehabilitation services. Since the older adult/adults are less affected by occupation, the explanatory variables of SEP include annual household per capita income and educational level. The higher the annual household per capita income or educational level, the higher the SEP. In the descriptive analysis, the annual disposable per capita income of urban residents in China in 2006 was 11,759 yuan, and the per capita net income of rural residents was 3,587 yuan, according to the data of the National Bureau of Statistics. In this study, the annual per capita income of urban households that is higher than 11,759 yuan and the per capita net income of rural households that is higher 3,587 yuan are defined as higher than the annual per capita income of national residents (22). In addition, according to regulation of the National Bureau of Statistics, the Eastern China includes Beijing, Tianjin, Hebei, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong and Hainan; the Central China includes Shanxi, Anhui, Jiangxi, Henan, Hubei and Hunan; the Western China includes Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Tibet, Shaanxi, Gansu, Qinghai, Ningxia and Xinjiang; and the Northeastern China includes Liaoning, Jilin, and Heilongjiang (23).

Ethical approval

These surveys were approved by the State Council [Guo Ban Fa No. 77 (1986); Guo Ban Fa No. 73 (2004)] and the survey plan was formulated in accordance with the Statistics Law of the People's Republic of China and the Law of the People's Republic of China on the Protection of Disabled Persons. During the surveys, all respondents provided informed consent to participate in the surveys and clinical diagnosis.

TABLE 1 Injury-related causes of disability in the CSSD.

Disability type	Causes of disability
Vision	Trauma, poisoning
Hearing	Drug poisoning, trauma or accidental injury, noise, detonation
Speech	Brain injury, birth injury, CO poisoning
Physical	Industrial injury, traffic accident, spinal cord injury, brain injury, other injuries, poisoning
Intellectual	Birth injury, industrial injury, traffic accident, other injuries, poisoning, allergic reaction

Statistical analysis

Stata 16.0 was used for data analysis. Chi square test was employed for univariate analysis, and binary logistic regression was adopted for multivariate analysis. Hosmer-Lemeshow test was used for the test of goodness of fit of the model. The significance level was 0.05.

Results

Prevalence of injury-caused disability in the older adults

A total of 354,859 elders were surveyed in CSSD, including 85,260 disabled elders. Among them, 10,314 older adults people were disabled by injury, with the prevalence of 291/10,000 (number of the disabled older adults by injury in CSSD/total number of the older adults in CSSD), accounting for 12.1% of all older adults disabled people. The prevalence of physical disability by injury is the highest in this group (151/10,000) (number of the older adults with physical disabilities caused by injury and without other kinds of disabilities in CSSD/total number of the older adults in CSSD), followed by hearing disability (71/10,000). On the contrary, the prevalence is relatively low for the visual (12/10,000), intellectual (2/10,000), and speech (0.4/10,000) disabilities caused by injury in the older adults. As for the disability grading, most injury-caused disability in the older adult is mild (grade IV), accounting for nearly 57% of the total, followed by moderate (grade III, nearly 28%). Severe (grade II) and extremely severe (grade I) disabled elders account for only 15%.

In terms of SEP factors, the injury-caused disability in the older adults shows a higher prevalence in the groups of those with the annual household per capita income lower than the national average (prevalence = 306/10,000, reference: those with the annual household per capita income higher than the national average, prevalence = 224/10,000), the illiteracy/with no schooling (prevalence = 321/10,000, reference: primary school or above, reference = 267/10,000) (Table 2).

TABLE 2 Comparison of the prevalence of the disabled older adults by injury with different SEP.

	Total	Disabled by injury	Prevalence/10,000	χ^2	*P*
Annual household per capita income					
≥National average	67,922	1,523	224	131.3268	<0.05
<National average	286,937	8,791	306		
Educational level					
Illiteracy/no schooling	158,014	5,066	321	90.5672	<0.05
Primary school or above	196,845	5,248	267		

TABLE 3 Demand and utilization of rehabilitation services of the older adults with injury-related disability.

	Medical services and assistance			Assistive devices			Rehabilitation training and services		
	Demand (*n*)	Usage (*n*)	# Gap (%)	Demand (*n*)	Usage (*n*)	Gap (%)	Demand (*n*)	Usage (*n*)	Gap (%)
Overview	7,191	4,500	37.42	4,983	1,251	74.89	2,952	1,086	63.21
Disability grade									
Mild (grade IV)	4,121	2,611	36.64%	2,438	621	74.53%	1,794	666	62.88%
Moderate to extremely severe (grade I–III)	3,070	1,889	38.47%	2,545	630	75.25%	1,158	420	63.73%
Gender									
Male	4,011	2,616	34.78	2,917	741	74.60	1,616	621	61.57
Female	3,180	1,884	40.75	2,066	510	75.31	1,336	465	65.19
Age groups									
60–69	2,703	1,669	38.25%	1,677	405	75.85%	1,150	410	64.35%
70–79	3,012	1,901	36.89%	2,185	554	74.65%	1,196	464	61.20%
≥1.	1,476	930	36.99%	1,121	292	73.95%	606	212	65.02%
Marital status									
Without spouse	2,827	1,641	41.95%	1,970	468	76.24%	1,156	397	65.66%
Having spouse	4,364	2,859	34.49%	3,013	783	74.01%	1,796	689	61.64%
Region									
Western China	2,563	1,454	43.27	1,736	345	80.13	1,131	302	73.30
Eastern China	2,377	1,822	23.35	1,802	566	68.59	971	455	53.14
Central China	1,755	803	54.25	1,092	219	79.95	592	187	68.41
Northeastern China	496	421	15.12	353	121	65.72	258	142	44.96
Residence									
Rural	4,872	2,688	44.83	3,257	627	80.75	1,886	587	68.88
Urban	2,319	1,812	21.86	1,726	624	63.85	1,066	499	53.19
Insurance (including endowment, medical, insurance, employment injury, and unemployment insurance)									
No	4,364	2,424	44.45%	2,934	693	76.38%	1,762	608	65.49%
Yes	2,827	2,076	26.57%	2,049	558	72.77%	1,190	478	59.83%
Disability certificate									
No	6,108	3,656	40.14%	4,321	992	77.04%	2,388	845	64.61%
Yes	1,083	844	22.07%	662	259	60.88%	564	241	57.27%
Annual household per capita income									
<National average	6,216	3,740	39.83	4,174	988	76.33	2,524	913	63.83
≥National average	975	760	22.05	809	263	67.49	428	173	59.58
Educational level									
Illiteracy/no schooling	3,634	2,008	44.74	2,397	499	79.18	1,405	454	67.69
Primary school or above	2,416	1,566	35.18	1,701	427	74.90	1,008	391	61.21
Chi-square test (the variables are demographic characteristics and whether they use rehabilitation services or not. Inside the brackets is *p*-value)									
Gender	5.9398 (<0.05)			28.6559 (<0.05)			10.7134 (<0.05)		
Age groups	1.5856 (=0.208)			1.8787 (=0.170)			0.0321 (=0.858)		
Marital status	0.9589 (=0.619)			15.4828 (<0.05)			1.5392 (=0.463)		

(Continued)

TABLE 3 (Continued)

	Medical services and assistance			Assistive devices			Rehabilitation training and services		
	Demand (*n*)	Usage (*n*)	# Gap (%)	Demand (*n*)	Usage (*n*)	Gap (%)	Demand (*n*)	Usage (*n*)	Gap (%)
Region	25.5373 (<0.05)			1.9741 (=0.160)			3.6353 (=0.057)		
Residence	304.0136 (<0.05)			116.2728 (<0.05)			134.4611 (<0.05)		
Insurance	200.2527 (<0.05)			187.7017 (<0.05)			94.7389 (<0.05)		
Disability certificate	101.8897 (<0.05)			9.5350 (<0.05)			5.9190 (<0.05)		
Annual household per capita income	54.8969 (<0.05)			26.4949 (<0.05)			38.1499 (<0.05)		
Educational level	28.5757 (<0.05)			44.2832 (<0.05)			1.3060 (=0.253)		

[#]The calculation of the rehabilitation gap: (1 – the number of people using/demanding the service) *100%.
*Indicates a significant difference, $p < 0.05$.

TABLE 4 Variables assignment.

Variables	Assignment
Dependent variables	
Usage of rehabilitation services	0 = Never used, 1 = have used
Control variables	
Disability grade	1 = Grade I, 2 = grade II, 3 = grade III, 4 = grade IV
Gender	0 = Female, 1 = male
Age	Continuous variable
Marital status	0 = Without spouse, 1 = having spouse
Region	0 = Western China, 1 = eastern China, 2 = central China, 3 = northeastern China
Residence	0 = Rural areas, 1 = urban areas
Insurance status	0 = No, 1 = yes
Disability certificate status	0 = No, 1 = yes
Explanatory variables	
Annual household per capita income	0 = Lower than the national average, 1 = Higher than the national average
Educational level	0 = Illiteracy/no schooling, 1 = Primary school or above

The demand and utilization of rehabilitation services of the older adults with injury-related disability

There is a large gap between the high demand and low utilization of rehabilitation services among the Chinese older adults disabled by injury (hereinafter referred to as the "rehabilitation gap"). Thirty-eight percentage of demand for medical treatment, 75% for assistive devices and 64% for rehabilitation training are left unsatisfied. Based on social and demographic factors, there is little difference in the rehabilitation gap among different disability grades, gender, age groups, and marital status. However, the rehabilitation gap is relatively larger among the older adults with injury-related disability who (1) live in the central or western regions, (2) are rural residents, (3) without insurance, (4) without disability certificate, (5) have the annual household per capita income lower than the national average, and (6) are illiterate or with no schooling (Table 3).

Associated SEP factors of rehabilitation service utilization among the older adults with disability caused by injury

Binary logistic regression analysis was carried out with "the usage of rehabilitation services" as the dependent variable; and disability grade, gender, age, marital status, region, residence (rural/urban), insurance status, and disability certificate status as the control variables; and annual household per capita income, educational level as the explanatory variables. The assignment of independent variables is shown in Table 4. Hosmer-Lemeshow goodness of fit test result shows that Hosmer-Lemeshow $\chi^2 = 12.77$, $P = 0.12 > 0.05$, which means that the model fits better.

The results show that after controlling the variables of disability grade, gender, age, marital status, region, residence (rural/urban), insurance status, and disability certificate status, the odds of utilization of rehabilitation services is much higher in the groups of participants that (1) with higher annual household per capita income (OR = 1.184, 95%CI 1.054–1.329, reference: annual household per capita income < national average), (2) have been to primary school or above (OR = 1.143, 95%CI 1.038–1.256, reference: illiteracy/no schooling) (Table 5).

Discussion

The gap between the utilization of rehabilitation services and the demand is large for the older adults disabled by injury. Rehabilitation services needs are universal (7). As for the older adults, their needs for rehabilitation services are neglected more serious (24, 25). There are few studies on the utilization of rehabilitation services for the older adult/adults disabled by injury in China. An similar study based on CSSD shows that the rehabilitation gap for the older adults disabled by injury is nearly 40% (26). This study pointed out the problem of low utilization rate

TABLE 5 Regression analysis of the SEP factors on whether the older adults disabled by injury utilize the rehabilitation services.

The usage of rehabilitation services	*B*	Robust S.E.	OR (95% CI)	*P*
Annual household per capita income (reference: <national average)				
≥National average	0.169	0.070	1.184 (1.054–1.329)	<0.05
Educational level (reference: illiteracy/no schooling)				
Primary school or above	0.132	0.056	1.142 (1.038–1.256)	<0.05

OR, odds ratio; CI, confidence intervals.

of rehabilitation services from the perspective of all the disabled by injury. In addition, this study revealed two relationship patterns ("high-low-high" and "low-high-low") among SEP, prevalence of injury-caused disability and odds of utilization of rehabilitation services among the Chinese older adults disabled by injury, that is, the older adults with higher SEP have a lower prevalence of injury-caused disability, but a higher odds of utilization of rehabilitation services; conversely, the older adults with lower SEP have a relatively higher prevalence but a lower odds of utilization of rehabilitation services.

Existing research showed a "inverse combination" pattern between individual health status and SEP (27), that is, the lower the SEP, the worse the individual health status (28). This explains the inverse combination of the SEP and the prevalence of disability by injury among the older adults in this study. educational level (29–31) and income (32, 33) are two important factors affecting the utilization of health services, and the mechanism by which they affect the individual behaviors mainly are the two intermediate factors of "intention" and "affordability". The essence of individual utilization of health services is consumption behavior. Based on the economic theory, "intention" and "affordability" are the two determinants of consumption behavior. Some foundation theories have emphasized the important effects of income and education on individual health services utilization behavior. Anderson health services utilization behavior model points out that "intention" comes from the individual awareness of the gap between their actual health level and the ideal state or the diagnosis from a medical professional, as well as the individual's analysis of the benefits of the health behaviors, which involves the individual's health literacy affected by the educational level deeply (34). Affordability is mainly determined by individual "ability resources", that is, the ability of individuals to obtain health service resources, in which income is the basic composition (34). There is also an important psychological variable between "intention" and "affordability". Social psychologist Icek Ajzen believes that "perceived behavioral control" is an important intermediary in the transformation path from intention to action (35). Through the judgment of affordability, individual clearly assesses the difficulty of taking practical actions, and then decides whether to adopt healthy behaviors. In addition, the social ecology model also reveals that individual behavior is determined by individual ability, knowledge, motivation, etc. (36).

Limitations

However, there are some limitations that require consideration. First, It fails to distinguish mentally disabled persons due to injury in the CSSD database. Therefore, this study lacks the situation of mentally disabled people. Second, The CSSD database is relatively old and has limited practical guidance. Nonetheless, it is still the latest national sampling survey on disability in China.

Conclusions

Facing the current situation of limited rehabilitation services in China, it is an essential means to improve the efficiency of rehabilitation services by clarifying the vulnerable groups of people with injury-caused disability and taking precise assistance measures. To be more specific, according to the distribution of the prevalence of injury-related disability and the utilization rate of rehabilitation services among different older adults groups, targeted measures should be taken based on their specific characteristics, especially the rural residents or people living in the central or western regions, poverty-stricken people, people with low educational level, or without insurance and disability certificate among the older adults. Strategies to improve the disability manage system, to strengthen the chain of "information discovery-information transmission-rehabilitation services supply-continuous health monitoring and management" for the older adults with injury-caused disability are warranted, especially for the vulnerable groups aforementioned. In view of the poor and illiterate groups, to enhance medical aids and popularize the scientific information to compensate for the lack of affordability and awareness of rehabilitation services utilization is essential. In addition, it is necessary to further expand the coverage and improve the payment system of medical insurance for rehabilitation services.

Data availability statement

The data that support the findings of this study are available from the Institute of Population Research of Peking University (IPR). Restrictions apply to the availability of these data, which were used under license for this study. Data are available with the permission of IPR. Requests to access these datasets should be directed to 00-86-010-62751974.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

Y-RW is responsible for conceptualizing, data analysis, formal interpretation of results, and writing the manuscript. Y-NL is responsible for conceptualizing, critical revision of article for important intellectual content, and writing—review and editing. Y-LF and Y-YF are responsibility for revision of article. X-YZ is responsible for conceptualizing the study, methodology, and supervision. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Is there a correlation between sensory impairments and social isolation in middle-aged and older Chinese population? Cross-sectional and longitudinal evidence from a nationally representative survey

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Purpose: The aim of this study is to investigate the cross-sectional and longitudinal associations between sensory impairments (SIs) including single vision impairment (SVI), single hearing impairment (SHI), and dual sensory impairments (DSI) with social isolation in the middle-aged and older Chinese population.

Methods: Data were obtained from the China Health and Retirement Longitudinal Survey (CHARLS). In total, 11,674 Chinese older adults aged over 45 were included at baseline 2011, and 6,859 participants who accomplished all four interviews from 2011 to 2018 were adapted for longitudinal analyses. Sensory status and social isolation measurements including social disconnectedness and self-perceived loneliness were collected. Assessment of social disconnectedness included the number of types of social activities in which they participated and the frequency of such participation. Loneliness referred to the subjective perception of loneliness. Other covariates included socio-demographic characteristics, medical conditions, and lifestyle-related factors. The impacts of baseline sensory status on social disconnectedness and loneliness were assessed using univariate and multivariate generalized linear models. A generalized linear model with generalized estimation equations (GEE) was used to assess the association between time-varying sensory statuses with social disconnectedness or loneliness over 8 years after being adjusted with multi-confounding factors.

Results: Participants with SIs had significantly higher levels of social disconnectedness and self-perceived loneliness, compared to those who were free of SI. All kinds of SIs were significantly associated with loneliness according to both cross-sectional and longitudinal data. The correlations between DSI and social disconnectedness or loneliness at baseline and over 8 years were also noticed. SHI was found to be significantly associated with both

frequency and types of social activities according to cross-sectional data and with the frequency of social activity participation in longitudinal analysis. SVI was only associated with the types of social activities at baseline (all p-values < 0.05).

Conclusion: Sensory impairments, especially dual sensory impairments, have explicitly detrimental effects on social isolation among the older Chinese population. Over time, single hearing impairment specifically jeopardizes their frequency rather than types of social activities participation.

KEYWORDS

China Health and Retirement Longitudinal Study (CHARLS), sensory impairment, social isolation, social disconnectedness, loneliness

1. Introduction

A substantial increase in the size of the aging population in our society generates an urgent requirement for attaining a successful aging life, which fosters daunting challenges for biological, social, and medical science (1). Successful aging is multidimensional, which includes three main components: the lower probability of disease and related disability, maintenance of physical and cognitive function, and sustained engagement in social and productive activities (2).

In aging life, elderly people no longer need to work or work less, and they have more time for social engagement (3), which has become an important approach for older people to obtain social resources and preserve an active and healthy aging life. On the contrary, increasing pieces of evidence have also indicated that impoverished social relationships, also known as social isolation, have become a global public health challenge that influences health status (4), including cognitive impairment (5, 6) and depression (7), physical dysfunction or disability (8–11), multi-morbidities and mortality among the older population (9, 12, 13). Especially during the COVID-19 pandemic, as many countries have carried out various containment or lockdown policies which would inevitably lead to contrived social isolation, researchers have noticed that even temporary social disconnectedness could also impact health-related quality of life (HRQoL) (14), cognitive function (15, 16), and mental health status (16–18). Thus, to strengthen social relationships, encourage social participation, and reduce loneliness in an aging life, the investigation of modifiable risk factors of social isolation has gained certain attention as an important approach over the past decades (19).

Sensory impairments (SIs), including single hearing impairment (SHI), single vision impairment (SVI), and dual sensory impairments (DSI), which refer to the simultaneous presence of VI and HI, are commonly observed with aging (20). The associations of SIs with various adverse events in an aging life, including cognitive decline, physical dysfunctions, and all-cause mortality, have been widely investigated (21–23), which could also aggravate social isolation. Thus far, cross-sectional studies from some western countries have indicated that SI could restrict interpersonal communication and therefore inhibit social participation (24–26), while weaker associations or conflicting results were also noticed from other studies as well, which could be related to disparities in sample race, gender, aging categories, and adjustments of confounders (26, 27). To date, there are limited longitudinal reports on this issue, especially from developing countries.

China is the most populous developing country which is also facing a severe social problem of aging. Older Chinese are likely to neglect SI and related problems owing to their traditional attitudes regarding SI as a normal part of aging life, which might further contribute to the higher prevalence of SI and SI-related problems in China than that in some western countries (28). Several studies have indicated the associations between SI and adverse health consequences in the older Chinese population (29–31). However, to the best of our knowledge, there is a paucity of literature on SIs and social isolation in our aging population. To address the research gap, we conducted a cross-sectional and longitudinal observation on the associations between SIs and social isolation in a large, population-based sample from the China Health and Retirement Longitudinal Study (CHARLS). Allowing for the specific social institution, cultural background, and public health system in China, the purpose of this study is to verify whether SIs are independently associated with social isolation in the middle-aged and older population in China.

2. Methods

2.1. Participants and public involvement

Data were obtained from the China Health and Retirement Longitudinal Study (CHARLS), which is the first nationally representative longitudinal survey sampling residents (adults over 45 years old) from 450 villages/neighborhoods, and 150 counties across 28 provinces in China. With response rates over 80%, CHARLS provides the most up-to-date longitudinal data for the investigation of the health status and wellbeing of the middle-aged and elderly population in China. Initiated in 2011, CHARLS enrolled 17,708 participants at baseline (Wave 1), 18,254 participants at Wave 2 (2013), 20,273 participants at Wave 3 (2015), and 19,816 participants at Wave 4 (2018).

2.2. Measures

2.2.1. Main outcome

Social isolation has been variously conceptualized. We quoted the definition of social isolation as "a state in which the individual

lacks a sense of belonging socially, lacks engagement with others, has a minimal number of social contacts and they are deficient in fulfilling and quality relationships" according to Nicholson et al. (32). Such definition emphasized both subjective and objective dimensions of social isolation that are conceptualized as social disconnectedness and loneliness (33). Such quotation has been adapted in related studies (5, 34). Thus, the main outcome in this study falls in these two dimensions of social isolation according to the CHARLS questionnaire.

Social disconnectedness is an objective state reflecting a restricted social network and social inactivity with low participation and engagement. We focused on two aspects of social disconnectedness for quantification in the present study. First, Types: Respondents were asked whether they had participated in any of the following 11 activities in the past month including (1) Interact with friends; (2) Play Ma-jong, chess, cards, or go to community club; (3) Provide help to family, friends, or neighbors; (4) Go to a sport, social, or other kind of club; (5) Take part in a community organization; (6) Do voluntary or charity work; (7) Care for a sick or disabled adult; (8) Attend an educational or training course; (9) Stock investment; (10) Use the Internet; (11) Other activities. We summed the responses and created an index representing multifarious social participation, which revise-represented social disconnectedness, with higher scores reflecting lower levels of social disconnectedness (range: 0–11). Then, participants were asked, "How often do you usually do certain activities in the last month? Almost daily, almost every week, or not regularly?" We defined almost daily = 28 scores, almost every week = 8 scores, and not regularly = 3 scores, to assess the frequency of social participation. Scores of frequencies were also summed as one index for statistical analysis.

Loneliness is a subjective assessment defined as "a distressing feeling that accompanies the perception that one's social needs are not being met by the quantity or especially the quality of one's social relationships" according to Hawkley and Cacioppo (35). Respondents were asked the frequency of feeling lonely in the last week: 1. rarely or none of the time (<1 day); 2. some or a little of the time (1–2 days); 3. occasionally or a moderate amount of the time (3–4 days); 4. most or all the time (5–7 days). Loneliness was dichotomized into 2 categories: 0, not lonely=those who reported feeling lonely rarely and none of the time, and 1, lonely=those who felt lonely sometimes, occasionally, or most of the time. This one-item measure correlates highly with multi-item loneliness scales and has been used in numerous studies (11, 34, 36).

2.3. Exposures

The main exposure in this present study is sensory status including no sensory impairment (NSI), single vision impairment (SVI), single hearing impairment (SHI), and dual sensory impairments (DSI). In CHARLS, VI consists of distal and near losses. Distal VI and near VI were evaluated by asking participants whether their eyesight was excellent, very good, good, fair, or poor when seeing things at a distance or up close, respectively. Reporting of fair or poor eyesight was classified as VI. Similarly, for the HI assessment, the question was: "Is your hearing excellent, very good, good, fair or poor." A response of fair or poor hearing was identified as HI. Such assessment of SI has been widely used in previous CHARLS-related studies (29–31). DSI refers to the condition in which participants reported both VI and HI, and single SI refers to sole VI or HI without the other one.

Sensory impairment in the aging population could be amended by medical supports such as cataract surgery and hearing aids, or vice versa, get worse due to aging or pathologic progressions. Thus, along with baseline sensory status, we also investigated the impacts of time-varying SI statuses during 8 years of follow-up to further explore its longitudinal effects on social isolation.

2.4. Other variates

2.4.1. Socio-demographic characteristics

Gender was a binary variable, male or female, and age was treated as a continuous variable. Marital status indicated whether the respondent lived alone or got accompanied. Participants who were separated, divorced, widowed, or never married were coded as "living alone," while those who were married or partnered were coded as "living with partner." Living area referred to urban or rural places where participants lived. Educational attainment represents one's social economic status, which was categorized into five groups: illiterate, less than elementary school, elementary school, middle school, and high school or above.

2.4.2. Medical condition

Data on the physical condition were collected with the following question: "Have you ever been diagnosed by a doctor as having the following diseases: hypertension, dyslipidemia, diabetes, cancer, chronic lung diseases, liver diseases, heart disease, stroke, kidney diseases, memory-related diseases, digestive diseases, arthritis, and asthma?." Suffering from more than two diseases was defined as multi-morbidities. Insurance covering referred to coverage of one or more kinds of health insurances, which represented an approach to health support.

2.4.3. Lifestyle-related factors

The lifestyle variables included smoking and drinking status. Smoking was categorized as current/former smoker or never smoked. Drinking was a three-category variable that indicated the frequency of drinking: none, less than once a month, or more than once a month.

2.5. Statistical analysis

Statistical analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC, USA). In this study, the primary exposures of interest were SIs, while the other independent variables served as control variables. Baseline characteristics were compared among participants according to SI statuses (four groups) using the one-way ANOVA, Kruskal–Wallis test, or Chi-square test analysis based on obtained data. Generalized linear models were conducted to assess the associations between SIs, multiple covariates, and

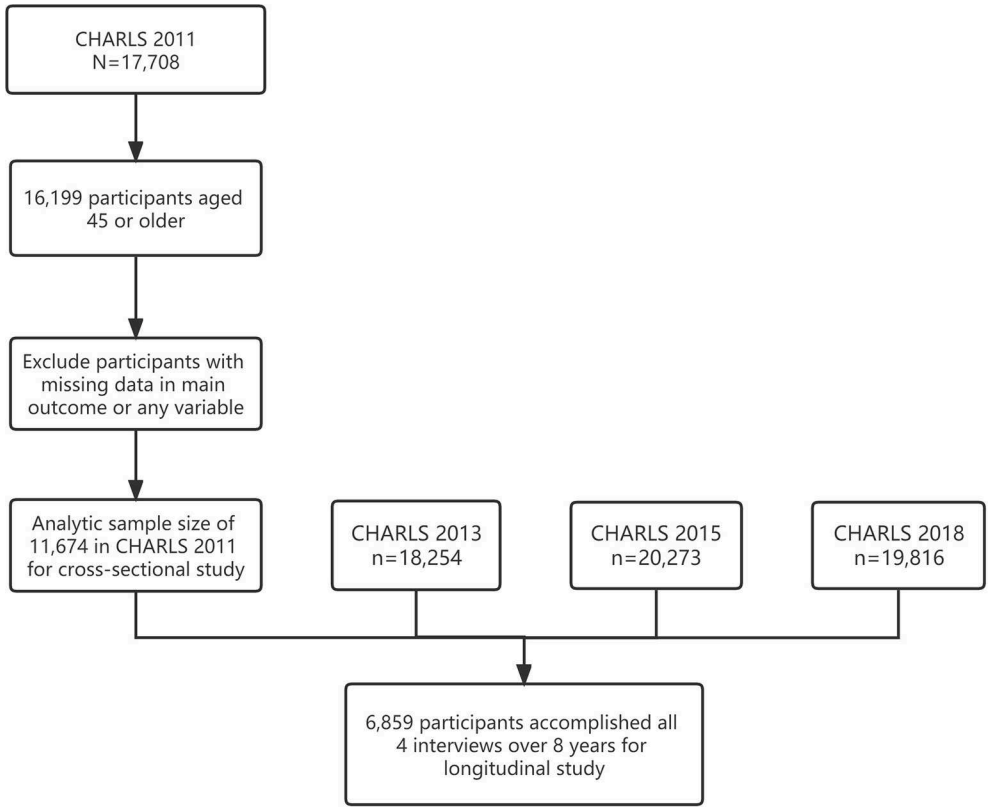

FIGURE 1
Graphic abstract of sample screening of the present study.

social isolation at baseline for cross-sectional analyses. Associations between time-variant SIs and social isolation measurements change over time (across four interviews over 8 years) were assessed using generalized linear models with generalized estimating equations (GEE), controlling for the intraindividual correlation between repeated measurements using an exchangeable correlation structure as previously described (37). To examine whether social isolation was dependent on the status of sensory impairments, models that adjusted for potential confounders as mentioned earlier were employed. Parameter estimates were shown with 95% confidence intervals and statistically significant was considered as a two-sided p-value of < 0.05. We begin our research with a hypothesis that a correlation exists between sensory impairments and social isolation, and the null hypothesis is the opposite stating that no such relationship exists.

3. Results

In total, 11,674 participants over 45 years old from baseline CHARLS 2011 were deemed eligible for the current study, among which, 6,859 participants accomplished all four interviews from 2011 to 2018 and were adopted in the longitudinal analyses (Figure 1). The baseline socio-demographic characteristics, medical conditions, lifestyle-related factors, and social participation measurements of the study sample were grouped by sensory statuses and shown in Table 1. Participants who were free from any kind of SI appeared to have explicitly more abundant social activities with higher frequency and lower levels of self-perception of loneliness at baseline. Variations in the number of activity types, frequency of social activities, and loneliness over 8 years are shown in Figure 2.

The univariate generalized linear models indicated the potential associated factors of social isolation measurements in our sample at baseline 2011. SIs including SVI, SHI, and DSI, along with other factors including gender, age, educational level, living area, smoking, alcohol consumption, and medical conditions were all found to have certain associations with loneliness and the types or frequency of social activities (Table 2). Compared to single SI, DSI had lower incidence rate ratios and higher odds ratios, which suggests its potentially greater impacts on social disconnectedness and loneliness.

The results of the univariate generalized linear models indicated certain covariables that could probably confound the relationship between SIs and social isolation measurements in multivariate models. Thus, to further clarify the cross-sectional associations between SIs and social isolation measurements, we reanalyzed their relevance by controlling the covariates (Table 3). For the subjective perception of loneliness, all kinds of SIs showed profound and detrimental impacts after being adjusted for various confounders (all p-values < 0.001). DSI, also showed significant correlations with both the frequency (IRR: 0.779, 95% CI: 0.704–0.862; $p <$

TABLE 1 Characteristics of participants in the present study from CHARLS 2011.

Variables	Total	NSI	SHI	SVI	DSI	*P*-value
Age	59.38 ± 9.69	56.86 ± 8.78	59.69 ± 9.92	59.22 ± 9.27	61.44 ± 9.97	<0.0001
Gender						<0.0001
Male	5,572 (47.73)	1,892 (50.68)	1,037 (51.57)	687 (43.90)	1,956 (44.81)	
Female	6,102 (25.27)	1,841 (49.32)	974 (48.43)	878 (56.10)	2,409 (55.19)	
Education						<0.0001
Illiterate	3,121 (26.73)	800 (21.43)	504 (25.06)	445 (28.43)	1,372 (31.43)	
Less than elementary school	2,103 (18.01)	568 (15.22)	372 (18.50)	285 (18.21)	878 (20.11)	
Middle school	2,529 (21.66)	754 (20.20)	457 (22.73)	351 (22.43)	967 (22.15)	
High school or vocational school	2,423 (20.76)	924 (24.75)	423 (21.03)	299 (19.11)	777 (17.80)	
College and above	1,489 (12.83)	687 (18.40)	255 (12.68)	185 (11.82)	371 (24.77)	
Marital status						<0.0001
Living with partner	9,668 (82.82)	3178 (85.22)	1,658 (82.45)	1,310 (83.71)	3,522 (80.69)	
Living alone	2,006 (17.18)	555 (14.87)	353 (17.55)	255 (16.29)	843 (19.31)	
Living area						<0.0001
Urban	4,727 (40.49)	1,728 (46.29)	773 (38.44)	644 (41.15)	1,582 (36.24)	
Rural	6,947 (59.51)	2,005 (53.71)	1,238 (61.56)	921 (58.85)	2,783 (63.76)	
Drinking status						0.0005
Drink more than once a month	2,900 (24.84)	975 (26.12)	531 (26.40)	383 (24.47)	1,011 (23.16)	
Drink but less than once a month	904 (7.74)	323 (8.65)	157 (7.81)	100 (6.39)	324 (7.42)	
None of these	7,870 (67.41)	2,435 (65.23)	1,323 (65.79)	1,082 (69.14)	3,030 (69.42)	
Smoking status						0.0064
Yes	4,588 (39.30)	1,466 (39.27)	856 (42.57)	588 (37.57)	1,678 (38.44)	
No	7,086 (60.70)	2,267 (60.73)	1,155 (27.43)	977 (62.43)	2,687 (61.56)	
Multi-morbidities						<0.0001
Yes	2,203 (18.87)	450 (12.05)	377 (18.75)	284 (18.15)	1,092 (25.02)	
No	9,471 (81.13)	3,283 (87.95)	1,634 (81.25)	1,281 (81.85)	3,273 (74.98)	
Insurance covering						0.3582
Yes	10,918 (93.52)	3,498 (93.70)	1,888 (93.88)	1,448 (92.52)	4,084 (93.56)	
No	756 (6.48)	235 (6.30)	123 (6.12)	117 (7.48)	281 (6.44)	
Social disconnectedness						
Type	0.74 ± 0.93	0.85 ± 1.03	0.74 ± 0.92	0.76 ± 0.93	0.64 ± 0.82	<0.0001
Frequency	10.60 ± 16.35	12.50 ± 18.18	10.49 ± 15.83	11.09 ± 16.60	8.85 ± 14.57	<0.0001
Loneliness						<0.0001
Yes	3,456 (29.60)	875 (23.44)	560 (27.85)	455 (29.07)	1,566 (35.88)	
No	8,218 (70.40)	2,858 (76.56)	1,451 (72.15)	1,110 (70.93)	2,799 (64.12)	

0.001) and types (IRR: 0.861, 95% CI: 0.816–0.909; $p < 0.001$) of social activities. However, associations between the types of social activities and SHI or SVI were attenuated after being adjusted for lifestyle-related factors and medical conditions. Only SHI showed profound associations with the frequency of social activities after receiving an adjustment of socio-economic factors (Models 1 and 2; Table 3).

In longitudinal analyses, associations between time-variant SIs and social isolation measurements over time were assessed using generalized linear models with generalized estimating equations, which could provide longitudinal observation of intraindividual correlations between repeated measurements. Consistent with cross-sectional analyses, we found that participants with DSI were more likely to involve in social activities with fewer types (IRR:

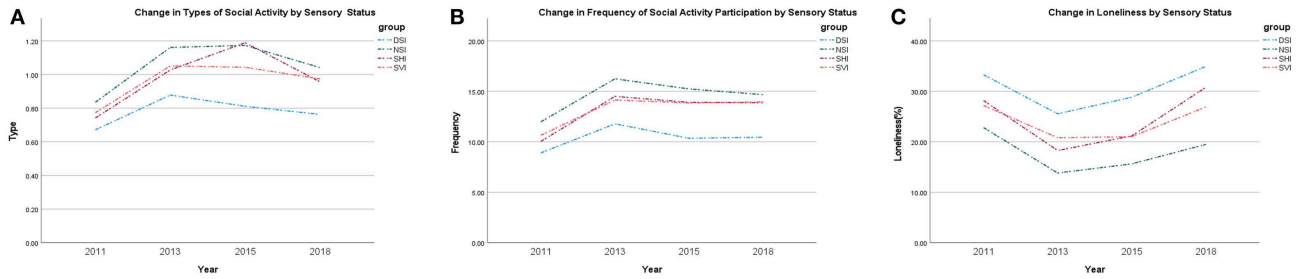

FIGURE 2
Changes of social disconnectedness and loneliness over time, 2011–2018. NSI, No sensory impairment; SVI, Single vision impairment; SHI, Single hearing impairment; DSI, Dual sensory impairments.

0.889, 95% CI: 0.855–0.925; $p < 0.001$) and less frequency (IRR: 0.825, 95% CI: 0.785–0.868; $p < 0.001$), and were more likely to experience loneliness (OR: 1.545, 95% CI: 1.418–1.684; $p < 0.001$) compared with participants without SIs after receiving adjustments of various confounders (Table 4). However, both single SI lost their associations with the types of social activities. Only SHI (IRR: 0.924, 95% CI: 0.859–0.994; $p < 0.05$) remained to be significantly associated with the frequency of social activities after being adjusted for covariates. We failed to find any profound correlation between SVI and the frequency of social activities in any of the four models.

4. Discussion

To the best of our knowledge, the present study is the very first study that provides explicit evidence of the detrimental impacts of sensory impairments on social isolation among a middle-aged and older Chinese population, using cross-sectional and longitudinal data from a nationally representative survey in China. The importance of social engagement to a healthy aging life has been highlighted as a global consensus (38). Thus, it is essential to investigate factors that may jeopardize social engagement, which consequently leads to social isolation and adverse events in aging life.

4.1. SIs and jeopardized social connection

Scales of sensory assessments, covariate adjustments, and evaluation of social isolation measurements including social disconnectedness and loneliness from previous study designs were widely divergent, which may lead to nuanced results and difficulties in direct comparisons among these studies (24, 26, 27, 39–42). Nevertheless, most findings still converged to a general and reasonable conclusion, that SIs and the consequent difficulties in communication could exert certain detrimental impacts on social participation to some extent (43). Results from both cross-sectional analyses and longitudinal observation in the present study reiterated that SIs, especially DSI, had explicit associations with higher social disconnectedness and increased loneliness among elderly Chinese. Our work echoed related cross-sectional studies in other countries (24, 26, 27, 39, 40), which also provided empirical longitudinal pieces of evidence on this issue in the Chinese population for the first time.

The complex mechanisms underlying "sensory-social isolation" correlation or interactions are yet to be explored. Along with direct obstructions to social interactions, older adults with sensory loss are more prone to functional (44) and mental health dysfunctions such as cognitive decline (44), depression, and anxiety (45), which may consequently jeopardize social communication. On the other hand, people experiencing sensory deprivation, especially over extended periods of time, often report perceptual disturbances such as visual and auditory hallucinations, which might be considered as a protective reaction of the social brain (46, 47). Even short-term sensory deprivation could induce psychotomimetic effects or cognitive appraisal distortion (48, 49). Such perceptual disorders propel them to become suspicious of interpersonal interaction and misinterpret social clues (46, 47).

4.2. DSI, combined effects, and compounded problems

Compared to single SI, DSI had more consistent and profound effects on social disconnectedness and loneliness according to both cross-sectional and longitudinal data in the present study. Links between SIs and social isolation are primarily mediated by communication difficulties (50). For people with single SIs, those who have SHI might compensate their inter-person communication using lip reading or sign language, while those who suffer from SVI can rely on spoken language. However, the combination of concurrent sensory deficits creates a compounded problem that restrains such cross-modal compensation (51, 52). Therefore, older people with DSI would more likely to be timid, hesitant, or confused, which inevitably leads to isolation, disappointment, and frustration during communication (24). Compared to people with single SI, those with DSI may appear to have a higher likelihood of social inactivity (27), and poorer scores in psychosocial variables and life quality evaluation (53). Also presumably, their communication partners might become impatient in an unjustified way, or pay inadequate attention in order to understand them (54). Thus, our findings underscore the importance of primary prevention and rehabilitation in both vision and hearing impairments as well as setting objectives to increase social participation and life satisfaction among people with sensory disabilities and the removal of environmental barriers (24).

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TABLE 2 Univariate generalized linear analysis of independent variables and social isolation measurements in 2011.

Variables	Social disconnectedness				Loneliness	
	Type		Frequency			
	IRR (95%CI)	*P*-value	IRR (95%CI)	*P*-value	OR (95%CI)	*P*-value
Gender						
Male		Reference				
Female	0.878 (0.840, 0.919)	<0.0001	1.006 (0.927, 1.092)	0.8813	1.462 (1.349, 1.584)	<0.0001
Age	0.986 (0.983, 0.988)	<0.0001	0.997 (0.993, 1.002)	0.2255	1.202 (1.016, 1.024)	<0.0001
Marital status						
Live with partner		Reference				
Living alone	0.969 (0.913, 1.029)	0.3063	1.072 (0.962, 1.194)	0.2111	3.118 (2.825, 3.442)	<0.0001
Education						
Illiterate		Reference				
Less than primary school	1.206 (1.120, 1.300)	<0.0001	1.101 (0.973, 1.247)	0.1269	0.779 (0.694, 0875)	<0.0001
Junior School	1.352 (1.262, 1.449)	<0.0001	1.235 (1.098, 1.389)	0.0004	0.647 (0.578, 0.556)	<0.0001
Middle school or vocational school	1.597 (1.493, 1.708)	<0.0001	1.383 (1.229, 1.558)	<0.0001	0.494 (0.439, 0.556)	<0.0001
High school and above	2.362 (2.204, 2.531)	<0.0001	2.181 (1.910, 2.503)	<0.0001	0.370 (0.319, 0.429)	<0.0001
Living area						
Urban area		Reference				
Rural area	0.712 (0.681, 0.745)	<0.0001	0.626 (0.576, 0.680)	<0.0001	1.611 (1.482, 1.751)	<0.0001
Smoke						
No		Reference				
Yes	1.147 (1.096, 1.200)	<0.0001	1.031 (0.948, 1.121)	0.4817	0.842 (0.775, 0.914)	<0.0001
Multi-morbidities						
Drinking status						
No drink		Reference				
Drink but less than once a month	1.420 (1.315, 1.533)	<0.0001	1.239 (1.061, 1.446)	0.0068	0.852 (0.731, 0.993)	0.0402
Drink more than once a month	1.247 (1.186, 1.313)	<0.0001	1.097 (0.996, 1.207)	0.0594	0.748 (0.680, 0.824)	<0.0001
Multi-morbidities						
No						
Yes	0.979 (0.924, 1.038)	<0.478	0.971 (0.875, 1.078)	0.581	1.869 (1.697, 2.058)	<0.0001
Insurance covering						
No		Reference				
Yes	1.171 (0.824, 1.2900)	0.0015	1.144 (0.969, 1.352)	0.112	0.836 (0.715, 0.978)	0.0252

(Continued)

TABLE 2 (Continued)

Variables	Social disconnectedness				Loneliness	
	Type		Frequency			
	IRR (95%CI)	*P*-value	IRR (95%CI)	*P*-value	OR (95%CI)	*P*-value
Sensory status						
No sensory impairment		Reference				
Hearing impairment	0.868 (0.813, 0.927)	<0.0001	0.839 (0.743, 0.948)	0.0048	1.260 (1.114, 1.426)	0.0002
Vision impairment	0.894 (0.832, 0.960)	0.0019	0.887 (0.777, 1.013)	0.0772	1.339 (1.172, 1.529)	<0.0001
Dual sensory impairment	0.754 (0.714, 0.796)	<0.0001	0.708 (0.642, 0.781)	<0.0001	1.827 (1.657, 2.015)	<0.0001

TABLE 3 Cross-sectional generalized linear analysis of sensory impairments and social isolation.

Sensory status	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]	
	IRR/OR	95%CI	IRR/OR	95%CI	IRR/OR	95%CI	IRR/OR	95%CI
Social disconnectedness: types								
Ref: NSI[e]								
SHI[f]	0.868***	(0.813, 0.927)	0.898**	(0.841, 0.960)	0.940	(0.882, 1.002)	0.938	(0.879, 0.999)
SVI[g]	0.894**	(0.832, 0.960)	0.929*	(0.865, 0.997)	0.975	(0.910, 1.045)	0.975	(0.910, 1.045)
DSI[h]	0.754***	(0.714, 0.796)	0.805***	(0.762, 0.850)	0.864***	(0.819, 0.912)	0.861***	(0.816, 0.909)
Social disconnectedness: frequency								
Ref: NSI								
SHI	0.708**	(0.642, 0.781)	0.839**	(0.742, 0.948)	0.906	(0.802, 1.023)	0.907	(0.803, 1.024)
SVI	0.887	(0.777, 1.013)	0.885	(0.774, 1.011)	0.945	(0.810, 1.056)	0.926	(0.811, 1.057)
DSI	0.708***	(0.642, 0.781)	0.706***	(0.638, 0.780)	0.778***	(0.704, 0.860)	0.779***	(0.704, 0.862)
Loneliness								
Ref: NSI								
SHI	1.260***	(1.114, 1.426)	1.208**	(1.013, 1.022)	1.156*	(1.017, 1.314)	1.116	(0.981, 1.270)
SVI	1.339***	(1.172, 1.529)	1.256**	(1.098, 1.436)	1.234**	(1.076, 1.416)	1.196*	(1.042, 1.374)
DSI	1.827***	(1.657, 2.015)	1.663***	(1.505, 1.838)	1.593***	(1.437, 1.766)	1.495***	(1.347, 1.660)

The results of the generalized linear models were expressed as the incidence rate ratio (IRR) or odds ratio (OR) with 95% confidence intervals (CI). The analytic sample size was 11,674.
[a]Model 1: adjusted for demographic factors including age and gender; [b]Model 2: adjusted for factors in Model 1, as well as social–economic including marital status, educational level, and living area; [c]Model 3: adjusted for factors in Model 2, as well as lifestyle factors including smoking status and alcohol consumption; [d]Model 4: adjusted for factors in Model 3, as well as medical conditions including multi-morbidities and insurance covering.
[e]NSI, No sensory impairment; [f]SVI, Single vision impairment; [g]SHI, Single hearing impairment; [h]DSI, Dual sensory impairment.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

4.3. Single SI jeopardizes the frequency, rather than the types of social activities

It engrossed our attention that, although cross-sectionally, single SI, especially SHI, could have certain impacts on both the frequency and types of social activities. However, during longitudinal observation, their impacts on types of social activities vanished and only SHI remained significantly associated with the frequency of social activities. We supposed that participation in specific types of social activities shall be regarded as very personal habits and customed lifestyles in the form of daily routine, which could have been preserved for a long time in one's aging life. Such personal habits might maintain to a certain extent through compensating for the use of another intact sensory organ as mentioned earlier during aging life with single SI. Such an explanation could partly account for the attenuated significance of the association between single SI and social disconnectedness, after being adjusted for lifestyle-related factors including smoking and alcohol consumption (Model 3; Table 3). Thus, we consider that the types of social activities in which one regularly takes part in could reflect his or her personal habits and customed lifestyle, which would not be so easily affected by single SI. On the contrary, sensory deficits, especially hearing impairment, might curtail the frequency of social activities by compromising physical functions, mobility,

TABLE 4 Longitudinal generalized linear analysis of sensory impairments and social isolation, 2011–2018.

Sensory status	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]	
	IRR/OR	95%CI	IRR/OR	95%CI	IRR/OR	95%CI	IRR/OR	95%CI
Social disconnectedness: types								
Ref: NSI[e]								
SHI[f]	0.955	(0.903, 1.011)	0.968	(0.915, 1.024)	0.977	(0.924, 1.032)	0.976	(0.924, 1.032)
SVI[g]	0.985	(0.942, 1.029)	0.992	(0.950, 1.036)	0.998	(0.957, 1.041)	0.997	(0.956, 1.040)
DSI[h]	0.854***	(0.820, 0.890)	0.869***	(0.835, 0.905)	0.891***	(0.857, 0.927)	0.889***	(0.855, 0.925)
Social disconnectedness: frequency								
Ref: NSI								
SHI	0.891**	(0.830, 0.956)	0.895**	(0.834, 0.962)	0.925*	(0.860, 0.995)	0.924*	(0.859, 0.994)
SVI	0.959	(0.909, 1.011)	0.956	(0.907, 1.008)	0.974	(0.923, 1.028)	0.973	(0.923, 1.027)
DSI	0.792***	(0.753, 0.833)	0.793***	(0.754, 0.834)	0.827***	(0.786, 0.870)	0.825***	(0.785, 0.868)
Loneliness								
Ref: NSI								
SHI	1.328***	(1.186, 1.486)	1.316***	(1.174, 1.475)	1.310***	(1.166, 1.473)	1.294***	(1.150, 1.456)
SVI	1.267***	(1.158, 1.387)	1.241***	(1.133, 1.360)	1.237***	(1.126, 1.359)	1.228***	(1.117, 1.350)
DSI	1.623***	(1.495, 1.763)	1.579***	(1.453, 1.716)	1.576***	(1.447, 1.716)	1.545***	(1.418, 1.684)

The results of the longitudinal generalized linear models were expressed as the incidence rate ratio (IRR) or odds ratio (OR) with 95% confidence intervals (CI). The analytic sample size was 6,859.

[a]Model 1: adjusted for demographic factors including age and gender; [b]Model 2: adjusted for factors in Model 1, as well as social–economic including marital status, educational level, and living area; [c]Model 3: adjusted for factors in Model 2, as well as lifestyle factors including smoking status and alcohol consumption; [d]Model 4: adjusted for factors in Model 3, as well as medical conditions including multi-morbidities and insurance covering.

[e]NSI, No sensory impairment; [f]SVI, Single vision impairment; [g]SHI, Single hearing impairment; [h]DSI, Dual sensory impairment.

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

mental status, and the ability to communicate (29, 30). Hence, for the first time, our study may highlight that it is the frequency, rather than the types of social activities, that receive detrimental impacts from SI, especially hearing deficits over time in aging life. Such findings deserve certain attention and further research in the future.

4.4. SHI may exert more explicit impacts than SVI

As for single SIs, some researchers pointed out that VI seems to have more profound impacts than HI on social participation (24, 26), which they supposed might be explained that VI would exert more profoundly detrimental impacts on functional activity (55), mobility and social interactions (26). However, according to our cross-sectional and longitudinal data, we found that SHI may exert more explicitly negative impacts than SVI on the frequency of social activities among older Chinese over time (Tables 3, 4). One possible explanation for such a situation might lay in the fact that there is less feasibility and probability in the amelioration of hearing impairment than the visual deficit over time among aging Chinese. Assistive devices such as glasses and portable magnifiers are relatively efficient, economic, and easy-to-carry interventions for quite a lot of people who suffer reversible VI (56). On the contrary, interventions like wearing hearing aids for improvement of hearing status would more likely confront financial constraints, unfamiliarity with hearing aids, and difficulties during manipulating, which might all contribute to the fact that the application level of hearing aids is far less than expected among Chinese population (57). In addition to amplifying desired sounds, hearing aids would amplify noises as well, thus making users feel too loud and noisy. Such a muffled effect also jeopardizes peoples' belief in hearing aids (57). Some authors argued that, even when listening aids are used, the promotion of satisfaction might be limited in people with hearing deficits (58, 59). Therefore, untreated HI and the subsequent sustaining hearing deficit might exert more explicitly longitudinal effects on SP among our population over time.

4.5. Limitations and strengths

We need to acknowledge some limitations. Self-reports provide information about subjective perception and, therefore, are clinically highly relevant and suitable for studies on social participation and subjective perception of loneliness like ours (27). Questionnaires have also been considered as effective strategies for the early identification of sensory problems (24). However, we still need to notice the potential bias owing to the nature of self-reported data. Previous related studies adopted various definitions and evaluation methods of social isolation, which renders direct comparisons of the results from our study and those studies to be difficult. During the COVID-19 pandemic, many countries have carried out kinds of containment or restriction policies, which

is different from the definition of social isolation in aging life from the current study. However, our study could still provide a meaningful reference for such social disconnectedness and call for even more attention to an aging population with sensory impairments. Interactions among social connections and physical and mental dysfunctions in an older population with sensory impairments deserve further exploration.

Nevertheless, our study is one of the very first studies to verify both cross-sectional and longitudinal associations between sensory impairments and social isolation. We obtained data from the first nationally representative survey on the health and wellbeing status of the middle-aged and elderly population in China (CHARLS) to provide explicit evidence on this topic. Findings from the current study could be generalized to the entire country or could be even used as a reference to other developing countries. Multiple associated factors were included and adjusted in this study analyses, which could otherwise potentially confound the relationship between sensory impairments and social isolation.

5. Conclusion

Sensory impairments, especially dual sensory impairments, have explicitly detrimental effects on social disconnectedness and loneliness among older Chinese. Single hearing impairment specifically jeopardized their frequency rather than types of social activities over time. Future studies are needed to determine the mechanisms underlying these associations.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: The original dataset of CHARLS is accessible on http://charls.pku.edu.cn/.

Ethics statement

The studies involving human participants were reviewed and approved by Institutional Review Board at Peking University. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual (s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

YZ and JL: conceptualization. JW and KA: investigation and methodology. QS and YL: data curation, formal analysis, and writing—original draft. HL, YH, and GG: writing—review and editing and manuscript revision. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Progress in biological age research

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Biological age (BA) is a common model to evaluate the function of aging individuals as it may provide a more accurate measure of the extent of human aging than chronological age (CA). Biological age is influenced by the used biomarkers and standards in selected aging biomarkers and the statistical method to construct BA. Traditional used BA estimation approaches include multiple linear regression (MLR), principal component analysis (PCA), Klemera and Doubal's method (KDM), and, in recent years, deep learning methods. This review summarizes the markers for each organ/system used to construct biological age and published literature using methods in BA research. Future research needs to explore the new aging markers and the standard in select markers and new methods in building BA models.

KEYWORDS

aging, biological age, aging biomarkers, chronological age, deep learning, age

Introduction

Aging is accompanied by a progressive decline in physiological functions and an accumulation of damage to the body, leading to an increased risk of morbidity and mortality (1). Based on birth date, chronological age (CA) is the traditional criterion for assessing aging. However, the degree of aging may vary significantly between individuals with the same CA (2). Therefore, CA is not the best indicator for evaluating the degree of aging in human individuals.

To seek a better index to assess the degree of aging of individuals, biological age (BA) (3, 4) are used as alternatives to CA to estimate aging status. BA is the most popularly used model. Aging markers are the basis for constructing biological age, in this article we summarize the markers used in constructing biological age. There are many ways to classify markers of aging, e.g., the aging markers can classify into two categories: histology-based data (DNA methylation, metabolomics, proteomics, etc.), and clinical biomarkers obtained from blood chemistry, hematology, anthropometry, and organ function test measurements (5, 6). The "aging clock" developed from omics data is another form of biological age, multiple omics data can be combined to build the clock (7). Until now, omics data have rarely been used in the construction of BA because of the high cost of its application in large-scale populations. Previously built BA models commonly choose aging biomarkers in multiple organs/systems, such as blood biomarkers (8, 9), genetic indicators (10), and physical activity data (11, 12). Biomarkers from diverse organs are more reflective of the overall body state. To build the BA

model, these biomarkers apply different model building methods like multiple linear regression (MLR) (13, 14), principal component analysis (PCA) (15, 16), Klemera and Doubal's method (KDM) (3, 17), deep learning (8, 12), and other methods.

Previous studies have focused on the construction of BA models using different methods, but fewer studies have compared the BA models constructed by these methods, especially the advantages and disadvantages between deep learning and traditional methods. This review focuses on BA models constructed by four common approaches, namely composite or combined biomarkers that include a lot of aging markers. A more accurate biological age can only be constructed on the basis of knowing the advantages and disadvantages of existing methods. Table 1 provides a review of the more important, influential, and newly published literature with the four approaches above (3, 4, 8–16, 18–51), including cross-sectional and longitudinal studies.

Selection of aging biomarkers

Candidate biomarkers

The candidate biomarkers are a crucial factor to determine the final selected aging biomarkers. The most frequently used candidate biomarkers are routine clinical tests. These include age, sex, blood pressure, respiratory rate, pulse, heart rate, routine blood tests, blood biochemistry, routine urine tests, lung function, endocrine hormones (27, 34), and inflammatory factors (3, 38). Several metrics can be used to evaluate the same organ, and the best one is generally picked. For example, urea nitrogen (BUN), blood creatinine, and cystatin C (CYSC) are relevant to renal function. CYSC is a more sensitive marker of the endogenous glomerular filtration rate than blood creatinine (52). It has proven to be more suitable for BA models than blood creatinine and BUN (16, 30). Changes in body morphology (27, 29, 40) reflect the growth and nutritional statuses of the target population, such as waist circumference (WC), waist-to-hip ratio, waist-to-height ratio (WHtR), body mass index, and body fat. Abdominal obesity can occur in older adults with increased abdominal fat accumulation. Studies have shown that WHtR and WC are good indices to identify obesity in the elderly (53). Cognitive tests (4, 22, 45) are available to examine brain function, such as the trail making test, the digit symbol test, and the mini-mental state examination. Sensory tests (15, 29, 54), such as hearing, visual acuity, and vibration perception, are relatively less applied due to the cumbersome and specialist nature of the measurement process. Some parameters reflecting physical exercise capacities, such as grip strength (13) and vertical jump (31), are not only valuable for the BA model. They have also been used to structure physical (fitness) age (18, 19, 21) to assess aging. Imaging indices, such as cardiac and carotid ultrasound, are suitable biomarkers of aging for estimating BA (10, 16).

Aging is not a single process but is rather governed by a comprehensive range of factors, including disease, environment, lifestyle habits, and genetics. Health status, work experience, lifestyle, and dietary habits are often obtained through questionnaires (4, 22). Some genetic indicators are also taken as candidate aging biomarkers in the BA model, such as single nucleotide polymorphisms and terminal telomere restriction fragments (TRF). Nevertheless, probably because of its high detection cost in the population, genetic indicators are less applied in biological age. Zhang et al. (16) investigated polymorphic loci on P16, Sirt1, IL6, and Klotho genes associated with aging. Limited by the size of the sample population and the genes tested, the genes could not be used in BA models. TRF length is considered a genetic biomarker of aging at the cellular level (55), reflecting the dynamic aging process (56). TRF was found to be a promising aging biomarker in healthy aging populations (10).

Selection criteria for aging biomarkers

Researchers or organizations in the field of aging have proposed criteria for selecting aging biomarkers, such as Butler et al. (57) and the American Federation for Aging Research (58), but no consensus has been reached. There are also some commonalities between the criteria, including aging biomarkers that predict age-related body functions, low or noninvasive assays, and high reproducibility (55). Costa and McCrae concluded that generic biomarkers of aging explain most of the changes that occur with increasing age (59, 60). This is similar to the criterion, proposed by Butler et al. (57), that aging biomarkers change with *CA*. An interesting question is if aging biomarkers can be selected according to their correlation with *CA*. First, it is associated with the method of estimating BA. When using MLR, PCA, and KDM methods, the initial step is to calculate the correlation between biomarkers and *CA*. This process is replaced by automatic machine learning in deep learning methods, which have a series of complex algorithms. Second, consider experiments that discovered biomarkers of aging and empirically found various physiological, biochemical, and imaging indicators that significantly correlate with age or analyzed age correlations from extensive data obtained from multiomics (2). In contrast, the selection of aging biomarkers in studies oriented to aging mechanisms is based on a hypothesis about the causes of aging (2). Finally, some investigators (61, 62) have given the more reasonable view that this correlation is not a reasonable criterion for selecting, validating, or weighting aging biomarkers, and some biomarkers moderately associated with CA may be utterly unrelated to aging. It follows that the correlation of aging biomarkers with CA is not equivalent to a causal relationship between aging biomarkers and senescence simply because there is no better alternative to correlation for screening markers. We summarized the standard selection criteria for aging biomarkers in the BA model (Table 2), including those significantly correlated with CA; nonredundant variables; monitoring the underlying mechanisms of the aging process rather than the effects of disease; repeatable measurements; reflecting different organ or physiological functions; and biomarkers used in previous studies.

Final selected aging biomarkers

It is critical to select the correct number of representative aging biomarkers to evaluate BA. The aging biomarkers of BA models in different systems are summarized in Table 3. In analyzing the differences in the final selection of aging biomarkers by different investigators, the preference is related to the study population. Some researchers (16, 18) choose all subjects to be healthy or almost healthy to exclude the effects of disease. There were also studies (31, 36) in

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TABLE 1 The basic information of BA models in different populations.

Assessment methods	Researchers	Year	Country	Sample size	Age range	Population	Aging biomarkers (Candidate → Final)
MLR	Hollingsworth et al.	1965	Japan	169 Males 268 Females	10–70+ years	General population	17 → 9
MLR	Webster and Logie	1976	Australia	1,080 Females	21–83 years	General population	37 → 7
MLR	Takeda et al.	1982	Japan	200 Males	20–69 years	Healthy population	10 → 5
MLR	Voitenko and Tokar	1983	Soviet Union	88 Males 109 Females	19–73 years	General population	122 → 11
MLR	Dubina et al.	1984	Soviet Union	100 Males 63 Females	60–100 years	Healthy population	21 → 3
MLR /PCA	Nakamura et al.	1988	Japan	462 Males	30–80 years	Healthy population	30 → 11
PCA	Nakamura et al.	1989	Japan	69 Males	Average 42.6 ± 9.4 years	Healthy population	18 → 7
PCA	Nakamura et al.	1990	Japan	65 Females	20–64 years	Healthy population	18 → 9
PCA	Nakamura et al.	1996	Japan	221 Males	20–85 years	Healthy population	17 → 8
PCA	Nakamura and Miyao	2003	Japan	86 Males	31–77 years	Healthy population (including some early functional decline or disease)	25 → 9
PCA	Ueno et al.	2003	Japan	981 Females (cross-sectional study) 110 Females (longitudinal study)	28–80 years	Healthy population	31 → 5
PCA	Nakamura and Miyao	2007	Japan	86 Males	31–77 years	Healthy population (including some early functional decline or disease)	29 → 5
MLR	Bae et al.	2008	Korea	1,302 Males 2,273 Females	40–88 years	General population	80 → 25
PCA	Nakamura and Miyao	2008	Japan	86 Males 93 Females	31–77 years	Healthy population (including some early functional decline or disease)	29 → 5
PCA	Park et al.	2009	Korea	1,588 Males	30–77 years	Healthy population (including some early functional decline or disease)	11
PCA	Bai et al.	2010	China	392 Males 460 Females	30–98 years	Healthy population (including some early functional decline or disease)	108 → 8
MLR/PCA/KDM	Cho et al.	2010	Korea	200 Males	30–70 years	General population	16 → 11/3 principal components
PCA	Jee et al.	2012	Korea	1,604 Males 760 Females	30–85 years	Healthy population	14 → 8
MLR	Bae et al.	2013	Korea	66,168 Males 55,021 Females	20–89 years	General population	34

(Continued)

TABLE 1 (Continued)

Assessment methods	Researchers	Year	Country	Sample size	Age range	Population	Aging biomarkers (Candidate → Final)
MLR/PCA/KDM	Levine	2013	United States	9,389 People	30–75 years	NHANES (1988–1994)	21 → 10
PCA	Zhang et al.	2014	China	505 People	35–91 years	Healthy population	114 → 7
PCA	Zhang et al.	2014	China	69 Males 70 Females	35–91 years	Healthy population	105 → 6
KDM	Belsky et al.	2015	New Zealand	954 People	38 years	The Dunedin Study (1972–1973)	10
KDM	Mitnitski et al.	2016	Canada	1,013 People (61.6% Females)	Average 80.8 ± 7.2 years	Canadian Study of Health and Aging (1991–1992)	22 → 10
DNN	Putin et al.	2016	Russia	62,419 People	0–100 years	Anonymous population	41
MLR/PCA/KDM	Jee and Park	2017	Korea	912 Females	30–80 years	Healthy population	31 → 8
PCA	Kang et al.	2017	Korea	165,395 Males 98,433 Females	Average 44.2 ± 10.6 years	Healthy population (including some early functional decline or disease)	5
PCA	Zhang et al.	2017	China	581 Males 792 Females	19–93 years	Healthy population	74 → 5
KDM	Brown et al.	2018	United States	1,356 Males 1,420 Females	70–79 years	The Health ABC Study (2013.11)	8
DNN	Mamoshina et al.	2018	Korea, Canada, Eastern Europe	142,379 People	≥20 years	Anonymous population	19
KDM	Murabito et al.	2018	United States	2,532–3,417 People	Average 45/62/67 years (Exam 2/7/8)	The Framingham Heart Study Exam 2 (1979–1983) Exam 7 (1998–2001) Exam 8 (2005–2008)	clinical BA:6 inflammatory BA:9
CNN	Pyrkov et al.	2018	United States	7,454 People (51% Females)	6–84 years	NHANES (2003–2006)	1-Week Activity Data
KDM	Hastings et al.	2019	United States	6,731 People (52% Males)	20–84 years	NHANES (1999–2002)	12
MLR/PCA/KDM	Jee	2019	Korea	940 Males	30–80 years	Healthy population	32 → 6
DNN	Mamoshina et al.	2019	Canada	149,000 People	Average 55 years	Anonymous population	18/20/23(three DNN models)
ConvLSTM	Rahman and Adjeroh	2019	United States	7,104 People	18–84 years	NHANES (2003–2006)	1-Week Activity Data
KDM	Gaydosh et al.	2020	China Taiwan	951 People	Average 67.7 ± 8.3 years	Social Environment and Biomarkers of Aging Study (2000)	11
KDM	Zuyun Liu et al.	2020	China	8,119 People (53.5% Females)	20–79 years	China Nutrition and Health Survey (2009)	27 → 12
KDM	Parker et al.	2020	United States	1,374 People (35% Males)	71–102 years	Duke Established Populations for Epidemiologic Studies of the Elderly (1991–1992)	10
MLR/PCA/KDM	Zhong et al.	2020	Singapore	2,844 People	55–94 years	Singapore Longitudinal Aging Studies (2008.03–2013.11)	68 → 8/10(Males/Females)

(Continued)

TABLE 1 (Continued)

Assessment methods	Researchers	Year	Country	Sample size	Age range	Population	Aging biomarkers (Candidate → Final)
PCA/KDM	Chan et al.	2021	UK	141,254 People	40–70 years	Healthy population	110 → 51 principal components
DNN	Gialluisi et al.	2021	Italy	23,858 People (51.7% Females)	Average 55.9 ± 12.0 years	The Moli-Sani Study (2005.03–2010.04)	36
KDM	Kuo et al.	2021	UK	294,293 People	Average 56.7 ± 8.0 years	UK Biobank (2006–2010)	7
CNN	Raghu et al.	2021	United States	116,035 People	40–100 years	General population	Chest X-ray dataset
MLR/KDM	Bahour et al.	2022	United States	2,459 People	20–80 years	Diabetes, pre-diabetes, and NHANES (2017–2018) population	8
Deep learning	Nusinovici et al.	2022	Korea	40,480 People	≥65 years	Korean Health Screening study	retinal photos

MLR, multiple linear regression; PCA, principal component analysis; KDM, Klemera and Doubal's method; DNN, deep neural networks; CNN, convolutional neural networks; ConvLSTM, deep convolutional long-term memory; NHANES, National Health and Nutrition Examination Survey.

TABLE 2 The selection criteria for aging biomarkers among MLR, PCA, and KDM.

Selection criteria	Assessment Methods
Significantly correlated with CA	MLR (3, 13, 14, 20–22, 27, 32, 35, 40, 45, 54), PCA (3, 4, 10, 16, 18, 19, 23–26, 28–30, 35, 40, 45, 54), KDM (3, 34, 35, 40, 45, 54)
Non-redundant variables	MLR (35, 40, 45), PCA (4, 10, 16, 25, 26, 28–31, 35, 36, 40, 45), KDM (35, 40, 43, 45)
Used in previous studies	MLR (3, 22, 27, 32, 54), PCA (3, 54), KDM (3, 33, 37–39, 42–44, 48, 54)
Monitors the underlying mechanisms of the aging process rather than the effects of disease	MLR (20, 32, 35, 40), PCA (29, 31, 35, 40), KDM (35, 40, 43)
Repeatable measurements	MLR (14, 35), PCA (35, 46), KDM (35, 38, 46)
Reflects different organs or physiological functions	MLR (13, 15, 54), PCA (15, 23, 54), KDM (38, 54)
Variables with higher loadings within the first principal component	MLR (3, 15), PCA (3, 10, 15), KDM (3)
Test results can be quantified	MLR (35), PCA (16, 30, 31, 35, 46), KDM (35, 46)

which people in the early stages of adisease were included. In addition, the sample size, gender composition, age, and ethnicity of the study population can also impact the results. Moreover, BA models for specific populations, such as the elderly (37, 44) and the young (33), offer the possibility to explore aging differences between individuals within the same age group and potential clinical applications. Second, the choice is associated with candidate aging biomarkers; candidate biomarkers and investigators' research directions and perceptions have a significant impact. Then, the choice of biomarkers is related to the selection criteria. The thresholds for correlation selection varied across trials. In recent years, some investigators (42, 44) building BA models referred to previously published biomarkers of aging, which are generally screened in large populations, used by others and have good reliability. Examples include the 10 biomarkers of aging that Levine initially selected in the third National Health and Nutrition Examination Survey (NHANES) population and the nine biomarkers of aging that were subsequently acquired through machine learning (3, 63). Finally, the selection is affected by the BA assessment approach. The MLR and PCA select aging biomarkers that correlate linearly with CA, and the KDM can be used in the nonlinear case of aging biomarkers (17). On the other hand, deep learning also answers whether candidate aging biomarkers can be selected through powerful fitting capabilities. One example is that chest radiographs, which researchers once discarded because they could not be quantified, have recently been used to construct BA models (49). Briefly, the final selection of aging biomarkers by research staff affected the study population, the candidate aging biomarkers, the selection criteria, and the method of BA evaluation.

Biological age assessment method

Multiple linear regression

Hollingsworth et al. (13) selected nine age-related indicators of physiological function and innovatively used MLR to predict BA in the Japanese Hiroshima population. This approach has since been widely used. The independent variable was selected according to the

TABLE 3 The common aging biomarkers of four methods in different systems.

System	MLR	PCA	KDM	Deep learning
Cardiovascular system	SBP (3, 13, 15, 20, 22, 27, 32, 35, 40)	SBP (3, 15, 18, 19, 23–26, 28, 29, 31, 35, 40)	SBP (3, 33, 35, 37–40, 42, 43, 48)	
	DBP (27, 32, 45)	DBP (45)	DBP (34, 45)	
	Pulse pressure (32)	Pulse pressure (4, 16, 30)		
		Mean arterial pressure (36)		
	Pulse (15)	Pulse (15, 18)		
	Pulse wave velocity (22)			
		Heart rate (19)		
		Intima-media thickness (10, 30)		
		Minimum intima-media thickness (4, 16)		
		End diastolic velocity (30)		
		mitral valve E/A peak (4, 30)		
		MVEL (30), MVES (16), MVEA (10)		
		Atherosclerosis index (18, 19)		
				NT-proBNP (47)
				Cardiac troponin I (47)
	Creatine phosphokinase (32)			
	Homocysteine (32)			
Respiratory system	FVC (15, 27, 32, 54)	FVC (15, 18, 19, 23, 24)	FVC (54)	
	FEV1 (3, 20, 21, 27, 32, 35, 40, 45)	FEV1 (3, 24–26, 28, 29, 31, 35, 40, 45)	FEV1 (3, 33, 35, 37, 38, 40, 45)	
	Vital capacity (13, 22)			
		Maximal midexpiratory flow rate 75/25 (16)		
		VO_2 max (29, 31)		
				Chest radiography (49)
Nervous system	MMSE (45)	MMSE (45)	MMSE (45)	
	Digital symbol test (22)	Digital symbol test (10)		
	Numeric memory (54)		Numeric memory (54)	
	Associated memory (54)		Associated memory (54)	
	Topological memory (54)		Topological memory (54)	
	Short-time memory (14)			
	Concentration (54)		Concentration (54)	
	Intellectuality -mental defect (22)			
		Trail making test (4, 16)		
Endocrine metabolic system	Glucose (27, 32)	Glucose (23, 25, 36)	Glucose (38)	Glucose (8, 9, 41, 47)
	HBA1C (3, 32)	HBA1C (3, 29)	HBA1C (3, 33, 37, 39, 42–44, 48)	HBA1C (41)
				C-peptide (47)
				Insulin (47)
	Triglyceride (20, 27, 32)	Triglyceride (19, 36)	Triglyceride (43)	Triglyceride (9, 47)
	TC (3, 13, 15, 20, 21, 27, 32, 35)	TC (3, 15, 23, 35)	TC (3, 33, 35, 37, 38, 42, 43, 48)	TC (8, 9)
	HDL (27), LDL (32)	HDL (36), LDL (29)		HDL (9, 47),LDL (9, 47)
				Apolipoprotein A1 and B (47)
	TSH (27)		TSH (34)	
	Testosterone (27)			Testosterone (47)
	Vitamin D (40)	Vitamin D (40)	Vitamin D (40)	Vitamin D (47)
			Calcium (34)	Calcium (9)
				Potassium (9)
				Sodium (9)
			Inorganic phosphorus (34)	

(Continued)

TABLE 3 (Continued)

System	MLR	PCA	KDM	Deep learning
Urinary system	Urea (3, 15, 20, 32, 35)	Urea (3, 15, 18, 19, 23, 24, 26, 28, 29, 35)	Urea (3, 33–35, 39, 42–44)	Urea (8, 9, 41)
	Creatinine (3, 27, 32, 35, 40)	Creatinine (35, 40)	Creatinine (3, 33, 34, 37, 39, 42–44, 48)	Creatinine (9, 47)
	eGFR (45)	eGFR (45)	eGFR (45)	
			Uric acid (39, 44)	Uric acid (47)
		Cystatin C (4, 10, 16, 30)		Cystatin C (47)
	Creatinine clearance (32)			
	Urine specific gravity (32)			
	Urine pH (32)			
Digestive system	ALT (32)	ALT (23)		ALT (47)
	AST (15, 32, 35)	AST (15, 18, 19, 35)	AST (35)	AST (47)
	ALP (3, 20, 32)	ALP (3)	ALP (3, 33, 34, 37, 39, 44, 48)	ALP (8)
	Total protein (32)		Total protein (34)	Total protein (9)
	Albumin (3, 15, 32)	Albumin (3, 15, 24, 26, 28, 29)	Albumin (3, 33, 34, 37, 39, 42–44, 48)	Albumin (8, 9, 47)
	A/G (15, 32)	A/G (15, 24, 25)		
	Total bilirubin (32)			Total bilirubin (9)
	Direct bilirubin (32)			
	Amylase (32)			
	Lactate dehydrogenase (21, 32)	Lactate dehydrogenase (19, 23)		
				Alpha 2 globulin (8)
	Gamma glutamyl transpeptidase (32)			
Hematologic System	Red blood cell (40)	Red blood cell (24, 28, 40)	Red blood cell (40, 43)	Red blood cell (8, 9, 47)
			Red blood cell volume distribution width (39)	Red blood cell volume distribution width (8, 47)
		Hematocrit (24, 26)		Hematocrit (8, 9)
			Mean corpuscular volume (39, 42, 44)	Mean corpuscular volume (9, 47)
		Mean corpuscular hemoglobin (25)		
				Mean corpuscular hemoglobin concentration (9, 47)
	Hemoglobin (15, 45)	Hemoglobin (15, 18, 19, 23, 24, 45)	Hemoglobin (34, 45)	Hemoglobin (9, 47)
			White blood cell (39, 42, 44)	White blood cell (47)
				Granulocytes (47)
				Neutrophils (47)
				Basophils (47), Eosinophils (47)
			Lymphocytes (39, 42, 44)	Lymphocytes (8, 47)
	Monocytes (45)	Monocytes (45)	Monocytes (45)	Monocytes (47)
			Platelet (43)	Platelet (9, 47)
				Mean platelet volume (47)
				Platelet distribution width (47)
	Erythrocyte	Erythrocyte		
	sedimentation rat (20, 27)	sedimentation rat (29)		
		D-dimer (10) Fibrinogen (30)		D-dimer (47)
	Ferritin (35)	Ferritin (35)	Ferritin (35, 43)	Ferritin (41)
			Fransferrin (43)	

(Continued)

TABLE 3 (Continued)

System	MLR	PCA	KDM	Deep learning
Sensory system	Visual accommodation (22, 54)		Visual accommodation (54)	
	Visual reaction time (54)		Visual reaction time (54)	
	Visual acuity (13, 15)	Visual acuity (15)		
	Hearing (13, 21, 22, 54)	Hearing (29)	Hearing (54)	
	Vibrotactile (13, 14, 54)		Vibrotactile (54)	
				Retinal photos
Inflammatory index	CRP (3)	CRP (3)	CRP (3, 33, 37–39, 42–44, 48)	CRP (47)
	Cytomegalovirus optical density (3)	Cytomegalovirus optical density (3)	Cytomegalovirus optical density (3, 33, 42)	
			Interleukin-6 (38)	
			P-selectin (38)	
Motion index	Grip strength (13, 14, 45, 54)	Grip strength (31, 45)	Grip strength (45, 54)	
		Vertical jump (31)		
	Timed up and go test (45)	Timed up and go test (45)	Timed up and go test (45)	
	Chair rise time (45)	Chair rise time (45)	Chair rise time (45)	
				1-week physical activity (11, 12)
Body morphology index	WC (32, 35)	WC (29, 31, 35, 36)	WC (35)	
	Waist-to-hip ratio (27, 32)			
	Waist-to-height ratio (40)	Waist-to-height ratio (40)	Waist-to-height ratio (40)	
	Body mass index (27, 32)			
	Weight (22)			
	Height (45)	Height (45)	Height (45)	
	Body fat (27, 32)	Body fat (29)		
	Lean body mass (27, 32)			
		Soft lean mass (31)		
Genetic index		Terminal telomere restriction fragment (10)		
Genetic index		Terminal telomere restriction fragment (10)		

SBP, systolic blood pressure; DBP, diastolic blood pressure; NT-proBNP, N-terminal pro brain natriuretic peptide; MVEA, mitral annulus peak E anterior wall; MVEL, mitral valve annulus lateral wall of peak velocity of early filling; MVES, mitral valve annulus ventricular septum of the peak velocity of early filling; FEV1, forced expiratory volume in 1.0 s; FVC, forced vital capacity; MMSE, mini-mental state examination; eGFR, estimated glomerular filtration rat; HBA1C, glycosylated hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; TSH, thyroid stimulating hormone; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; ALP, alkaline *phosphatase; A/G, ratio of albumin to globulin; CRP, c-reactive protein; WC, waist circumference.*

correlation between biomarkers and CA, and the individual's BA was used as the dependent variable to establish the MLR equation:

$$BA_i = b_0 + \sum_{j=1}^{m} b_j x_{ji} \quad (1)$$

In Eq. (1), m is the number of aging biomarkers, and x_{ji} ($i = 1...n$, $j = 1...m$) represents the jth aging biomarker of the ith individual (54). Moreover, b_0 and b_j are the intercept and regression coefficients, respectively, calculated by the least-squares method. The BA model constructed using the MLR requires an F test for the significance of the regression equation, a t test for the significance of variables, and a goodness-of-fit test for how well the model fits the variables.

MLR has collinearity problems (54, 62), which can be diagnosed by the variance expansion factor method and characteristic root determination method, eliminating some unimportant independent variables and increasing the sample size to eliminate collinearity. MLR fails to avoid the biomarker paradox, where biomarkers perfectly associated with CA are insensitive in individuals (54). In addition, the BA values calculated by MLR are distorted at both ends of the regression equation (54, 62). Dubine et al. (14) proposed using the Z score to solve this problem. The equation for the Z score corrected BA equation is as follows:

$$Corrected\ BA = BA_i + Z \quad (2)$$

Here, $Z = (CA_i\text{-}MEAN_{CA}) \times (1\text{-}b)$, where CA_i is the chronological age of the individual, $MEAN_{CA}$ is the average chronological age of the population in which the individual is located, and b is the slope in the simple linear regression, representing the relationship between BA and *CA*.

Principal component analysis

PCA was first used by Nakamura et al. (15) to estimate BA in Japanese populations, subsequently becoming popular in Korea, China, and other countries (3, 16, 29, 30). Our team was the first to utilize PCA to evaluate BA in healthy populations in China (30). For nearly 20 years, we have structured BA models based on data from single-centered and multicentered populations, finding that aging biomarkers such as CYSC and carotid intima-media thickness were closely associated with aging in the Chinese population (4, 10, 16, 30).

The steps of building a BA model by PCA are summarized as follows: (1) select aging biomarkers by correlation analysis, stability analysis, and redundancy analysis (64); (2) convert potentially relevant aging biomarkers into linearly uncorrelated principal components by orthogonal transformation; and (3) select the first principal component or multiple principal components to create the formula for predicting BA. When the PCA selects only the first principal component, the critical aging biomarkers can be further screened by principal component loading (3). The colinearity problem can be avoided if multiple principal components are selected as new variables (54). Both approaches have their advantages. The biological age score (BAS) formula constructed by selecting the first principal component as an example is as follows:

$$BAS = a_1 X_1^{'} + a_2 X_2^{'} + \ldots + a_n X_n^{'} \tag{3}$$

Here, X' is the standardized biomarker of aging, a_n is the score coefficient of aging biomarkers, where X' is computed from the equation $\frac{X - MEAN(X)}{SD(X)}$ and $MEAN(X)$ and $SD(X)$ are the mean and standard deviation of the aging biomarkers, respectively. Because the BAS is not measured in years, Nakamura et al. (15) used the T-score to convert BAS to BA:

$$BA = BAS \times SD_{CA} + MEAN_{CA} \tag{4}$$

In Equation (4), SD_{CA} and $MEAN_{CA}$ are the variance and mean of the chronological age of subjects, respectively. Similar to the MLR method, to avoid regression of BA values toward the mean age of the sample, the Z score was used to correct BA (10, 16), as in Formula (2).

Klemera and Doubal's method

KDM was first proposed by Klemera and Doubal (17) in 2006 and is now broadly available for aging and aging-related research. The KDM formula development process incorporates certain core hypotheses (17): (1) The hypothesis is that "the difference in BA is the difference among individuals aging in the same CA population." A random variable $R_{BA}\left(0;S_{BA}^2\right)$ with mean 0 and variance S_{BA}^2 was used to replace the differences in individual BA, establishing the formula:

$$BA = CA + R_{BA}\left(0;S_{BA}^2\right) \tag{5}$$

(2) Another hypothesis is that "the actual value of aging biomarker X is not only regulated by BA but also influenced by transient effects that are not BA dependent" (17). A random variable $R_X\left(0;S_X^2\right)$ with mean 0 and variance S_X^2 is used to represent the transient effect. An inverse regression equation similar to the Hochschild (65) view is obtained:

$$X = F_X\left(BA\right) + R_X\left(0;S_X^2\right) \tag{6}$$

Here, $F_X\left(BA\right)$ is considered a simple linear equation with independent variable BA, intercept q, and slope k. Subsequently, Klemera and Doubal developed two formulations, shown in Eqs (7) and (8), for calculating BA through sophisticated mathematical derivations, the distinction being the inclusion of CA as an independent variable in Eq. (8) (17).

$$BA_E = \frac{\sum_{j=1}^{m}\left(x_j - q_j\right)\left(\frac{k_j}{s_j^2}\right)}{\sum_{j=1}^{m}\left(\frac{k_j}{s_j}\right)^2} \tag{7}$$

$$BA_{EC} = \frac{\sum_{j=1}^{m}\left(x_j - q_j\right)\left(\frac{k_j}{s_j^2}\right) + \frac{CA}{S_{BA}^2}}{\sum_{j=1}^{m}\left(\frac{k_j}{s_j}\right)^2 + \frac{1}{S_{BA}^2}} \tag{8}$$

where x_j, q_j, k_j, and s_j^2 $(j=1...m)$ represent the *jth* aging biomarker and its intercept, slope, and transient effect, respectively. The detailed derivation process is available in their paper. Cho et al. (54) improved the algorithm of KDM to simplify the computing flow. In the KDM2 model they developed, PCA was introduced, and multiple sets of principal components were selected instead of the original aging biomarkers (54). Levine (3) used the modified method that combined PCA to construct the KDM2 model, with the difference being that they selected the key aging biomarkers within the first principal component. In addition, the Δage (Δage = BA-CA) was determined by the KDM method and is more practical than calculating the BA of an individual (34). Recently Kwon and Belsky developed an R package containing the KDM method: BioAge, for facilitating biological age measurement (66).

Deep learning

Deep learning is a subfield of machine learning, where good features can be learned automatically using a general-purpose learning procedure (67). Deep neural networks (DNNs) (8, 9, 41, 47), convolutional neural networks (CNNs) (11, 49), and recurrent neural networks (RNNs) (12) have been employed to build BA models in recent years.

A DNN consists of an input layer that receives external data, several hidden layers responsible for feature extraction, and an output layer that outputs the final result. Round-by-round iterations are performed with activation functions (68), gradient descent (69), and backpropagation algorithms to transform the input data into results for solving regression or classification problems. In 2016, Putin et al. constructed a model for predicting BA using a DNN, which is placed at www.aging.ai for public usage; the BA can be estimated by entering the complete 41 blood markers or just the most crucial 10 markers (8). The model performed poorly in non-Eastern European populations due to population differences (70). Mamoshina et al. trained a DNN with a dataset containing ethnically diverse populations to enhance accuracy in computing BA in Canadian, Korean, and Eastern European populations (9). More recently, Gialluisi et al. created a DNN based on 36 circulating biomarkers to estimate BA in Italians (47). It is worth considering that suitable approaches should be explored in deep learning to clarify the weight and importance ranking of individual aging biomarkers to assess their importance. Permutation feature importance (PFI) is an algorithm derived from the random forest that explains the importance of aging biomarkers in DNNs (8, 9). To explore the effect of smoking on BA, Mamoshina et al. used PFI to rank biomarkers and selected the top-ranked biomarkers to construct three DNNs and found that smoking accelerates aging (41).

Used chiefly for image analysis, CNNs are mainly composed of convolutional and pooling layers with features such as local connectivity and weight sharing, simplifying the number of parameters and the complexity of calculations (67). The convolutional layer converts the input information into an output feature map with multiple feature mappings employing a specific number of filters. The pooling layer is intended to reduce the information output from the convolution layer. It is executed immediately after the convolution, completed by the maximum, minimum, or average value of operations. Pyrkov et al. selected physical activity data recorded by wearable devices of NHANES participants for 1 week as a biomarker of aging and generated a BA model with a CNN (11). Raghu et al. built a BA model using chest radiograph data combined with a CNN (49).

RNNs are designed with a loop/repeat structure to preserve valuable historical information in sequences through "state vectors" to better process sequence data. RNNs suffer from long-term dependency problems (71) such as vanishing or exploding gradient when learning on long sequences. Hochreiter and Schmidhuber (72) proposed the long short-term memory network (LSTM) to solve this problem, adding the *cell state* unit and the *gate unit* based on the ordinary RNN. Thus, LSTM can handle short-term information sensitively and remember valuable information for a long time, which improves the network's learning ability. Rahman and Adjeroh (12) also used physical activity data from 1 week. Considering the temporal information contained in the data, they adopted a deep convolutional long-term memory (ConvLSTM) method to develop a BA model that outperformed other deep learning approaches (12).

Other methods

In addition to the four popular methods mentioned above, some researchers have tried to find the best model to assess BA, starting from the aspect of the impact of aging markers on life expectancy. Hochschild (62, 65, 73) suggested a nonstandard, complex, but reasonable approach to estimating BA. Taking a questionnaire format, he collected mortality risk factors, such as smoking, diet, and exercise, and aggregated these indicators into a "composite validation variable (CVV)." The standardized biological age was then calculated by the correlation coefficient between CVV and aging markers and finally transformed into BA in years. Some studies used correlations with mortality to identify aging variables. Twelve clinical indicators associated with mortality were selected by Drewelies et al. and validated in two independent birth cohorts (74). Levin and coworkers (63, 75) determined the "phenotypic age" through a multifactorial analysis of mortality risk, an algorithm known to some researchers (39, 44) as "LM BA." First, nine aging biomarkers associated with mortality were selected with machine learning. Then, two Gompertz proportional hazards models were developed to predict the mortality risk, called the "mortality score," and converted to biological age values. In addition, Pyrkov et al. constructed BA models to predict both CA and life expectancy, further discussing the relative performance of the models in stratifying the effects of diseases and lifestyles (11). However, these approaches are not widely used for two main reasons: one, a mortality event is required to calculate the aging rate, which is a lengthy process for the follow-up of a normally aging population; second, even if death occurs, many cannot distinguish whether it is due to death from disease or natural death from aging.

Comparison of the four assessment methods

There is no perfect way to evaluate BA. Each researcher should select the proper approach according to the study's purpose, sample population, laboratory conditions, funding, statistical knowledge, and programming ability. A summary of the strengths, limitations, and possible practical improvements of the four BA assessment methods is presented in Table 4. MLR is the simplest way to measure BA but suffers from the biomarker paradox, edge distortion, and colinearity (54). "collinearity" refers to linear regression in which the accuracy of the model may be affected by the presence of highly correlated relationships among the independent variables, and "edge distortion" refers to distortion at both ends of the linear regression, where the estimated BA values are too large or too small. PCA can further screen aging biomarkers or solve the covariance problem. However, PCA selects aging markers based on correlation with CA and cannot settle the paradox of biomarkers. KDM uses a reverse regression equation that solves the biological paradox (65) and avoids distortion at both ends of the regression equation (76). The KDM2 model combined with PCA allows for a better valuation of mortality (3). Although BA_{EC} is superior to BA_E in predicting BA, assigning CA a similar role to other biomarkers would be controversial, as proposed by Klemera and Doubal (17). Mitnitski et al. (34) argued that CA is made an independent variable to avoid extreme values (to prevent BA from being overcalculated, e.g., 120 years) at the expense of BA clarity. Deep learning allows machines to extract features and construct BA models autonomously by learning about biomarkers. Their strengths include the ability to handle high-dimensional datasets with complex interactions and correlations to resolve problems that people do not fully understand. However, it is challenging to structure large datasets (8), and there is a "black box" in deep learning, where the specific learning process is unknown, and the results are uncontrollable.

Performance evaluation of biological age

Currently constructed BA models are mainly used to Predict the occurrence of disease or predict life expectancy. Their performance

TABLE 4 The advantages and disadvantages of the four methods and possible effective improvements.

Methods	Advantages	Disadvantages	Improvements
MLR	Simple and easy to operate	(1) Biomarkers paradox (2) co-linearity (3) Regression equation edge distortion	(1) Z-score correction edge distortion (14) (2) Co-linearity diagnosis and removal of redundant variables
PCA	(1) Avoid co-linearity (54) (2) Further screen aging biomarkers (3)	(1) Biomarkers paradox (2) Regression equation edge distortion	Z-score correction edge distortion (14)
KDM	(1) Resolving the biomarker paradox (2) Avoiding distortion at the edges of the regression equation (76) (3) Suitable for non-linear biomarkers (17)	(1) Complicated calculation (54) (2) CA as a marker of aging is controversial (34)	(1) Cho et al. improved the calculation process (54) (2) Calculating individual △age is more practical than BA (34)
Deep learning	(1) Good at handling high-dimensional dataset (67) (2) The machine extracts features autonomously by learning (67)	(1) Difficulty in building large data (8) (2) The existence of a "black box" and uncontrollable results (3) Excellent programming skills and computer hardware and software support required	(1) Suitable methods can be explored to clarify the weighting of each aging biomarker (2) Multidisciplinary Cooperation

MLR, multiple linear regression; PCA, principal component analysis; KDM, Klemera and Doubal's method.

evaluation metrics, such as R (2), reflect the superiority of the training model by the degree of fit between the estimated BA and the actual CA, however, the nonlinear fitting strategy in machine learning can cause R^2 to suffer from overfitting problems. In contrast, Δage is superior, which response to the acceleration of biological age. The validity of the model was recently confirmed by Li and Zhang et al. who trained the BA model using a healthy Beijing population and later validated the acceleration of aging by disease in a diseased population (77). However, the value of Δage may only serve a qualitative purpose, as relative acceleration or retardation of aging compared to a healthy population with the same *CA*. Some researchers have checked the efficacy of BA models through mortality (78). The introduction of a BA model with mortality training is similar to the inclusion of endpoint events in clinical trials. On the one hand, the incorporated life-length data may improve the accuracy of BA models more than the iteration of statistical methods alone; on the other hand, the exploration of endpoint mortality events may be more likely to generate public interest in BA. However, some emergencies or sudden events may affect the accuracy of biological age judgment.

Summary and prospects

BA is an integral part of the aging field. Only by accurately evaluating the individualized aging status, prompting an earlier window of aging prevention, and timely intervention for disease-prone and diseased individuals can we improve the quality of life of the elderly and prolong their lifespan (79). We investigated the selection and assessment methods of aging biomarkers in BA. Although researchers in aging have identified some aging biomarkers, due to the continuous application of new technologies, new ideas, and new groups of people, there are still many potentially better biomarkers waiting to be discovered. For example, with the increasing availability of longitudinal biological data, the organic state recovery time (resilience) has been found to be an important marker of aging, which cannot be obtained from cross-sectional data (80, 81). Moreover, the development of sequencing omics and image acquisition has provided a direction for exploring new aging biomarkers.

This review focuses on statistical methods for quantifying BA, discusses the advantages and disadvantages of different statistical methods, summarizes the different kinds of aging markers applied in biological age, also mentioned the selection criteria of aging markers. It compares traditional methods and new deep learning methods in BA research and helps clarify how to construct a more accurate new biological age. Of course, this paper has the following shortcomings: on the one hand, candidate markers and selected markers are different for each article, it cannot reflect the importance of each marker by the frequency of aging markers use; on the other hand, only a brief discussion on the performance aspects of statistical methods is made in this paper, and longitudinal or mortality verification is less; Third, there are few studies using the same population to compare the pros and cons of different methods, and more are theoretically compared. We suggest that, regarding the selection of aging markers, it is necessary to focus on both the discovery of new aging markers and the reassessment of the role of old aging markers. It is very important to develop standardized or equivalent screening criteria for aging markers. The new method is more accurate but requires a larger amount of data, and it is easy to overfit if the amount of data is small, so it is not the latest that is the best, but the right one is the best. Common BA evaluation methods have their own merits and demerits and are continuously optimized in practice. The combined use of multiple methods may yield superior results and facilitate the creation of new methods. Biological age is mostly constructed in healthy or community populations to avoid the influence of disease factors. We should pay more attention to the accuracy of applying biological age in different populations such as disease populations, progeria populations, and longevity populations. In the future, we should pay attention to the clinical translation of BA models and do further exploration for clinical utility, such as developing

assessment models suitable for different disease individuals and further revealing the complex interaction between disease and aging.

Author contributions

ZL and WZ was written the first draft of the manuscript. YD, YN, YC, XL, ZD, YZ, XzC, ZF, YW, and DZ commented on previous versions of the manuscript. XS, GC, HJ, and XmC provided enough scientific suggestions and concrete actions during the revision. All authors read and approved the final version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The role of resistance training and creatine supplementation on oxidative stress, antioxidant defense, muscle strength, and quality of life in older adults

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Background: The aim of this study was to evaluate the effect of resistance training (RT) with creatine monohydrate supplementation (CS) on serum levels of *8-hydroxydeoxyguanosine* (8-OHdG), malondialdehyde (MDA), glutathione peroxidase (GPX), and total antioxidant capacity (TAC) in older adults.

Objectives: This study evaluated the effect of resistance training with creatine monohydrate supplementation on oxidative stress and antioxidant defense, muscle strength and quality of life in older adults.

Methods: We examined 45 non-athlete volunteer older men and women (mean, 68.1±7.2 years old), were randomly selected and divided into three groups of 15: RT with creatine supplementation (RT+CS), RT with placebo (RT+P) and control group. RT protocol was performed for 10 weeks, three sessions per week. Creatine supplement was taken daily at a dose of 0.1g/kg of body weight, while the placebo group consumed the same amount of starch. Fasting blood samples were taken before the start of program and at the end of the RT period.

Results: In the training groups, after 10 weeks of RT, a significant decrease in MDA and 8 - OHDG as well as a significant increase in serum levels of GPX and TAC were observed (in all cases, $p = 0.001$). In addition, creatinine levels were enhanced in the RT+CS ($p = 0.014$). Training intervention also improved quality of life and muscle strength in the experimental groups ($p = 0.001$), although muscle strength changes were more visible in the RT+CS group than in the RT+P group ($p < 0/05$).

Conclusion: Regular resistance training can be recommended as a very suitable non-pharmacological approach to strengthen the body's antioxidant system, muscle strength and quality of life in older adults. There are no definite findings on the role of creatine on the antioxidant system and quality of life in older adults, but the use of this supplement in addition to RT can double the amount of strength gained from resistance training.

KEYWORDS

creatine, antioxidant defense, aging, quality of life, muscular endurance

1. Introduction

The production of free radicals increases from the fourth decade of life onwards, and the amount of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPX) decreases (1). Reactive oxygen species (ROS) lead to oxidative damage in lipid membranes and DNA through programmed cell death (2). Lipid peroxidation produces substances such as malondialdehyde (MDA) (3), and DNA damage is measured through *8-hydroxydeoxyguanosine* (8-OHdG) (4). One of the factors that plays an important role in the loss of an active lifestyle is the progressive reduction of muscle mass or sarcopenia (5). Muscle mass forms more than 50% of the body weight of young people, while this amount reaches approximately 25% in older adults (6).

Cumulative damage to skeletal muscle and nerve cells in sarcopenia may result from oxidative stress. Sarcopenia could be caused by an increase of endogenous ROS formation in skeletal muscle but the source of ROS in sarcopenic muscle is still relatively unknown. However, an age-associated increase of ROS levels in muscle mass, as a consequence of an upregulation of NADPH oxidase 2 enzyme (NOX_2), has been reported (7). Moreover, a study by Sullivan-Gunn and Lewandowski (8) has highlighted the role of NOX_2 enzyme in a healthy mouse model of aging, suggesting that elevated levels of H_2O_2 from NOX_2, as well as the lack of antioxidant protection from catalase and glutathione peroxidase (GPX), carry out a key role in the onset of sarcopenia. The lack of SOD_1 also causes a reduction of skeletal muscle mass, impairment of neurotransmitter release, and neuronal degeneration in mice (9).

Moreover, irrespective of the mechanism, oxidative stress causes the onset of many types of disease such as cardiovascular disease (CVD) and cancer (10, 11) as well as modulation of cancer treatment-related outcomes (12, 13). Excessive ROS levels have been linked to tumor initiation, growth and progression (14). As mentioned before, the production of ROS increases with age. Therefore, the possibility of getting diseases related to ROS increases in older adults. Therapeutic benefits of creatine supplementation (CS) in some diseases associated with oxidative stress have been confirmed (15, 16).

In the body as a whole, creatine is synthesized in the kidney and in the liver (17). Specifically, the kidney accomplishes the first step of the synthesis, forming guanidinoacetic acid from arginine and glycine. Guanidinoacetic acid is then transported to the liver, where it is converted into creatine with the intervention of the methyl donor S-adenosyl-methionine (17). Creatine monohydrate is a common and popular supplement used by many athletes to improve strength, endurance and athletic performance (18). The antioxidant properties of creatine might be due to the presence of arginine, which disintegrates nitric oxide (19). The NO formed undergoes oxidative degradation to the stable inorganic nitrogen oxides, nitrite (NO_2), and nitrate (NO_3), which are detectable in plasma and urine (20).

Resistance training (RT) has the beneficial effects of preventing the complications of aging and leads to improved health through a variety of mechanisms (21). RT has been shown to reduce MDA and hydrogen peroxidase, while boosting GPX and SOD activity (22). On the other hand, in aging, we face a phenomenon called anabolic resistance which reduces the response of muscles to RT (23).

Long-term creatine supplementation along with moderate-intensity resistance and endurance training can probably reduce oxidative stress and increase the antioxidant defense system; however, in the short-term, creatine consumption and its effect on oxidative stress due to endurance exercise is not well known, although it seems that the short-term creatine ingestion possibly reduces oxidative stress due to intense resistance exercise. Considering the antioxidant effects of regular physical activity and creatine, it seems that the combined effect of physical activity and creatine consumption can reduce oxidative stress (12).

Stefani et al. (24) noted that creatine consumption combined with resistance exercise could reduce oxidative stress (reduced lipoperoxidation in plasma, heart and liver, and gastrocnemius). Moreover, this supplement had positive effects on the SOD activity in all groups. Creatine consumption possibly have a synergistic effect with resistance training in modulating SOD activity in the heart (24). Additionally, Rahimi stated that consuming 20 g of creatine per day for 7 days reduces MDA and 8-hydroxy-20 -deoxyguanosine (8-OHdG) after resistance training. Additionally, the antioxidant effects of creatine may be related to its compounds (arginine, glycine and methionine) (25).

Most studies on the effect of resistance training (RT) and creatine supplementation (CS) on oxidant/antioxidant equilibrium have focused on young people (25). To date, the effects of regular RT alone and with CS on various oxidative markers and antioxidant defense system in older adults have not been studied.

2. Materials and methods

2.1. Ethical considerations

Before the start of the study, a meeting session was held to coordinate and explain the objectives of the project and to mention the possible risks and benefits for the participants. At the end of this session, consent forms for participation in the research were signed by the subjects. The research design was approved by the Ethics Committee of the University of Kurdistan (IR.UOK.REC.1399.010), and was also reviewed and approved at the Clinical Trial Registration Center (IRCT20201121049453N1).

2.2. Participants and study design

The current study was an experimental research with pre-test and post-test control group design. The statistical population of the present study consisted of older men and women (age: 61.5 ± 5.7 y; height: 165.9 ± 11.1 cm; weight: 75.6 ± 19.8 kg; BMI: 27.8 ± 1.6 kg/m^2) in Kermanshah city, Iran. After announcing the research call at parks and sport spaces of the city, 45 qualified people (with inclusion criteria) were randomly selected as subjects. Subjects were then randomly, in a double-blind design, assigned to three groups of 15: resistance training with creatine supplementation (RT + CS), resistance training with placebo (RT + P) and control group (Table 1; Figure 1).

2.3. Inclusion and exclusion criteria

People ranging in age from 60 to 70 years were considered. According to the information in the health questionnaire, they were in good health and did not take any medication. They also did not have a history of taking dietary supplements or regular exercise training 3 months prior to the start of the study. Exclusion criteria

TABLE 1 Baseline characteristics of subjects according to study groups.

Variable	Control group (*n* =15)	Training+placebo (*n* =15)	Training+creatine supplement (*n* =15)
Age (year)	62.5 ± 25.47	61.3 ± 31.57	61.2 ± 0.7.06
Weight (kg)	74.08 ± 18.8	75.37 ± 10.7	77.23 ± 16.9
Height (cm)	168.16 ± 9.50	162.37 ± 6.35	167.38 ± 10.92
BMI (kg/m2)	25.83 ± 5.4	28.37 ± 2.9	27.84 ± 5.1

BMI, body mass index. Values are reported as mean ± SD.

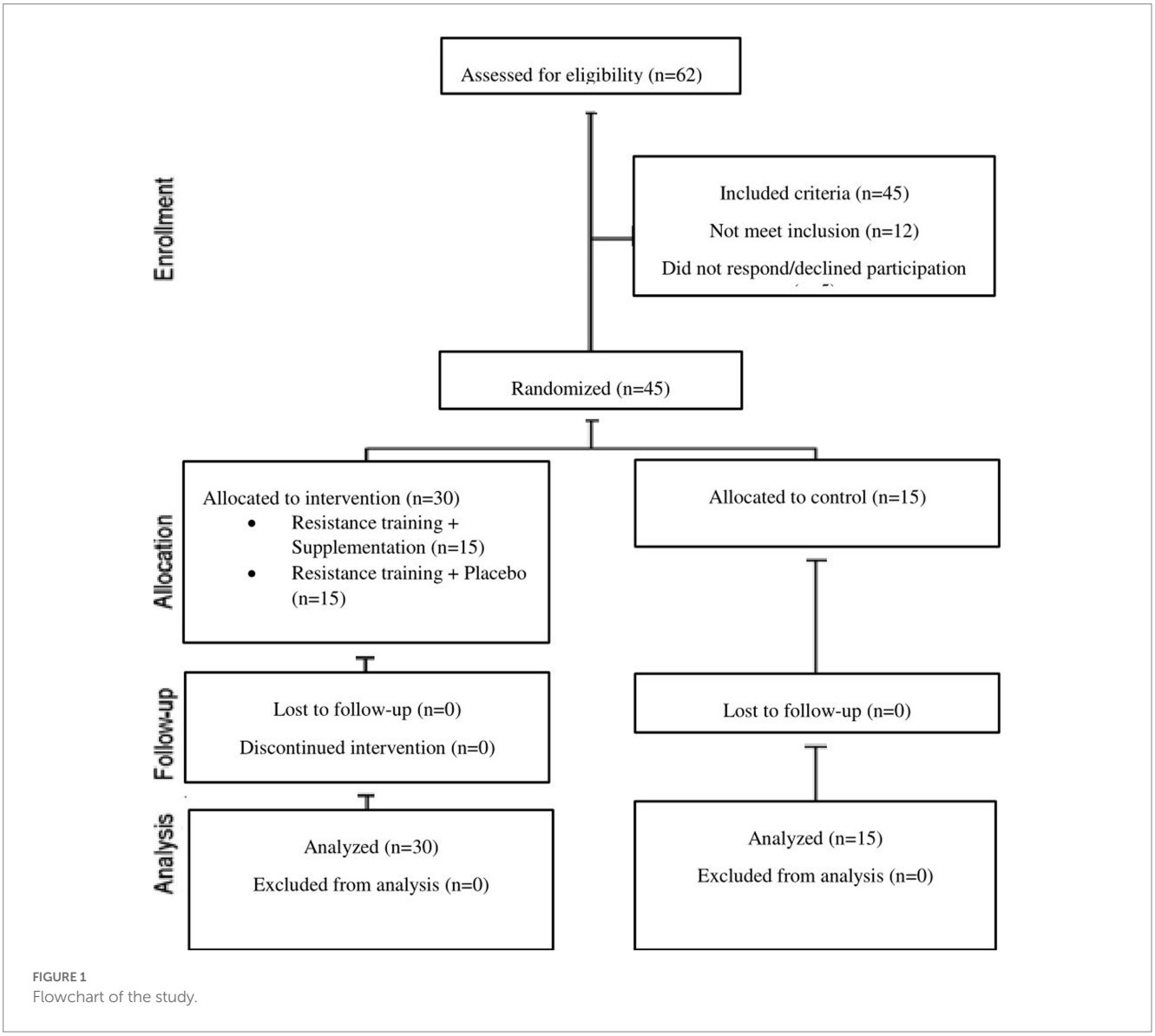

FIGURE 1
Flowchart of the study.

included any illness that required medical attention, the unwillingness of the subjects to continue cooperation, and having more than three absences in the training sessions (Figure 1).

2.4. Resistance training protocol

Resistance training program was performed for 10 weeks, three sessions per week (1 day in between). Each workout lasted approximately 70 mins and consisted of three parts: warm-up (10 mins), specific resistance exercise program (50 mins), and cool-down (10 mins). Resistance movements included leg extension and leg curl machine, barbell bench press, lateral pulldown, barbell curl, overhead press, and triceps extension machine. Resistance movements were performed in three sets with 10 repetitions and an intensity of 75% of one repetition maximum (1-RM). Rest intervals between sets and between movements were 2 and 3 mins, respectively. To maintain training intensity, 1-RM test was measured once every 2 weeks in all movements and for all subjects. The one repetition maximum (1-RM) test was calculated based on the Brzycki equation (26).

2.5. Creatine supplementation

Creatine monohydrate supplementation consisted of 0.1 g/kg/d which was consumed daily in a single dose and dissolved in a glass of water immediately after the end of the exercise session by the subjects in the RT + CS group (27, 28). Supplementation on non-training days was consumed at the same hour (6 pm). The placebo group took maltodextrin in the same way as the supplementation group. The control group did not receive any intervention and participated only in pre-test and post-test evaluations.

2.6. Sampling and data collection

48 hours before the start of the first training session and creatine supplementation as well as 48 hours after the end of the 10-week course of interventions, blood samples were taken at 8 am in the amount of 6 cc (after approximately 10 hrs of night fasting). The samples were then centrifuged at 3000 g for 10 mins and the extracted serums were frozen at −70°C until final assay.

Malondialdehyde (MDA), glutathione peroxidase (GPX) and total antioxidant capacity (TAC) serum levels were determined using commercial kits (Human ELISA; ZellBio Company, Berlin, Deutschland) according to the manufacturer's protocol with a lower detection limit of 0.1 μM, 5 U/ml, and 0.1 mM, respectively. The measurement of *8-hydroxydeoxyguanosine* (8OHdG) was performed by a commercial ELISA kit with a lower detection limit of 0.25 ng/ml (BT Lab, Shanghai, China).

As previously mentioned, in order to measure the maximum muscle strength, the Brzycki equation was used (26). Quality of life was measured by the short-form 36 (SF-36) questionnaire (29). This questionnaire comprised of the following sections: physical component score (PCS), mental component score (MCS), physical functioning, role-physical, bodily pain, general health and mental health.

In order to control the participants' nutritional status, a 24-h dietary recall was taken 48 hrs before the start of both blood sampling steps. In this regard, the calorie intake was analyzed through nutrition software, and there was no significant difference in terms of calorie intake of the subjects in the three groups.

2.7. Data analysis

The Shapiro–Wilk test was used to examine the normal distribution of data. Analyses of variance (ANOVA) with repeated measure and Bonferroni post-hoc test were used to determine within-group (time effect), between-group (group effect) and time–group interactions. Data was analyzed with IBM SPSS software (version 23; IBM Corporation, Armonk, NY, United States), and the statistical significance level was set at $p \leq 0.05$.

3. Results

There was no significant difference ($p > 0.05$) between the three groups regarding any of the research variables in the pre-test.

There were significant main effect of time ($F = 127.38$, $p = 0.001$, and $F = 468.47$, $p = 0.001$) and group × time interaction ($F = 21.98$, $p = 0.001$, and $F = 106.21$, p = 0.001) respectively for malondialdehyde (MDA) and *8-hydroxydeoxyguanosine* (8-OHdG). These serum indices of oxidative damage were significantly reduced in both experimental groups (RT + CS and RT + P) after 10 weeks of RT (in all cases, $p = 0.001$) and there was no difference between the training groups ($p > 0.05$; Figures 2A,B).

In relation to the glutathione peroxidase (GPX), there was a significant main effect of time ($F = 155.32$, p = 0.001), group × time interaction ($F = 37.47$, $p = 0.001$) and main effect of group ($F = 5.39$, $p = 0.009$). Serum concentrations of GPX was higher in both training groups (RT + CS and RT + P) compared with the control group in the post-test ($p = 0.001$ and $p = 0.006$, respectively). Indeed, in the post-test, the levels of this enzyme in the RT + CS was higher than the RT + P group ($p = 0.004$). GPX substantially increased in the RT + CS and RT + P groups after the 10-week intervention compared with the pre-test ($p = 0.001$, eta = 0.87 and $p = 0.001$, eta = 0.86; Figure 2C).

In regards total antioxidant capacity (TAC), there was a significant main effect of time ($F = 41.77$, $p = 0.001$) and group × time interaction ($F = 15.51$, $p = 0.001$). This index of antioxidant capacity also had an interesting rise in both training groups after 10 weeks (in both cases, $p = 0.001$), while no significant difference was observed between the groups in the post-test ($p > 0.05$; Figure 2D).

Regarding body mass index (BMI), there was a significant main effect of time ($F = 3.68$, $p = 0.049$) and group × time interaction ($F = 23.93$, $p = 0.001$). Intragroup changes showed that the body mass index decreased ($p = 0.001$) only in the RT + P group in comparison with the pre-test (Figure 2E).

However, with regard to creatinine, the interaction of time and group was significant ($F = 6.40$, $p = 0.004$). Creatinine levels elevated only in the RT + CS group after 10 weeks of supplementation ($p = 0.014$). No significant difference was observed between the groups in the post-test ($p > 0.05$; Figure 2F).

There was also a significant main effect of time ($F = 1831.58$, $p = 0.001$), group × time interaction ($F = 441.69$, p = 0.001) and main effect of group ($F = 111.97$, $p = 0.001$) for quality of life (Figure 2G). This index in the experimental groups (RT + CS and RT + P) improved after 10 weeks of intervention (in both groups, $p = 0.001$). Indeed, there was a difference between the groups in the post-test so much so that the quality-of-life index in the training groups was better than in the control group (Table 2).

Changes in muscle strength in all seven resistance movements including leg extension and leg curl machine, barbell bench press, lateral pulldown, barbell curl, overhead press, and triceps extension machine indicated that the training groups (RT + CS and RT + P) had a sharp increase compared to the pre-test ($p < 0.05$) as well as compared to the control groups in the post-test ($p < 0.05$). In addition, the increase in muscle strength of the RT + CS group was greater than that of the RT + P group ($p < 0.05$; Table 2).

4. Discussion

Findings of the present study showed that 10 weeks of RT reduced the oxidative damage indices in older adults by strengthening the antioxidant defense system. In fact, after 10 weeks of regular RT, MDA and *8-hydroxydeoxyguanosine* (8-OHdG) in the training groups decreased, while the amount of GPX and total antioxidant

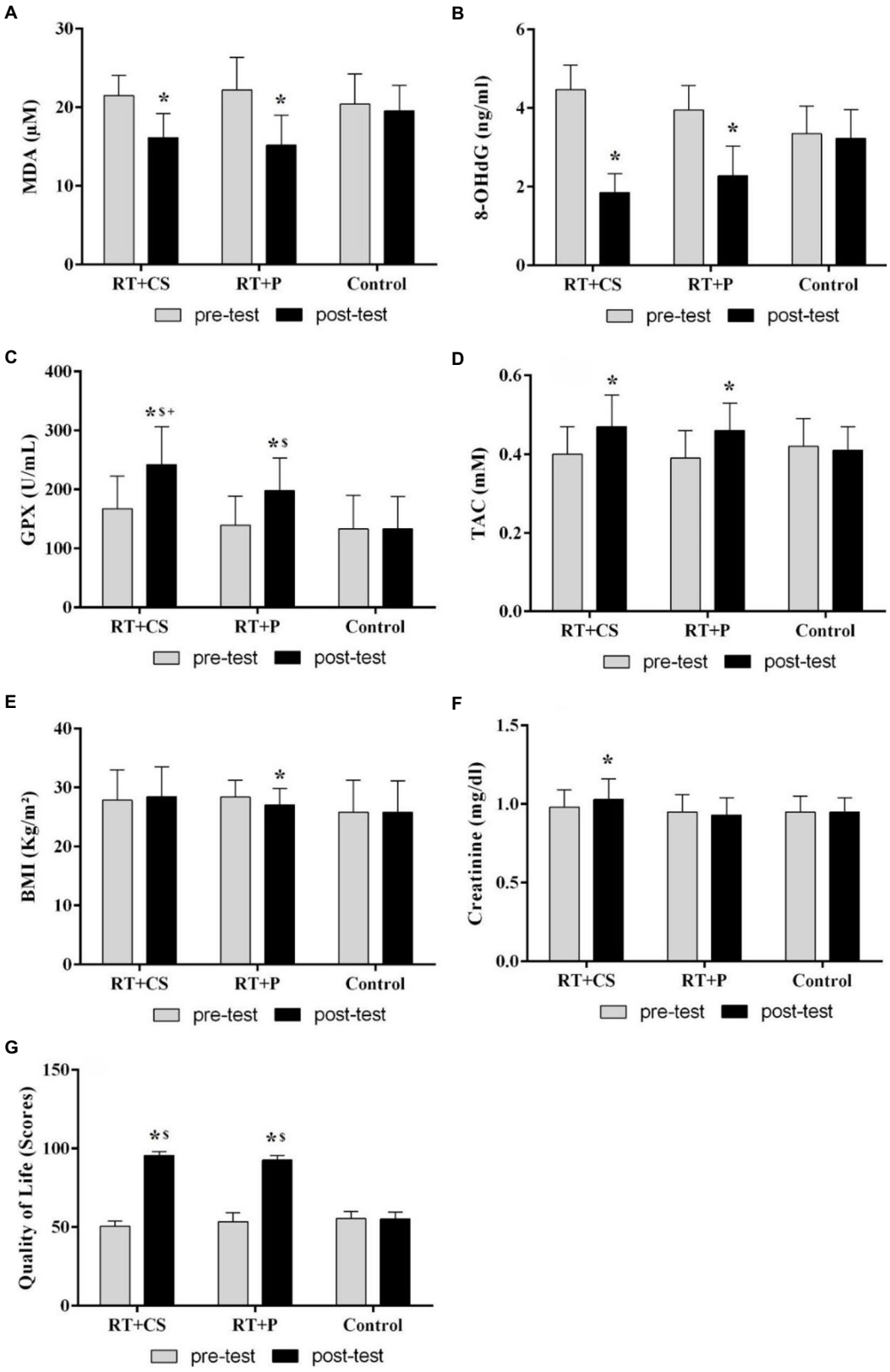

FIGURE 2
Changes in oxidative and antioxidant indices, as well as creatinine, BMI and quality of life in the older adults after 10-week of resistance training and creatine supplementation. **(A)** Malondialdehyde (MDA); **(B)** *8-hydroxydeoxyguanosine* (8-OHdG); **(C)** Glutathione peroxidase (GPX); **(D)** Total antioxidant capacity (TAC); **(E)** Body mass index (BMI); **(F)** Creatinine; **(G)** Quality of life. *Significant difference with the pre-test. $^{\$}$Significant difference with the control group.

TABLE 2 Changes in subjects' quality of life and muscle strength following 10-week of resistance training and creatine supplementation.

		Groups	Pre-test (M±SD)	Post-test (M±SD)	Repeated Measure	*f*	*p*
Muscle strength (kg)	Leg extension	RT + CS	33.61 ± 36.38	50.53 ± 52.61	Time	20.57	0.001*
		RT + P	16.87 ± 23.50	22.87 ± 23.58	Group	2.01	0.14
		Control	26.91 ± 5.53	26.83 ± 5.16	Time × Group	8.25	0.001*
	Leg curl	RT + CS	15.92 ± 14.66	29.46 ± 26.73	Time	26.38	0.001*
		RT + P	9.62 ± 9.16	14.43 ± 12.69	Group	3.59	0. 03*
		Control	9.08 ± 3.34	9.08 ± 3.22	Time × Group	10.40	0.001*
	Barbell bench press	RT + CS	32.15 ± 21.83	47 ± 31.53	Time	35.81	0.001*
		RT + P	19.62 ± 9.81	25.68 ± 14.40	Group	4.14	0.024*
		Control	23.83 ± 6.75	23.58 ± 6 ± 43	Time × Group	13.50	0.001*
	Lat pulldown	RT + CS	38.76 ± 10.96	57 ± 16.03	Time	77.50	0.001*
		RT + P	31.18 ± 6.24	40.87 ± 6 ± 81	Group	19	0.001*
		Control	27.58 ± 4.16	27.16 ± 3.80	Time × Group	24.87	0.001*
	Barbell curl	RT + CS	19.38 ± 10 ± 73	30.07 ± 15.56	Time	46.70	0.001*
		RT + P	14.87 ± 7.67	18.56 ± 10.54	Group	6.01	0.005*
		Control	11.75 ± 3.98	11.58 ± 4.01	Time × Group	19.75	0.001*
	Overhead press	RT + CS	8.84 ± 4.01	15.46 ± 6.67	Time	80.19	0.001*
		RT + P	6.93 ± 3.19	10.43 ± 4.42	Group	6.31	0.001*
		Control	6.83 ± 1.74	6.66 ± 1.82	Time × Group	25.89	0.004*
	Triceps extension	RT + CS	32.61 ± 15.56	50.30 ± 22.62	Time	76.66	0.001*
		RT + P	24.12 ± 6.35	32.06 ± 10.89	Group	8.24	0.001*
		Control	22.25 ± 5.59	22.25 ± 5.59	Time × Group	35.59	0.001*
Quality of life (scores)		RT + CS	50.50 ± 3.58	95.61 ± 2.34	Time	1831.58	0.001*
		RT + P	53.59 ± 5.59	92.70 ± 2.79	Group	111.97	0.001*
		Control	55.45 ± 4.59	55.20 ± 4.25	Time × Group	441.69	0.001*

RT + CS resistance training with creatine supplementation. RT + P resistance training with placebo.
*Significant difference at $p < 0.05$.

capacity (TAC) increased. An interesting result is that creatine supplementation did not have an incremental effect on reducing oxidative damage. However, the rate of increase in GPX enzyme in the supplement group was higher than the placebo group demonstrating the synergistic effect of creatine supplementation on the levels of this antioxidant enzyme.

Alikhani and colleagues in line with the present study illustrated an improvement in MDA and TAC in older and younger people after 12 weeks of RT. (30) Consistent with the current findings, two other studies also confirmed the positive effects of regular exercise training on improving the activity of antioxidant enzymes such as catalase, superoxide dismutase and glutathione peroxidase in the older adults (31, 32). The effect of combined training (aerobic and resistance training) on DNA oxidative damage and antioxidant properties in middle-aged and older people was investigated by (33) which indicated the positive role of the above exercise program in improving antioxidant capacity and reducing 8-OHdG. Ghahramani Moghadam's study also demonstrated a reduction in 8-OHdG levels in older women after 8 weeks of exercise training (34). In another study by Padilha, three sessions of RT per week (for 12-weeks) reduced oxidative stress indices in older women (35). In a research conducted by Koechlin, the effect of RT with an intensity of 40% of 1-RM with N-acetylcystein supplementation on the older adults with chronic obstructive pulmonary disease was evaluated and indicated that the TAC index did not change (36). It appears that the low intensity of the exercise program, the type of supplement used and also the illnesses of the subjects are the reasons for the contradiction in the findings of the above research with the results of the present study.

Kinksly et al. examined the effect of cycling and creatine consumption on non-enzymatic indicators of antioxidant defense. The finding of the above study indicated that creatine had no effect on improving the antioxidant system (37). However, in a study conducted on young subjects stated that 7 days of creatine supplementation reduced MDA and 8-OHdG following acute RT. Candow et al. reported that creatine supplementation improved body composition and muscle strength in older adults without any adverse effects on the kidney (27). Canadow in another study illustrated that creatine supplementation had anti-sarcopenic effects and would improve bone mineral density (38). In addition, Deminice et al. stated that short-term creatine supplementation (for 7 days) had no effect on catalase and superoxide dismutase activity after an anaerobic test (39).

According to the results of previous research, it seems that short-term use of creatine supplementation has no effect on strengthening the antioxidant system. Available findings are limited and relatively contradictory in regards the long-term effects of this supplement which makes the final conclusion difficult. As mentioned, in the present study, 10 weeks of creatine monohydrate supplementation doubled the activity of GPX enzyme, while no synergistic effect of this

supplement on TAC were observed. Therefore, further research is needed to prove the possible effects of creatine on boosting the antioxidant system. Nevertheless, it has been found that regular RT can be a logical approach for reducing exercise training-induced oxidative damage by enhancing the antioxidant capacity of older adults.

The finding of the present study regarding changes in muscle strength showed that after 10 weeks of RT and creatine supplementation, the average increase in muscle strength (mean of the seven muscle groups studied) in the training-placebo group was 35.9% and in the training-creatine group was equal to 57%. These findings generally indicate the positive effect of RT on increasing muscle strength in the older adults, and in particular the synergistic effects of creatine supplementation on elevating strength in these individuals. Moreover, the results of the current study demonstrated that there was a significant decrease in body mass index only in the training-placebo group. The present research finding have been confirmed by previous research on the effect of RT on upgrading muscle strength and body composition, as well as the dual role of creatine supplementation in improving muscle strength in older adults (27).

The present results showed an improvement of 79.9% and 89.2% of quality of life index in the training-placebo and training-creatine groups, respectively.

4.1. Limitations

To our knowledge, the present study is the first study that examines the long-term effect of resistance training along with creatine supplementation on antioxidant indices in older adults. One of the limitation of the current study include the lake of measurement of nitric oxide metabolites. In addition, it is better to measure the level of muscle tissue at the same time as blood sampling in future studies to check the changes in oxidant/antioxidant indices more precisely.

5. Conclusion

Regular resistance training can be recommended as a very suitable non-pharmacological approach to strengthen the body's antioxidant system, muscle strength and quality of life in older adults. There are no definite findings on the role of creatine on the antioxidant system and quality of life in older adults, but the use of this supplement in addition to RT can double the amount of strength gained from resistance training. From a clinical viewpoint, our findings indicated that these results can be obtained using a modest exercise prescription for an aging population.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the research design was approved by the Ethics Committee of the University of Kurdistan (IR.UOK.REC.1399.010). The patients/participants provided their written informed consent to participate in this study.

Author contributions

EA: writing original draft of the manuscript. DS-V: methodology, editing the manuscript, and supervision. EA and DS-V: data analysis and interpretation. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Changes of the acute myocardial infarction-related resident deaths in a transitioning region: a real-world study involving 3.17 million people

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Background: The impact of acute myocardial infarction (AMI) on the life span of residents in a transitioning region has not been studied in depth. Therefore, we aimed to evaluate the changes in AMI-related resident deaths in a transitioning region in China.

Methods: A longitudinal, population-based study was performed to analyze the deaths with/of AMI in Pudong New Area (PNA), Shanghai from 2005 to 2021. The average annual percentage change (AAPC) of AMI in crude mortality rates (CMR), age-standardized mortality rates worldwide (ASMRW), and rates of years of life lost (YLLr) were calculated by the joinpoint regression. The impact of demographic and non-demographic factors on the mortality of residents who died with/of AMI was quantitatively analyzed by the decomposition method.

Results: In 7,353 residents who died with AMI, 91.74% (6,746) of them were died of AMI from 2005 to 2021. In this period, the CMR and ASMRW of residents died with/of AMI were 15.23/10^5 and 5.17/10^5 person-years, the AAPC of CMR was 0.01% (95% CI: −0.71,0.72, p =0.989) and 0.06% (95% CI: −0.71,0.84, p =0.868), and the ASMRW decreased by 2.83% (95% CI: −3.66,−2.00, p <0.001) and 2.76% (95% CI: −3.56,-1.95, p <0.001), respectively. The CMR of people died of AMI showed a downward trend (all p <0.05) in people ≥60 years but an upward trend [AAPC=2.47% (95% CI: 0.07,4.94, p =0.045)] in people of 45–59 years. The change in CMR of people died with/of AMI caused by demographic factors was 28.70% (95% CI: 12.99,46.60, p =0.001) and 28.07% (95% CI: 12.71,45.52, p =0.001) per year, respectively.

Conclusion: Preventative strategies for AMI should be applied to enhance the health management of residents aged 45–59 years or with comorbidities in the transitioning region.

KEYWORDS

acute myocardial infarction, mortality, years of life lost, comorbidities, trend analysis

Introduction

Cardiovascular diseases (CVDs) have become one of the most important causes of death in the global population (1, 2). Among the multiple categories of CVDs, acute myocardial infarction (AMI) is a severe and acute clinical syndrome associated with multiple life-threatening comorbidities such as malignant arrhythmia, cardiac shock, and heart failure (3). Post-AMI patients suffer from impaired quality of life, despite the increased use of revascularization therapy such as percutaneous coronary intervention (PCI) to save the ischemic myocardium in current clinical practice (4).

On the other hand, data regarding the long-term trend of the influence of AMI on the resident mortality are relatively lacking in Asia (5), particularly in a transitioning region where there is economic growth, advanced medical services, and aging population. Pudong New Area (PNA) is the largest municipal district of Shanghai, the forefront of China's reform and opening up, and a typical transitioning area in China (6). The PNA residents' working environment and living style has drastically changed in recent decades (7).

In this study, by collecting AMI-related mortality data in the death-cause monitoring database of the registered population in PNA from 2005 to 2021, we estimated the trend of the average annual percentage change (AAPC) of AMI in crude mortality rates (CMR), age-standardized mortality rates worldwide (ASMRW), and rates of years of life lost (YLLr) in this population. These real-world data provided us with insight on the influence of AMI on the mortality of the population in this particular region, which may be important for the designating of effective strategies for the prevention of AMI-related deaths.

Methods

Data source

Registered residents of PNA were included in the research population, and the data on AMI-related death were collected from 1 January 2005 to 31 December 2021 by screening the death-cause monitoring database of PNA residents. The main reasons we chose the population of PNA as the research object were: (1) The PNA covers an area of 1210.41 km^2, including both the central urban area and the suburbs (8). The registered resident population is 3.17 million in 2021, accounting for more than 50% of the total population of Shanghai (9). (2) The economy of PNA has experienced a period of rapid development. The total economic volume has increased from 210.8 billion RMB in 2005 to 1,535.3 billion RMB in 2021 (https://www.pudong.gov.cn/006001/20220221/665255.html, First line of the first paragraph), with an average annual growth rate of 13.21%. (3) There are 760,250 people over the age of 65 among the registered residents in 2021, accounting for 23.99% of the entire registered population of PNA (https://wsjkw.sh.gov.cn/cmsres/59/5983e677030440f18a034ce02a0c10e5/d55b3444b8c63b77d3b73231f4f66a28.pdf, in page 9). The huge aging population base and the features of super-aging can provide a more realistic reflection for analyzing the impact of aging on the characteristics of dying with/of AMI. (4) Since 2005, PNA has established a unified, standardized death information registration system based on the whole population, which provides reliable data guarantee for the analysis of AMI death cause (7). Therefore, PNA would be an epitome for most transitioning countries or regions with aging population.

The demographic data in this study came from the PNA Public Security Bureau (PSB). They mainly included data regarding the name, gender, date of birth, date of death, cause of death, place of death, and other basic information of the participants. The community health service center and the Center for Disease Control and Prevention (CDC) collected the death certificates of residents from PSB's household registration department on a monthly basis. They built a database of the death causes of residents in PNA (10). All causes of death were coded by strictly trained clinicians according to the actual situation of patients with predefined coding rules and further checked by the CDC to ensure the homogeneity and accuracy of the data (8).

ICD-10 codes

International Classification of Diseases (ICD) is a system expressed by coding, which classifies diseases according to some characteristics of diseases and certain rules. At present, the mature version is ICD-10,[1] which standardizes and formats the names of causes of death, and provides a research basis for analyzing the international comparability of mortality data (11). According to the ICD-10, acute myocardial infarction has code I21, including acute transmural myocardial infarction of the anterior wall (I21.0), acute transmural myocardial infarction of the inferior wall (I21.1), acute transmural myocardial infarction of other sites (I21.2), acute transmural myocardial infarction of unspecified site (I21.3), acute subendocardial myocardial infarction (I21.4), acute myocardial infarction, unspecified (I21.9). We use the recommended method to evaluate data quality which defines and classifies garbage codes into different types (10). In addition, the definition of "died with AMI" means all-cause of death included AMI. Meanwhile, "died of AMI" means the underlying cause of death was AMI.

Statistical analyses

The primary outcome parameter of the study was mortality. Segi's world population composition was used as the referenced population to standardize the mortality of AMI. Subsequently, CMR and ASMRW of AMI were calculated and presented as data per 100,000 persons ($/10^5$). Z test and Mantel–Haenszel test were used to compare if CMR and ASMRW were different by gender of the study population. YLL refers to the number of years lost due to a certain disease, which can

Abbreviations: AAPC, Average annual percent change; AMI, Acute myocardial infarction; APC, Annual percentage change; ASMRW, Age-standardized mortality rates worldwide; CDC, Center for Disease Control and Prevention; CHD, Coronary heart disease; CI, Confidence interval; CMR, Crude mortality rates; CVD, Cardiovascular disease; GBD, Global Burden of Disease; GDP, Gross domestic product; ICD, International Classification of Diseases; PNA, Pudong New Area; PSB, Public Security Bureau; RMB, Ren Min Bi; TCM, Traditional Chinese Medicine; YLLr, rates of Years of life lost.

1 https://www.cdc.gov/nchs/icd/icd10.htm

reflect the social burden of the disease more accurately (7). The efficacies of the interventions were analyzed by evaluating the changes in premature death and the mortality differences of different subgroups, as indicated by YYL (12). In this study, YLL was used to analyze the burden of AMI according to the method proposed by Murray and Lopez (13).

Ages were divided into eight groups according to previous studies (6). However, considering that there are no or very few deaths due to AMI in residents younger than 30 years old, the calculation and trend analysis of age-specific CMR, age-specific proportion, and age-specific YLLr are only performed in the following six age groups: 0–29 years, 30–44 years, 45–59 years, 60–69 years, 70–79 years, and ≥80 years. Joinpoint regression model has been widely used in disease mortality trend research (14). Therefore, we used Joinpoint regression to calculate the CMR, ASMRW, and YLLr over time and expressed the degree of change trend with average annual percent change (AAPC) and its 95% confidence interval (CI).

The Bayesian Information Criterion (BIC) was used to compare whether AAPC values were statistically different from zero. When the difference was statistically significant ($p < 0.05$), it indicated that the trend presented an "increase" or "decrease" change, and when the difference was not, it indicated that the trend was "stable." The quantitative contribution of demographic and non-demographic factors to the change in AMI mortality was evaluated by the decomposition method (15). The statistical analyses were performed using SPSS (version 26.0; SPSS, Inc., Chicago, IL), R (version 3.4.3), and the Joinpoint Regression Program 4.3.1.0 (National Cancer Institute, Bethesda, MD, United States; source: https://surveillance.cancer.gov/joinpoint/), with $p < 0.05$ indicating a statistically significant difference.

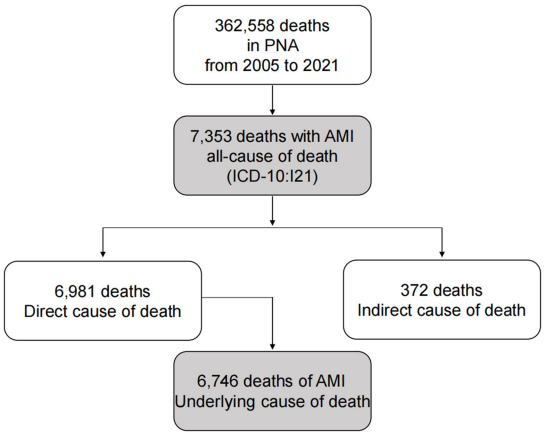

FIGURE 1
Flow chart for the selection of AMI-related deaths in PNA, Shanghai from 2005 to 2021.

Results

Baseline characteristics

From 1 January 2005 to 31 December 2021, a total of 48,276,547 registered residents in PNA were included in this study, and a total of 362,558 people died during the period. Specifically, 7,353 of the participants died with AMI, including 6,746 participants who died of AMI (Figure 1). For participants who died with AMI, the average age at death was 78.11 ± 11.15 years, and the median age at death was 80.27 years. The CMR and ASMRW were ($15.23/10^5$and $5.17/10^5$) person-years, higher in males than in females ($U = 10.01$, $p < 0.001$; $Z = -22.06$, $p < 0.001$) and the proportion of females was 44.27%. The CMR, ASMRW, and the YLLs, YLLr of both gender are presented in Table 1. In addition, the YLLr of participants in 60–69 years, 70–79 years, and ≥80 years were $196.83/10^5$, $527.84/10^5$, and $937.59/10^5$, respectively (Table 2). For participants who died of AMI, the CMR and ASMRW were ($13.97/10^5$and $4.73/10^5$) person-years, higher in males than in females ($U = 9.42$, $p < 0.001$; $Z = -21.07$, $p < 0.001$) and the proportion of females was 44.37% (Table 1).

Main comorbidities

For participants who died with AMI, the top 3 prevalent comorbidities were coronary heart disease (92.06%), cerebrovascular disease (1.92%), and diabetes mellitus (1.89%; Table 1; Supplementary Table S1). The top 10 comorbidities for participants who died with AMI by gender are shown in Figure 2A. For participants who died of AMI, the top 3 prevalent comorbidities were coronary heart disease (34.24%), hypertensive diseases (15.29%), and heart disease (9.20%; Table 1; Supplementary Table S2), and the gender-specific data are shown in Figure 2B. For participants who died with/of AMI, the spectrum types, rankings, and proportions of specific comorbidity can be found in Supplementary Tables S1, S2, and the data of YLLs, YLLr (Table 1), and the number of comorbidities (Supplementary Table S3) are also presented.

Trends of burden

The AAPC value of CMR of residents who died with AMI was 0.01% (95% CI: −0.71,0.72, $p = 0.989$), in the overall participants but increased in males and decreased in females (all $p > 0.05$). However, the ASMRW of both gender showed a downward trend, which was −2.83% (95% CI: −3.66,−2.00, $p < 0.001$; Figure 3A). Similar trends were also observed in deaths of AMI (Figure 3B). The case number, proportion, and CMR of the residents who died with/of AMI in different age groups are shown in Table 2. The case number, CMR and ASMRW of the residents who died with/of AMI according to gender in each year are shown in Supplementary Tables S4, S5 and the CMR data in different age groups of each year are shown in Supplementary Table S6. The trends of the proportion of the different types of deaths in PNA are shown in Supplementary Figure S1, and the population aging trend chart of PNA, Shanghai, is shown in Supplementary Figure S2. The YLLr by gender and age groups and the proportion by age groups of death with/of AMI in PNA are shown in Supplementary Tables S7, S8. The median age at death of residents died of AMI in PNA is shown in Supplementary Table S9.

For deaths with AMI, the total YLLr decreased by 0.40% (95% CI: −1.25,0.45, $p = 0.331$) per year. A gender difference was observed, which was increased in males ($p = 0.318$) but decreased in females ($p = 0.009$). Analyses according to the age group showed that for participants of ≥60 years, a downward trend was observed, and the

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TABLE 1 Baseline characteristics of the residents who died with/of AMI during 2005–2021.

Characteristic	Deaths (*n*, %)	Age at death (mean±SD)	Age at death (median)	Age at death (range)	CMR (/10^5)	ASMRW (/10^5)	YLL (years)	YLL rate (/10^5)
In the residents death with AMI								
Gender								
Male	4,098(55.73)	75.31 ± 11.83	77.47	20.19–101.65	17.01	6.87	37308.07	154.88
Female	3,255(44.27)	81.64 ± 9.09	83.06	22.47–106.29	13.46	3.61	24583.41	101.63
Total	7,353(100.00)	78.11 ± 11.15	80.27	20.19–106.29	15.23	5.17	61891.48	128.20
The top 3 underlying cause of death of residents died with AMI								
Coronary heart disease (I20–I25)	6,769(92.06)	78.2 ± 11.21	80.38	20.19–106.29	14.02	4.75	80231.26	166.19
Cerebrovascular disease (I60–I69)	141(1.92)	79.24 ± 9.43	81.88	50.12–94.00	0.29	0.09	1687.97	3.50
Diabetes mellitus (E10–E14)	139(1.89)	76.63 ± 9.45	77.95	42.48–97.03	0.29	0.12	1889.32	3.91
In the residents death of AMI								
Gender								
Male	3,753(55.63)	75.27 ± 11.92	77.52	20.19–101.65	15.58	6.30	34236.05	142.13
Female	2,993(44.37)	81.89 ± 8.96	83.29	22.47–106.29	12.37	3.30	22347.96	92.39
Total	6,746(100.00)	78.20 ± 11.20	80.38	20.19–106.29	13.97	4.73	56584.01	117.21
The top 3 comorbid diseases of residents died of AMI (a person suffering from multiple diseases of the same ICD code is calculated only once)								
Coronary heart disease (I20–I25)	6,746(34.24)	78.2 ± 11.20	80.38	20.19–106.29	13.97	4.73	79947.90	165.60
Hypertensive diseases (I10–I15)	3,013(15.29)	78.61 ± 10.17	80.21	27.23–106.29	6.24	2.08	35458.99	73.45
Heart disease (I05–09, I16–19, I26–I27, I30–I52)	1813(9.20)	77.81 ± 11.1	79.98	30.28–100.12	3.76	1.28	21621.96	44.79

CMR, crude mortality rate; ASMRW, age-standardized mortality rate by Segi's world standard population; YLL, years of life lost.

age-specific YLLr increased by −4.06% (95% CI: −5.63 to −2.47%), −4.60% (95% CI: −5.87 to −3.32%), and − 2.72% (95% CI: −3.74 to −1.69%) per year, all $p < 0.001$, respectively (Figure 3A). Similar results were also observed for participants who died of AMI (Figure 3B). Interestingly, an age-group difference was found between residents who died of and died with AMI. Specifically, among the middle-aged (45–59 years) group, the YLLr increased by 2.47% (95% CI: 0.07,4.94, $p = 0.045$) per year, which showed an upward trend in those who died of AMI. The YLLs and YLLr of the deaths with/of AMI by age groups are shown in Table 2.

Quantitative analyses for the influences of the demographic and non-demographic factors on mortality

Among deaths with AMI, the total effects of demographic and non-demographic factors on CMR were different, with AAPC of 28.70% (95% CI: 12.99,46.60, $p = 0.001$) and −14.42% (95% CI: −20.14,−8.29, $p < 0.001$), respectively. In males, the AAPC for the effects of demographic and non-demographic factors were 30.04% (95% CI: 13.83,48.56, $p = 0.001$) and − 12.61% (95% CI: −19.63,−4.99, $p = 0.004$) respectively. For females, the AAPC for the effects of demographic and non-demographic factors were 27.28% (95% CI: 11.86,44.81, $p = 0.001$) and −15.24% (95% CI: −25.05,−4.14, $p = 0.012$; Figures 4A1,2). In addition, compared with participants who died with AMI, the influences of demographic and non-demographic factors on CMR in deaths of AMI were similar but weaker (Figures 4B1,2). The increments of CMR caused by demographic and non-demographic factors between 2005 and 2021 are also displayed in Supplementary Table S10.

Discussion

Over the past 40 years of reform and opening up, China's economy has developed rapidly. Although people's physical living standards have greatly improved, the gross domestic product (GDP) *per capita* level still has room for improvement. However, chronic diseases are also prevalent among Chinese residents, particularly for CVDs (16). According to the calculation, the current number of patients with CVDs in China is 330 million, including 11.39 million patients with coronary heart disease (CHD) (16). As the most common acute and critical disease in CHD (3), AMI is associated with high morbidity

and mortality and is an economic burden for the Chinese population (17). As a typical transition region in China, research regarding the trend of changes in the death characteristics and burden of AMI in PNA may provide information on the prevalence of AMI-related deaths in similar regions in the transition process, which may be critical for the subsequent development of effective preventative strategies.

TABLE 2 Age-specific mortality and burden of residents who dies with/of AMI during 2005–2021.

Age group (years)	Deaths (*N*)	Proportion (%)	CMR (/10^5)	YLL (years)	YLL rate (/10^5)
Residents who died with AMI					
0–29	8	0.11	0.11	216.24	2.87
30–44	68	0.92	0.62	1610.39	14.70
45–59	469	6.38	3.80	8689.97	70.39
60–69	965	13.12	14.22	13355.49	196.83
70–79	2064	28.07	57.60	18914.69	527.84
≥80	3,779	51.39	185.46	19104.68	937.59
Total	7,353	100.00	15.23	61891.48	128.20
Residents who died of AMI					
0–29	8	0.12	0.11	216.24	2.87
30–44	62	0.92	0.57	1464.71	13.37
45–59	437	6.48	3.54	8093.17	65.56
60–69	857	12.70	12.63	11865.39	174.87
70–79	1891	28.03	52.77	17336.89	483.81
≥80	3,491	51.75	171.33	17607.60	864.12
Total	6,746	100.00	13.97	56584.01	117.21

CMR, crude mortality rate; YLL, years of life lost.

Burden of AMI

From Figure 3, the total CMR of AMI in PNA showed a slight upward trend from 2005 to 2021, although the difference was not statistically significant. Interestingly, the ASMRW after age structure adjustment diminished this trend. Analysis of the total population showed a significant downward trend, which was more remarkable for the females. At the same time, combined with the aging trend chart in PNA (Supplementary Figure S2), it became obvious that aging factors play a key role in the increase of CMR. This is consistent with earlier findings of a study by Chang et al. (18), which showed that the increase in AMI mortality was primarily attributable to population aging.

In terms of age groups, the CMR of the groups of older adults (60–69 years, 70–79 years, and ≥80 years) all showed downward trends. This trend was similar to the conclusion of a previous German study, which showed a decline in AMI-related mortality in the older adult population (>64 years), indicating progress in prevention and treatment for the older adult population (19). Similar to Germany (developed country), China (developing country) can also achieve such prevention and control effects of AMI. The reason is inseparable from the implementation of the National Basic Public Health Service Project in China (20). The project (21) stipulates that health records should be established for adults aged 60 and above, and health care services and management should be executed in accordance with technical specifications and requirements, including providing community day care services and home-based door-to-door services such as living and medical care. In addition, based on the establishment of health records, health management services for older adults aged 65 and above are provided once a year, including lifestyle and health status assessment, Traditional Chinese Medicine (TCM) constitution identification, physical examination, auxiliary examination, and health guidance. Similar services for newborns and pregnant women have achieved remarkable benefits in reducing neonatal and maternal mortality (22, 23). This project can also be expected to serve as a

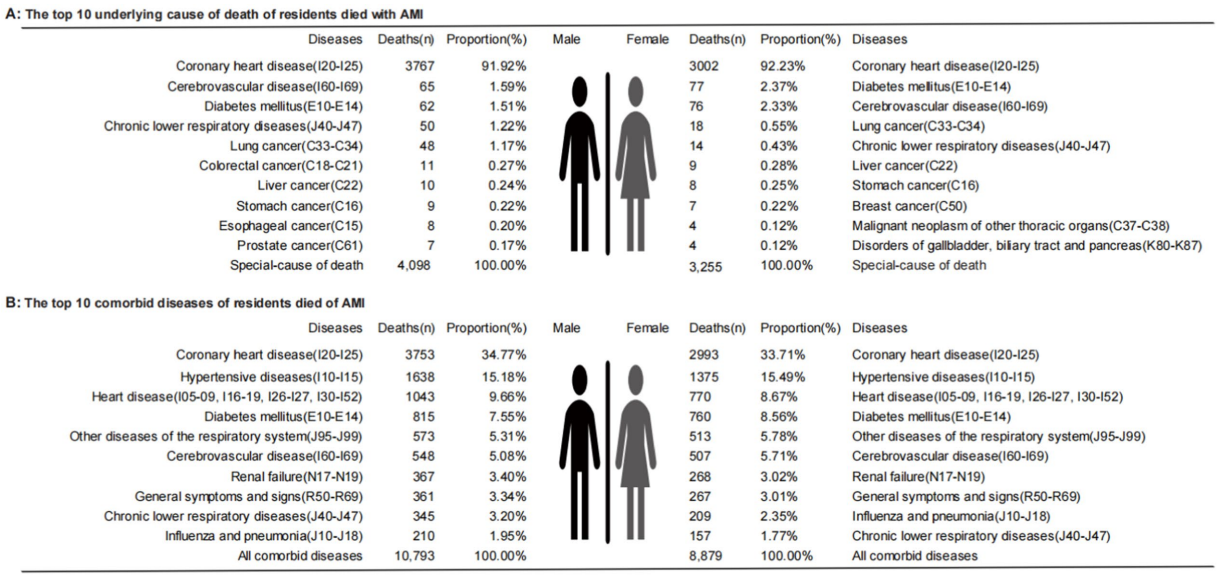

FIGURE 2
Sequence map of causes of death by gender. **(A)** The top 10 underlying cause of death of residents died with AMI; **(B)** The top 10 comorbid diseases of residents died of AMI.

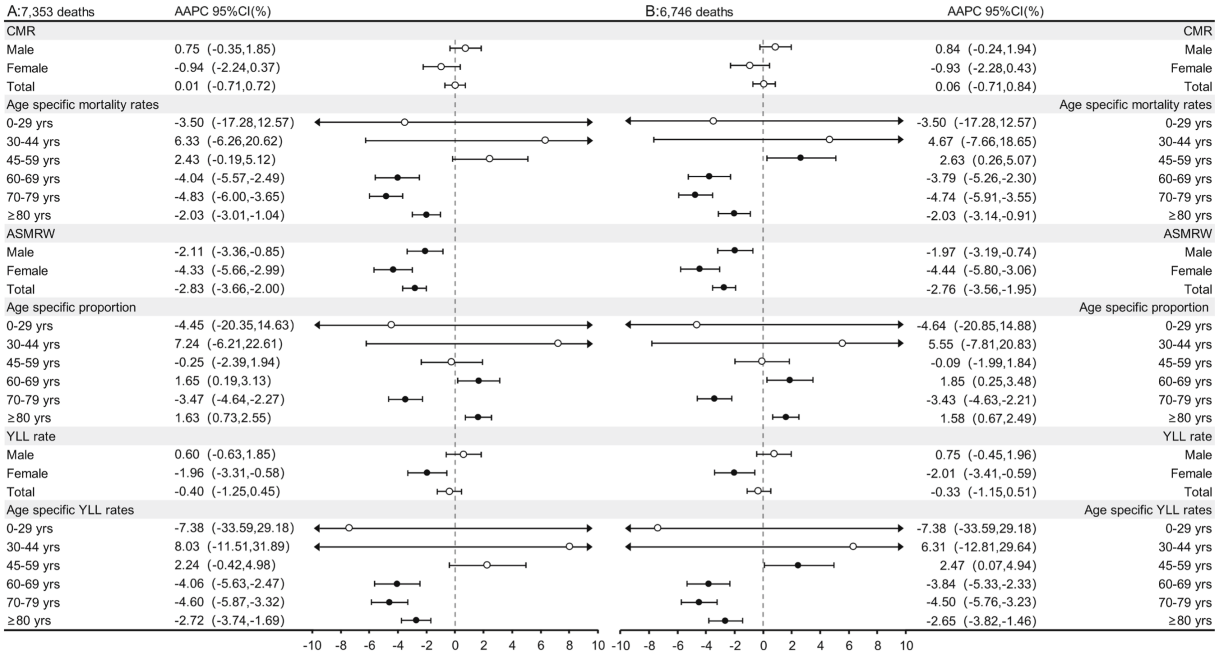

FIGURE 3
The trends in CMR, ASMRW, age specific proportions, and YLL of residents who died with/of AMI in genders and age groups in PNA, Shanghai, China, 2005–2021. **(A)** The trends in CMR, ASMRW, age specific proportions, and YLL of residents who died with AMI; **(B)** The trends in CMR, ASMRW, age specific proportions, and YLL of residents who died of AMI. CMR, crude mortality rate (per 100,000); ASMRW, age-standardized mortality rate by Segi's world standard population (per 100,000); YLL, year of lost. AAPC, average annual percent change; CI, confidence interval.

positive example for other developing countries looking to reduce AMI-related mortality in the older adults.

However, unexpected findings of increased AMI-related deaths were observed in the middle-aged population. In the 45–59 years age group (Figure 3), the CMR and YLLr showed an increasing trend by year, which to our knowledge, has not been reported in similar studies (18, 19, 24). People in this age group are in the transition period from youth to old. They are "middle-aged" adults, but they have a trend of increased mortality and higher YLL (Table 2). An analysis of 1,462,168 young adults with their first AMI showed that, in participants aged 45–59 years, hypertension (59.8%), dyslipidemia (57.5%), and smoking (51.9%) were most prevalent, and 92% of patients had at least one risk factor (25). These findings suggest that the prevention of AMI-related death in this "middle-aged" population may be the key objective in the future. For example, the age limits of the service of the national project mentioned above should be younger if permitted, e.g., from above 60 years to over 45 years old or 50 years old. Further cost-effective studies should also be performed to validate this strategy. For example, a previous study in India confirms that policies to expand treatment and preventive care for AMI are cost-effective based on GDP *per capita* comparisons (26). Although we have seen a downward trend in the CMR of older adults and the proportion of AMI in all death (Supplementary Figure S1), the rising trend in the proportion of AMI deaths in the last few years may be related to the lack of effective treatment due to stress, closed management, and medical resource runs caused by COVID-19 (27). We should also see that there are differences in this trend among different age groups since the proportion of deaths with/of AMI in the number of deaths in this age group still has a certain upward trend in some age groups (Figure 3). For participants aged 60–69 years and ≥80 years (Figure 3 Age specific proportion), measures for older adults in the above-mentioned national project should continue to be implemented and strengthened.

Main comorbidities

Comorbidities have been related to the poor long-term survival of patients after AMI (28). Pathophysiologically, AMI is mainly caused by coronary atherosclerotic stenosis in patients with CHD (29). During the pathogenesis of AMI, the coronary atherosclerotic plaque ruptures, and the platelets in the blood gather on the surface of the ruptured plaque, forming blood clots (thrombi), which suddenly block the coronary artery lumen, resulting in acute myocardial ischemic necrosis (3). Therefore, from Table 1, it can be seen that CHD is the first comorbid disease of AMI, whether it is in participants who died with or of AMI. At the same time, we also found that cerebrovascular disease and diabetes mellitus also account for a higher proportion of dying with AMI. Hall et al. (28) also found that the coexistence of multiple diseases in patients with AMI is very common, primarily with diseases such as hypertension, heart failure, and peripheral vascular disease. Our findings support that most residents who died of AMI also have multiple cardiovascular diseases such as hypertension and heart diseases.

In addition, from the gender-specific analyses in Figure 2, besides CVDs, diabetes is within the top 3 comorbidities for both genders. Diabetes can lead to several serious complications in the heart, blood vessels, kidneys, eyes, and nerves (30). Diabetes has a high prevalence in the Chinese population. A survey from 2015 to 2017 showed that the prevalence of diabetes in Chinese people aged ≥ 18 was 11.2%, which has contributed significantly to the burden of mortality and morbidity (30, 31). Globally, the number of people with diabetes quadrupled in more than 30 years between 1980 and 2014, reducing the life expectancy and causing severe loss of life (32), which has a strong public health impact worldwide (33). In the past 10 years, the prevalence of diabetes with AMI also increased (34). Our study

showed that diabetes is within the top 4 in death with/of AMI (Supplementary Tables S1, S2) and causes a severe loss of life in PNA residents (Table 1). Although genetic factors may have a certain influence on the high prevalence of diabetes, it is generally believed that diabetes is related to unhealthy lifestyles (35), and a healthy lifestyle also has a certain counteracting effect on genetic susceptibility (36). Therefore, health guidance is necessary for the high-risk population of diabetes, too.

Besides, chronic obstructive pulmonary disease and lung cancer may also have great impacts on early death with AMI. Although there is little difference in the ranks of respiratory comorbidities in men and women, they all rank within the top 5 of comorbidities (Figure 2A). The cardiovascular and pulmonary systems often interact with and influence each other, and injury to one system will also affect the other, leading to the occurrence of diseases (37–39). Therefore, in the secondary prevention of CHD progressing to AMI, treatments for respiratory comorbidity should be regarded as the concomitant treatment goal of improving cardiovascular outcomes.

Demographic and non-demographic factors

Among demographic factors, the impact of population aging on mortality is very important. The expert panel of the "China Cardiovascular Health and Disease Report 2021" (16) pointed out that China is facing the pressure of an aging population, and the CVD burden will continue to increase. Research shows that PNA took 26 years from being an aging society (in 1982) to an aged society (in 2008), while it took only 10 years from being an aged society to a super-aged society (in 2018) (7). Our research (Figure 4; Supplementary Figure S2) also confirmed that population aging in PNA is accelerating. Analyzed by gender, the aging of both men and women who died with/of AMI both showed an upward trend, but the trend in men was slightly higher than that of women (Figure 4), which may be related to the lower baseline life expectancy of men (40). Non-demographic factors mainly included economic development, the level of medical technology, the accessibility of medical services, health literacy of the residents, environmental factors, etc. (7). Figure 4 showed that non-demographic factors have hindered the increase in the CMR of AMI, indicating that the corresponding public health policies and specific clinical intervention measures have played positive roles in the prevention of AMI-related deaths (41).

With the increase in the contribution of aging to the CMR, the proportions of non-demographic factors have also gradually decreased (Figure 4). In gender-specific analyses, although a downward trend was shown in both men and women, the decline is faster for women (Figures 4A2,B2), indicating that the impact of intervention measures on women can be strengthened. A British study also confirmed that according to AMI quality indicators, women less frequently received guideline-indicated care and had significantly higher severity than men (42) and the use of measures for secondary prevention treatment is particularly low in women (43). The female population should be listed as the key target population in this regard, and women should receive greater attention regarding the delivery of recommended AMI prevention and treatment measures.

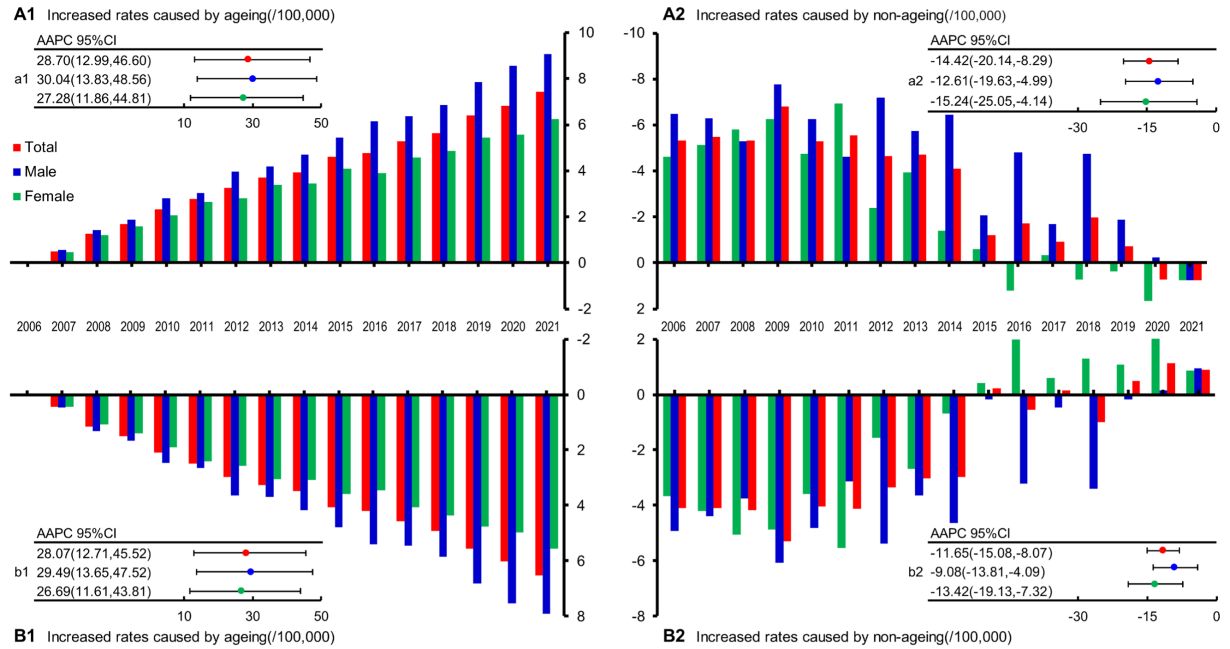

FIGURE 4
Influences of demographic and non-demographic factors on AMI-related deaths during the period from 2005 to 2021 in PNA, Shanghai, China. **(A1)** The increased rates caused by demographic age structure in death with AMI; **(A2)** The increased rates caused by non-demographic age structure in death with AMI; **(a1)** The trend of the mortality rate caused by demographic age structure in death with AMI; **(a2)** The trend of the mortality rate caused by non-demographic age structure in death with AMI; **(B1)** The increased rates caused by demographic age structure in death of AMI; **(B2)** The increased rates caused by non-demographic age structure in death of AMI; **(b1)** The trend of the mortality rate caused by demographic age structure in death of AMI; **(b2)** The trend of the mortality rate caused by non-demographic age structure in death of AMI; AAPC, average annual percent change; CI, confidence interval.

Further analyses of the overall population showed that the contribution of aging factors to mortality is greater than that of non-demographic factors in death with/of AMI. With the development of the economy and the progress of medical care, the average life expectancy has correspondingly prolonged, and aging has become an irreversible trend in various countries. Therefore, how to age healthily has become an important topic in the field of modern medical research (44). At present, the life expectancy of Shanghai residents in 2021 is 84.11 years old, which is 81.76 years for men and 86.56 years for women (http://wsjkw.sh.gov.cn/tjsj2/20220704/a540b90305ae4c54bf870b3804c6f84c.html, first line of the first paragraph). The median age of people who die of AMI is 81.16 years in 2021, which is close to the above life expectancy. This may be related to the "1 + 1 + 1" signing service (http://www.gov.cn/xinwen/2016-12/27/content_5153507.htm, in paragraph 2), which has become an important measure to implement healthy aging, implemented in Shanghai (45, 46). Specifically, the "1 + 1 + 1" signing service includes a general practitioner, a district-level medical institution, and a municipal-level medical institution, giving priority to meeting the signing needs of the older adult over 60 years old with chronic diseases. After signing the contract, residents can enjoy convenient medical diagnosis and treatment, health care, health education, rehabilitation, and other services. By providing continuous, comprehensive, and life-cycle signing services, every older adult is expected to have their own family doctor who knows their condition and who will help them achieve healthy aging (47).

In addition, the role of environmental problems in human health has also attracted more attention from scientists. Studies have shown that transient exposure to air pollutants, including PM (2.5), NO_2, SO_2, etc., may be important inducing factors for AMI, even at concentrations below the World Health Organization air quality guidelines (48, 49). Besides solving the traditional cardiovascular disease risk factors, the government must also formulate relevant policies to reduce the harm of air pollution to citizens' health (49). In recent years, China has issued a series of policies and regulations to control air pollution in the form of legislation, including the first time in 2012 that China incorporated PM2.5 into the National Ambient Air Quality Standards (50). Economic development cannot be at the expense of the environment because clear waters and green mountains are as valuable as mountains of gold and silver. Whether it is the "1 + 1 + 1″ signing service or environmental legislation in non-demographic factors, we hope that healthy aging can be implemented and transformed from treatment-centered to health-centered.

Future

China is facing the continuous pressure of the aging population and the control of metabolic risk factors, which has put forward new demands for CVD prevention and control strategies. These include optimization of the medical resource allocation, reducing the number of patients through primary prevention, increasing the allocation of medical resources for cardiovascular emergency treatment, and providing medical services of rehabilitation and secondary prevention to reduce the risk of recurrence, rehospitalization, and disability of a large number of CVD survivors. Specific prevention and treatment technologies should be implemented in different countries and regions to address the growing health needs associated with population aging, especially for patients with serious life-threatening diseases, such as AMI.

Strengths and limitations

The strengths of this study include the followings. Firstly, we selected PNA as the region of study, which involves a population of more than 3 million and is a highly representative transitioning area. Therefore, the results of the study could provide important reference significance for the prevention and treatment of AMI in other regions or countries with similar economic development and aging trends. Secondly, we not only analyzed the CMR trend of the all-cause of death (dying with AMI) but also further analyzed the changing trend of AMI as the underlying cause of death (dying of AMI), as well as ASMRW and YLLr, which could provide a comprehensive dataset. Besides, we also quantitatively analyzed the effect of demographic and non-demographic factors on CMR, which to our knowledge, has not been reported in other similar literature. Finally, AMI, as an acute and critical disease, differs from other chronic diseases. AMI often has typical symptoms, an evolution process, and strict diagnostic criteria, and researches regarding all-cause or underlying cause deaths related to AMI are likely to be more reliable. Despite these strengths, this study also has limitations. For example, due to the limitation of conditions, this study only includes the death data of residents in PNA for 16 years, not like the GBD 2019 for 30 years, and the impact of the intervention measures taken in this area on the changes of AMI mortality needs to be further observed. In addition, this study only discussed the impact of aging factors on the long-term changes of the CMR in AMI but did not discriminate against non-aging factors. At last, this study is an observational study, and the causal relationship between influencing factors and mortality changes in AMI could not be derived based on the findings.

Conclusion

Aging population and comorbidities may have played a role in the difference in trends between CMR stability and ASMRW decline in AMI in the transitioning region. Preventative strategies should be applied to enhance the health management of residents aged 45–59 years or with comorbidities, such as improving the lifestyle, targeted management of comorbidities, and intensified medical treatments for AMI.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study was approved by the Ethics Committee of the School of Public Health, Fudan University (No: IRB#2016-04-0586). Written informed consent for participation was not required for this study in

accordance with the national legislation and the institutional requirements.

Author contributions

YZ and XL: conceptualization, methodology, software, and writing—original draft. YZ, JZo, and YC: formal analysis. XL and SJ: validation and funding acquisition. JZo, YC, JZh, WD, and MP: writing—review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1096348/full#supplementary-material

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A baseline sarcopenia index based on creatinine/cystatin C for the prediction of stroke recurrence and mortality in older survivors of first ischemic strokes

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Objective: Older adults individuals have a higher risk of stroke recurrence, leading to high mortality and disability rates, which, in turn, hinders the achievement of healthy aging. This study aimed to assess the utility of a baseline sarcopenia index (SI) based on serum creatinine (Cr)/cystatin C (CysC) as a prognostic marker for the risk of stroke recurrence and mortality in first-ever ischemic stroke older survivors (ISOS).

Materials and methods: Data were obtained from an ischemic stroke cohort study. The baseline information was collected from medical records and face-to-face interviews with patients admitted between January 2010 and June 2016. Follow-up information was obtained from telephone interviews every 3 months to determine stroke recurrence and survival status. The SI was calculated from the Cr and CysC values in the medical records as Cr/CysC × 100. Using the first quantile of the SI as the cut-off value, the study participants were divided into the low muscle-mass group (low SI) and the high muscle-mass group (high SI). Cox regression analysis was used to assess the association between SI and recurrence and mortality.

Results: A total of 415 first-ever ISOS were enrolled, including 242 (58.31%) male and 173 (41.69%) female participants. In the high-SI group, the relapse and mortality rates were lower than those in the low-SI group (relapse: 20.58% vs. 30.77%; mortality:13.5% vs. 29.81%). After adjusting for confounding factors, the high-SI group was found to have a lower risk of relapse and mortality than the low-SI group (relapse: HR = 0.571; mortality: HR = 0.294).

Conclusion: The SI was predictive of the long-term prognosis of IS recurrence and mortality in first-ever ISOS. After discharge, in addition to conventional medication, it is recommended that patients with low SI values actively receive treatment for sarcopenia to reduce the risk of stroke recurrence and mortality and promote healthy aging.

KEYWORDS

ischemic stroke, sarcopenia index, creatinine, cystatin C, recurrence, mortality

Introduction

In May 1987, the World Health Organization Assembly first proposed the term "healthy aging." Healthy aging has two levels of meaning, one of which indicates a healthy old age with disability or loss of function only apparent in later years and of short duration, resulting in improved quality of life in the older adults and a more meaningful later life. Disability or loss of function in the older adults is often associated with stroke. Stroke has a high likelihood of recurrence and is associated with high rates of both disability and mortality (1–3).

Ischemic stroke (IS) is a common type of stroke. It is estimated that approximately 17 million people throughout the world suffer a first IS. The recurrence rate of IS ranges from 16 to 29% in the United States (4) and has been found to be 29.43% in China, where it is the leading cause of death and adult disability (5). The high rate of recurrence is directly proportional to increased mortality (6, 7) as well as a reduced capacity to compensate for functional injury (6). Therefore, the prediction of stroke prognosis is extremely important for its overall prevention and treatment.

Previous studies have shown that older patients have an elevated risk of stroke recurrence (8–10) and patients with sarcopenia before stroke have poor functional outcomes, including longer hospital stays (11), worse neurological impairment (11, 12), and reduced ability to walk (13). Sarcopenia is a common disease in the older population and is associated with significant risks of impaired mobility, falls, reduced quality of life, and mortality (14). Sarcopenia is generally diagnosed by the presence of reduced skeletal muscle mass and low muscle function (15). The assessment of muscle mass is commonly made by computed tomography (CT), magnetic resonance imaging (MRI), dual-energy X-ray absorptiometry (DXA), and bioelectrical impedance analysis (BIA). However, these methods have disadvantages, as CT and MRI have no clear cut-offs for muscle mass, DXA is time-consuming, and BIA requires patients to maintain a specific position for extended periods, often difficult for stroke patients. While muscle function can also be assessed by handgrip strength and gait speed, this can be challenging for patients with limb hemiplegia.

It would thus be economical and effective to evaluate sarcopenia in stroke patients using routine detection indices. Several recent studies (16–18) have shown that the ratio of creatinine to cystatin C can be used as an indicator of both muscle mass and muscle function and, therefore, the Creatinine/CystatinC (Cr/CysC)*100 was proposed as a sarcopenia index (SI). A three-month follow-up study (19) demonstrated that the Cr/CysC ratio at admission was an effective predictor of 30-day mortality and poor long-term prognosis (modified Rankin Scale score ≥ 4) in patients with acute IS. However, the authors found no association between the Cr/CysC ratio and stroke recurrence. Wang et al. (20) reported that the serum Cr/CysC ratio at admission could be used to predict poor long-term prognosis in neurocritically ill cases (including patients with IS and patients without IS) but not 30-day mortality. The inconsistencies between these findings may have resulted from differences in follow-up times or subjects. There is a lack of long-term follow-up investigations on the relationship between SI and IS prognosis (recurrence or death). The present study was based on a long-term cohort of IS survivors and explored the relationship between SI and recurrence and mortality in first-ever ISOS, with the aim of providing a reference for the prevention of stroke recurrence and the promotion of healthy aging.

Materials and methods

Study population

The dataset was derived from an IS cohort study. Details of the cohort design were reported previously (21). Between January 2010 and June 2016, a total of 764 patients with a primary and first diagnosis of IS were recruited during admission to two medical groups in the Department of Neurology, West China Hospital, Sichuan University. From this cohort, we chose patients who were 60 years old and over at admission. Patients with iatrogenic stroke, such as carotid endarterectomy, cardiac surgery, or angioplasty, were excluded due to medical issues and compliance. Patients with eGFR <15 mL/min/1.73 m^2, those who had received renal replacement treatment, had acute kidney injury, or refused clinical follow-up, were also excluded. The inclusion criteria are shown in the flow chart (Figure 1). The study was approved by the Ethics Committee of the West China Hospital, Sichuan University, Chengdu, China. All patients signed informed consent.

Study design

After obtaining written consent, trained interviewers used a semi-structured questionnaire in a face-to-face setting to obtain information on the basic characteristics and lifestyle of patients before the stroke. Proxies were interviewed when patients had cognitive or language impairments. At baseline, the researchers collected basic information including age, sex, marital status, education, physiological and biochemical indices, TOAST classification, lesion location, smoking history, drinking history, BMI, Rankin score, chronic disease, and exercise from the medical records and face-to-face interviews. During the follow-up, the researchers conducted phone interviews every 3 months after discharge until June 2016 to obtain information, including stroke recurrence (the first relapse was selected as the terminal event) and death (all-cause mortality). According to the purpose of this study, we retrospectively collected further data, including cystatin C and ALB levels, from the patient's medical records.

Sarcopenia index

We used the following equation to calculate the SI: serum Cr/CysC $\times$ 100. Based on a previous study (22), we divided all participants into two groups using the first quantile as the cut-off value, namely, the low muscle-mass group, representing the lowest to the first quartile and high muscle-mass group, above the first quartile.

Statistical analysis

All data were analyzed with SAS 9.4 software (Statistical Analysis System, SAS Institute Inc., Cary, NC, United States); reference.[1] All quantitative data are presented as mean and standard deviation or

1 https://www.sas.com/en_us/legal/editorial-guidelines.html

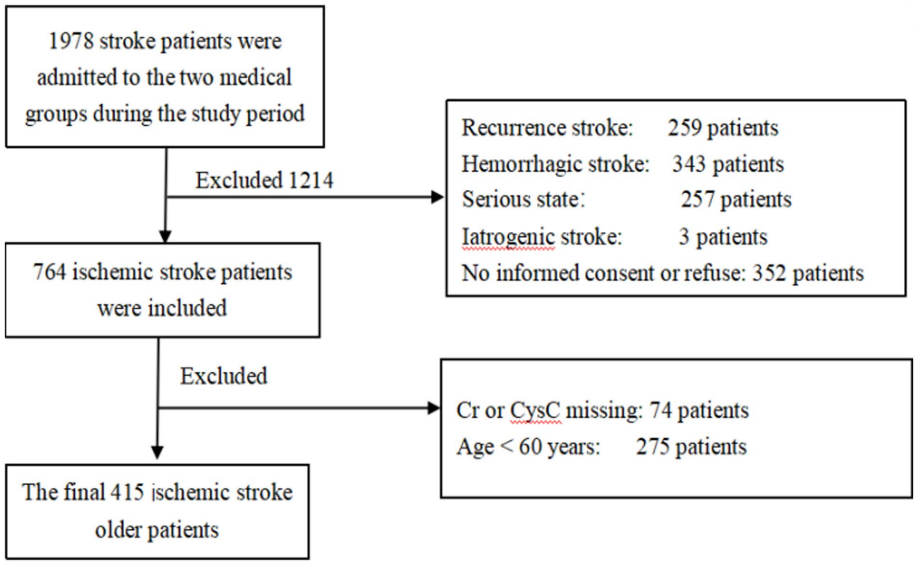

FIGURE 1
Flow chart of study participants.

median and interquartile based on distribution. Categorical variables are presented as frequencies and proportions. Various tests, including the rank-sum, Pearson's chi-square, and Student's *t*-test, were used for the comparison of the baseline features. The Kaplan–Meier method was used to evaluate survival outcomes to recurrence and death in relation to SI among different patients. The correlations between SI and stroke recurrence and mortality were determined using Cox regression analysis. A value of $p < 0.05$ indicated statistical significance.

Results

General characteristics

A total of 415 older first-ever IS patients were recruited; these included 242 (58.31%) males and 173 (41.69%) females. The ages of the subjects ranged from 60 to 90 years at the baseline. The median follow-up time was 42.75 months. Table 1 presents the characteristics of the different groups in relation to recurrence and death status. Compared with patients with high SI, those with low SI were more likely to relapse and die ($p < 0.05$).

In this study, the first quartile of the sarcopenia index was 76.12, and subjects were divided into two groups, namely the low-SI (<76.12) and high-SI groups (≥76.12). We demonstrated differences in age, sex, marital status, drinking history, smoking history, and eGFR between the low and high muscle-mass groups (Table 2).

Recurrence

After discharge from the hospital, 96 (23.13%) older patients with their first IS experienced stroke recurrence, which occurred within 1 year of discharge in 42 patients. During the follow-up period, 64 patients (30.77%) in the low-SI group experienced recurrence while compared with 32 (20.58%) in the high-SI group. The relapse rate at 75 months was 78.50% in the low-SI group and 38.60% in the high-SI group. The median survival time for recurrence in the low and high muscle-mass groups was 66.55 months and > 75 months, respectively, and this difference between the two groups was statistically significant (Figure 2; $p = 0.02$). Table 3 shows that after adjusting for confounding factors, the high-SI group had a lower relapse risk than the low-SI group (HR = 0.571, 95%CI: 0.336–0.969, $p = 0.038$).

Mortality

After discharge, 73 patients (17.4%) died, with 16 (21.3%) within 1 year of discharge. During the follow-up period, the mortality of the low- and high-SI groups was 29.81 and 13.5%, respectively. Although the median overall survival time in both groups was >75 months, the discrepancy between the two groups was statistically significant (Figure 3; $p < 0.001$). Table 3 illustrates that after adjusting for confounding factors, the high-SI group had a lower mortality risk than the low-SI group (HR = 0.294, 95%CI: 0.155–0.558, $p < 0.01$).

Discussion

In the present research, 96 (23.13%) older patients with their first IS experienced stroke recurrence, with 72 (17.4%) of patients dying during the median 42.75 months' follow-up. We found a significant association between SI with both stroke recurrence and mortality among first-ever ISOS. The high-SI group had a lower relapse risk and mortality, suggesting that active intervention to improve SI may prevent stroke recurrence and death and promote healthy aging in the older adults.

First-ever ISOS patients in the low-SI group showed significantly higher mortality. Patients with high SI scores were 0.294 times less likely to die than patients with lower scores, which is similar to the findings of a previous study (19). There are several possible reasons for this. First, the low-SI group represents the low muscle-mass group which includes patients who tend to have low levels of protein

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TABLE 1 Baseline characteristics of participants by the recurrence and death.

Variable	Recurrence			Death		
	No (n = 319)	Yes (n = 96)	P	No (n = 342)	Yes (n = 73)	P
Age, years, median(IQR)	69(64,75)	70(64,77.75)	0.214	68(63,74)	74(68.5,79.5)	<0.001
Sex n(%)			0.448			0.947
Male	190(78.19)	53(21.81)		200(82.3)	43(17.7)	
Female	129(75)	43(25)		142(82.56)	30(17.44)	
Marital status n(%)			0.59			0.025
Married	49(74.24)	17(25.76)		48(72.73)	18(27.27)	
Single/divorced, widowed	269(77.3)	79(22.7)		293(84.2)	55(15.8)	
Education n(%)			0.09			0.052
Elementary school and below	134(72.83)	50(27.17)		144(78.26)	40(21.74)	
Junior high school and above	183(79.91)	46(20.09)		196(85.59)	33(14.41)	
Toast classification n(%)			0.884			0.635
LAA	150(77.32)	44(22.68)		158(81.44)	36(18.56)	
SAOL	118(75.64)	38(24.36)		132(84.62)	24(15.38)	
CE	51(78.46)	14(21.54)		52(80)	13(20)	
Lesion location n(%)			0.077			0.741
Right	92(77.97)	26(22.03)		98(83.05)	20(16.95)	
Left	88(81.48)	20(18.52)		86(79.63)	22(20.37)	
Both	52(82.54)	11(17.46)		51(80.95)	12(19.05)	
Others	87(69.05)	39(30.95)		107(82.54)	19(17.46)	
Smoking history n(%)			0.208			0.379
No	153(74.27)	53(25.73)		166(80.58)	40(19.42)	
Yes	163(79.51)	42(20.49)		172(83.9)	33(16.1)	
Drinking history n(%)			0.744			0.094
No	217(76.41)	67(23.59)		228(80.28)	56(19.72)	
Yes	102(77.86)	29(22.14)		114(85.07)	17(14.93)	
BMI, kg/m^2, mean(SD)	23.26(5.11)	23.29(6.46)	0.971	23.46(5.32)	22.38(5.95)	0.126
eGFR, ml/min/1.73 m^2, mean(SD)	84.04(23.85)	83.63(23.48)	0.882	84.93(23.98)	79.34(22.13)	0.068
ALB, g/L, median(iqr range)	41.25(38.55,43.6)	41.1(38.2,43.5)	0.845	41.5(38.9,43.8)	40.3(37.25,42.1)	0.001
Rank score n(%)			0.547			0.008
0–2	96(78.69)	26(21.31)		110(90.16)	12(9.84)	
3–5	221(75.95)	70(24.05)		231(79.38)	60(20.62)	
Hypertension n(%)			0.427			0.139
No	96(74.42)	33(25.58)		101(78.29)	28(21.71)	
Yes	223(77.97)	63(22.03)		241(84.27)	45(15.73)	
Diabetes n(%)			0.728			0.853
No	220(76.39)	68(23.61)		238(82.64)	50(17.36)	
Yes	99(77.95)	28(22.05)		104(81.89)	23(18.11)	
Hyperlipidemia n(%)			0.964			0.184

(Continued)

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TABLE 1 (Continued)

Variable	Recurrence			Death		
	No (n = 319)	Yes (n = 96)	P	No (n = 342)	Yes (n = 73)	P
No	209(77.12)	62(22.88)		219(80.81)	52(19.19)	
Yes	110(76.92)	33(23.08)		123(86.01)	20(13.99)	
Heart disease n(%)			0.32			0.663
No	242(78.06)	68(21.94)		254(81.94)	56(18.06)	
Yes	77(73.33)	28(26.67)		88(83.81)	17(16.19)	
Peripheral vascular disease n(%)			0.861			0.905
No	306(76.88)	92(23.12)		328(82.42)	70(17.58)	
Yes	12(75)	4(25)		13(81.25)	3(18.75)	
Medication compliance n(%)			0.004			0.361
Good	143(83.14)	29(16.86)		148(86.05)	24(13.95)	
Bad	137(70.26)	58(29.74)		161(82.56)	34(17.44)	
Healthy exercise n(%)			0.837			0.505
No	160(77.29)	47(22.71)		168(81.16)	39(18.84)	
Yes	159(76.44)	49(23.56)		174(83.65)	34(16.35)	
SI. n(%)			0.033			<0.001
Low SI	72(69.23)	32(30.77)		73(70.19)	31(29.81)	
High SI	247(79.42)	64(20.58)		269(86.5)	42(13.5)	

involvement, associated with malnutrition. Patients with low muscle mass tend to be malnourished, which affects their prognosis (23). Second, patients with sarcopenia tend to have difficulty swallowing and are more likely to develop aspiration pneumonia (24). Third, sarcopenia patients are more likely to fall (15), causing fractures that can lead to death in older adults. Fourth, this study confirmed that low muscle mass was associated with a higher rate of stroke, also potentially leading to death. Fifth, sarcopenia is closely linked to mechanical ventilation and infectious complications, both of which are frequently fatal in older adults (25, 26). All these demonstrate the important role of the SI level in the prognosis of the first IS.

The findings of the present study showed that patients with high skeletal muscle mass had a lower rate of stroke recurrence. It has also been found that patients with low skeletal muscle mass may be at a higher risk of developing IS (13). This could result from fewer changes in the white matter and silent infarctions that are known to be associated with higher skeletal muscle mass, which may prevent stroke occurrence and thus reduce the recurrence rate (27).

In the present study, we chose the Cr/CysC ratio rather than muscle mass itself to assess the presence or absence of muscle loss. There were several reasons for this choice. Serum creatinine is an endogenous product derived from creatine phosphate and its production is influenced by skeletal muscle. However, serum creatinine levels are also affected by renal function, thus limiting the reliability of this biomarker in assessing muscle (28). Cystatin C is a small protein originating in nucleated cells that is reabsorbed by proximal tubules and completely decomposed. Its production is less affected by muscle mass. Therefore, Cr/CysC can effectively assess muscle mass without renal imaging (18).

The study has some strengths. The availability of data at multiple time points is one of the strengths of this study. Over the median follow-up period of 42.75 months, patients were assessed every 3 months. Therefore, we could compile accurate survival curves for the low-and high-muscle mass groups throughout this period. However, the study does have some limitations. First, we assessed the outcomes every 3 months by phone, making the data prone to memory bias. The rate of stroke recurrence might have been underestimated as some patients may have experienced a transient ischemic attack without recognizing it. Second, we only considered the first relapse of patients but some cases had more than one stroke recurrence. Third, as almost 50% of patients lacked NIHSS scores in their medical records, the modified Rankin Scale (mRS) was included in the model as a confounding factor. Fourth, the SI we used lacks a comparison with the gold standard for diagnosing sarcopenia, so the SI as an indicator of sarcopenia in the stroke population requires further study. Therefore, future research should collect more comprehensive basic information for analysis.

Conclusion

The study found a significant association between the sarcopenia index and both stroke recurrence and mortality in individuals with their first-ever ischemic stroke. These findings provide important insights and references for the secondary prevention of stroke. It is imperative to prioritize the modification of risk factors that contribute to both sarcopenia and stroke, such as smoking, unhealthy diet, and a lack of physical activity, in conjunction with regular medication after discharge. Furthermore, regular assessment of the sarcopenia index or sarcopenia status in stroke survivors is important. It is also recommended that patients receive personalized nutritional support and rehabilitation exercises to improve muscle mass and functionality. By implementing active and effective interventions and treatments

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TABLE 2 Baseline characteristics of participants according to the sarcopenia index (SI).

Variable	Low SI (n = 104)	High SI (n = 311)	p
Age, years, Median (iqr range)	72(65.5–79)	69(64–74)	<0.01
Sex n(%)			<0.01
Male	39(37.50)	203(65.27)	
Female	65(62.50)	108(34.73)	
Marital status n(%)			0.019
Married	24(23.30)	42(13.50)	
Single/divorced, widowed	79(76.70)	269(86.50)	
Education n(%)			0.202
Elementary school and below	51(50.00)	133(42.77)	
Junior high school and above	51(50.00)	178(57.23)	
Toast classification n(%)			0.7
LAA	47(45.19)	147(47.27)	
SAOL	38(36.54)	118(37.04)	
CE	19(18.27)	46(14.79)	
Lesion location n(%)			0.485
Right	33(31.73)	85(27.33)	
Left	30(28.85)	78(25.08)	
Both	12(11.54)	51(16.40)	
Others	29(27.88)	97(31.19)	
Smoking history n(%)			0.01
No	63(61.17)	143(46.43)	
Yes	40(38.83)	165(53.57)	
Drinking history n(%)			0.008
No	82(78.85)	202(64.95)	
Yes	22(21.15)	109(35.05)	
BMI, kg/m^2, mean(SD)	22.90(3.70)	23.64(4.11)	0.105
eGFR, ml/min/1.73 m^2, mean(SD)	95.30(28.66)	80.14(20.53)	<0.01
ALB, g/L, median(iqr range)	40.15(37.6–42.50)	41.65(39.10–43.80)	0.624
Rank score n(%)			0.209
0–2	25(25.00)	97(31.51)	
3–5	78(75.00)	213(68.49)	
Hypertension n(%)			0.165
No	38(36.54)	91(29.26)	
Yes	66(63.46)	220(70.74)	
Diabetes n(%)			0.093
No	79(75.96)	209(67.20)	
Yes	25(24.04)	102(32.80)	
Hyperlipidemia n(%)			0.241
No	73(70.19)	198(63.87)	
Yes	31(29.81)	112(36.13)	
Heart disease n(%)			0.081
No	71(68.27)	239(76.85)	
Yes	33(31.73)	72(23.15)	

(Continued)

TABLE 2 (Continued)

Variable	Low SI (n = 104)	High SI (n = 311)	p
Peripheral vascular disease n(%)			0.564
No	99(95.19)	299(96.45)	
Yes	5(4.81)	11(3.55)	
Medication compliance n(%)			0.480
Good	47(50.00)	125(45.79)	
Bad	47(50.00)	148(54.21)	
Healthy exercise n(%)			0.515
No	49(47.12)	158(50.80)	
Yes	55(52.88)	153(49.20)	

LAA, large-artery atherosclerosis; SAOL, small-artery occlusion lacunnar; CE, Cardioembolism; ALB, Serum albumin.

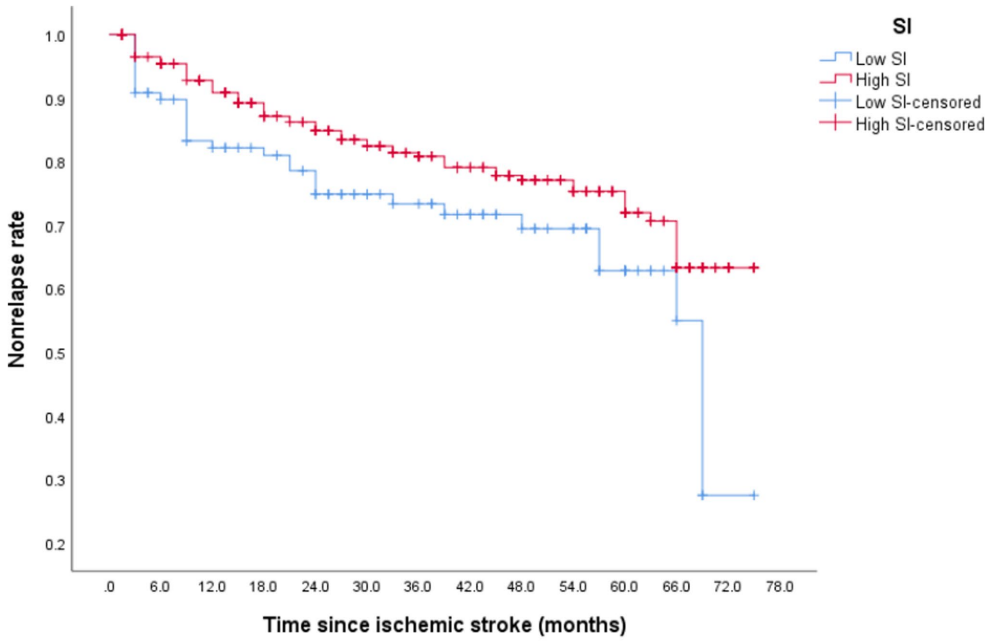

FIGURE 2
The survival curve of recurrence was evaluated by sarcopenia index (SI).

TABLE 3 Correlations between SI and recurrence and mortality.

Variable	High SI vs. Low SI	
	P value	HR (95% *CI*)
Recurrence		
Model 1	0.023	0.61(0.399–0.934)
Model 2	0.038	0.571(0.336–0.969)
Mortality		
Model 1	<0.01	0.442(0.277–0.705)
Model 2	<0.01	0.294(0.155–0.558)

Model 1: non-adjusted model. Model 2: adjusting for age, sex, marital status, education, toast classification, lesion location, Smoking history, drinking history, ALB level, eGFR, BMI, rank score, hypertension, diabetes, hyperlipidemia, heart disease, peripheral vascular disease, medication compliance, healthy exercise.

aimed at reducing stroke recurrence, we can successfully prevent the occurrence of secondary strokes and promote healthy aging.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Ethics Committee of the West China Hospital, Sichuan University, Chengdu, China. All patients signed informed consent. The studies were

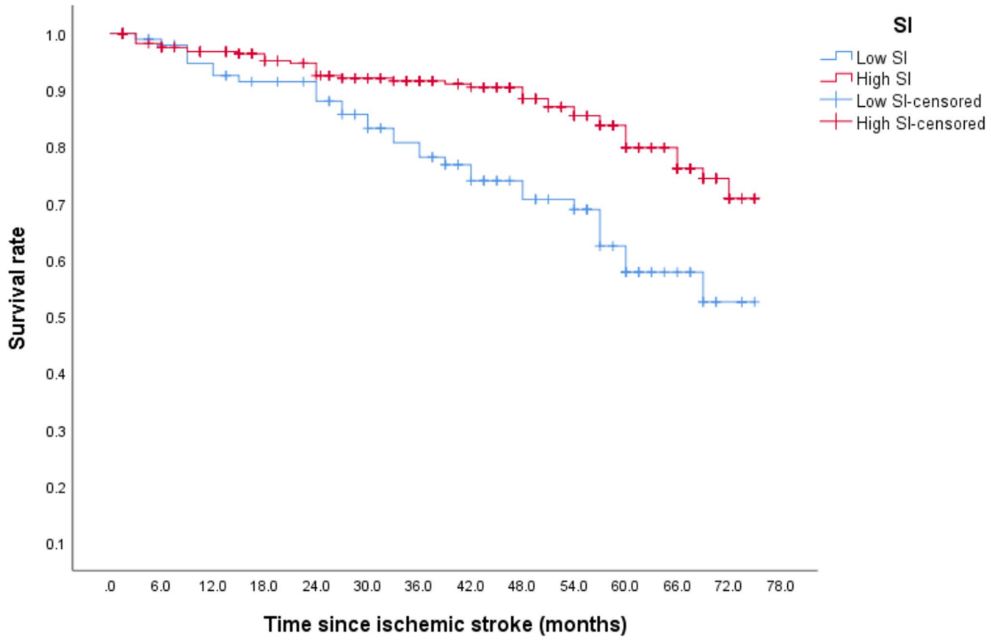

FIGURE 3
The survival curve of death was evaluated by SI.

conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

LH, XC, and CZ: study concept and design, and analysis and interpretation of data. LH and XC: acquisition of data and drafting of the manuscript. CZ: critical revision of the manuscript for important intellectual content. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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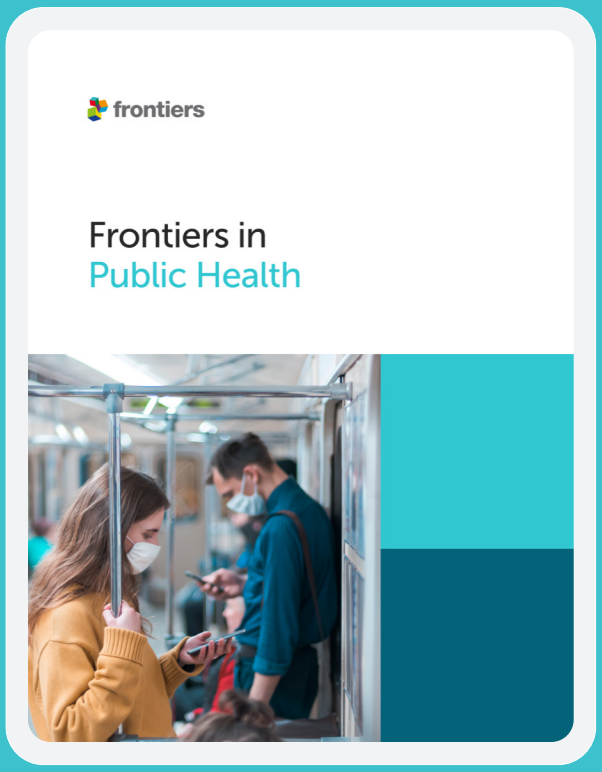

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