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Evidence-based approaches in aging and public health

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Evidence-based approaches in aging and public health

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Editorial: Evidence-based approaches in aging and public health

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Editorial on the Research Topic
Evidence-based approaches in aging and public health

Introduction

The past decade has seen a significant increase in aging research, driven by scientific breakthroughs and the need created by a growing global aging population. Clinical trials have made remarkable progress in providing insights into the underlying mechanisms of aging and exploring new treatments. However, it is crucial to recognize that human aging is a complex phenomenon that involves an intricate interplay of biological, social, cultural, and environmental factors. Any effective approach to aging research must therefore embrace this complexity.

Evidence-based medicine, which relies on randomized controlled trials (RCTs) for better diagnosis and treatment, often excludes older populations due to their co-morbidities and lower adherence rates. As a result, there has been a growing interest in observational studies based on real-world settings and data. These studies can supplement RCTs, monitor long-term cost-effectiveness and safety, and develop guidelines for treatment use. Given the significant impact of aging on health, finance, the economy, and society, an evidence-based approach is crucial for understanding disease causes and prevention. This Research Topic "*Evidence-based approaches in aging and public health*" welcomed opinions, reviews, systematic reviews, and original research articles on essential tools, epidemiological studies, artificial intelligence (AI), and geriatric syndromes.

For many years, aging research has been conducted in isolation, with researchers focusing on specific pathways or diseases. While this approach yielded valuable insights, it often failed to consider the interconnectedness of the various factors that contribute to aging. Today, there is a growing recognition of the need for a more holistic approach to aging research. Researchers are increasingly acknowledging the importance of genetics, lifestyle, environment, and emotional well-being in shaping the aging process. This requires a shift toward more innovative research methodologies that can integrate diverse disciplines and move beyond reductionist approaches.

This change presents considerable challenges. Traditional clinical trial designs, developed for single-target interventions, may not effectively capture the full impact of interventions aimed at the intricate web of aging. Ethical considerations become paramount, necessitating nuanced informed consent procedures that account for the long-term nature of interventions and the potential for unforeseen consequences. Furthermore, fostering interdisciplinary collaboration, while enriching, requires constructing bridges between diverse scientific cultures and methodologies. "A Call to Action for Collective Efforts: The apex research institutions," as a platform for pioneering medical advancements, must champion this critical transition. We urge scientists, clinicians, policymakers, and funding agencies to unite in supporting and nurturing to developing innovative clinical trial designs. Trials incorporating multidimensional endpoints, longitudinal assessments, and adaptive methodologies will be vital for evaluating holistic interventions.

Precision medicine has transformed cancer treatment by leveraging next-generation sequencing and tailored therapies. This has resulted in the emergence of novel trial designs, including basket and umbrella trials, master platform trials, and N-of-1 patient-centric studies. Additionally, real-world data, digital applications, and machine learning are being employed to expedite knowledge acquisition. Clinical trials have shifted from focusing on specific tumor types to being gene-directed and histology-agnostic, with personalized treatment plans tailored to individual biomarker profiles (1). Fostering interdisciplinary collaboration: encouraging partnerships between biologists, gerontologists, social and behavioral scientists, data scientists, and ethicists will be crucial for designing and implementing comprehensive aging research programs (2). Promoting public engagement and openly discussing the complexities and uncertainties of aging research, while emphasizing its potential benefits, will gain public trust and foster broader understanding.

Late-life learning programs can help answer research questions and enhance our comprehension of active and healthy aging. Such programs can be utilized to target age-related diseases such as dementia and cognitive decline. Research on the multidimensional health impact of late-life learning can strengthen national strategies and inform policies. These programs are cost-effective, scalable, and suitable for use in low-resource settings. More implementation research is needed to ensure that these programs reach vulnerable groups and older adults. The COVID-19 pandemic has accelerated the shift to online learning, promoting digital inclusion (3).

Scientific research has advanced significantly in domains like immunology and genetics over the last 30 years. Unfortunately, due to the high failure rate and inefficiencies in the healthcare system, clinical research is still moving slowly. Innovative approaches are required to solve this, in order to involve patients and produce evidence for novel medical advancements. The COVID-19 pandemic revealed structural flaws in the way clinical trials are conducted, which spurred scientists to create patient-centric trials of the future. Deep neural networks, multimodal biomedical AI, and machine learning have the potential to revitalize clinical research by enhancing image interpretation, workflow, and drug discovery (4). The fast advancements in precision medicine, immunology, and genomics require adjustments to clinical trial design. Although RCTs are regarded as the gold standard in drug discovery, they come with a high price and risk. Numerous practical uses of AI are being investigated as a means of achieving sustainable and optimal medication development. Utilizing AI models, data are transformed into meaningful insights, accelerating the process of drug research. Opportunities include how AI can help find focused therapeutics and rare illness treatments, improve patient recruitment and protocol design efficiency, and use AI to monitor patients. Furthermore, to help businesses decide whether to engage in AI integration and to ascertain the areas where regulation will have the greatest influence, this research attempts to identify opportunities, obstacles, and future implications for AI in RCTs (5–9).

ASReview is an open-source program that researchers have created to make the process of screening abstracts and titles for systematic reviews and meta-analyses more efficient. Only a small percentage of the screened research are deemed significant in the scientific literature, a problem that the new technology is intended to remedy. With the help of this tool, review procedures will be able to become more transparent and efficient by mitigating the error-prone and inefficient process of manually screening thousands of research publications (10).

Contribution to the field

It is vital to recognize and take lessons from the health system measures that can improve healthy aging. Considering the need for more and better evidence-based policies and care for our aging populations, we present 15 papers from across the globe in this Research Topic on "*Evidence-based approaches in aging and public health*" of *Frontiers in Public Health*. These papers cover different research methods ranging from hospital-based study (Chen S. et al.) to community based study (Peng et al.) to epidemiological study (Jiao et al.), and from RCTs (Xu et al.), to studies based on statistical modeling (Elamin and Ansah; Ye et al.) to a review (Chen J. et al.) as well as several systematic reviews with meta-analyses (Gao et al.; Dai et al.; Li et al.; Zhou et al.)

As is to be expected from Public Health as a broad discipline, the diseases and issues addressed in the 15 papers are also wide-ranging. "*Evidence-based approaches in aging and public health*" covers diverse topics such as dentistry, sarcopenia, physical activity, sleep, Alzheimer's and Parkinson's, arterial fibrillation, hip fracture, rehabilitation, unmet needs, medical costs, reducing blood pressure, inappropriate medications and much more. Interestingly, the overwhelming majority (11/15) of papers in this Research Topic were submitted from authors based in China, with one study each focusing on Italy (De Cola et al.), the United Kingdom (Elamin and Ansah), Singapore (Ansah et al.), and Vietnam (Phi et al.).

According to the Chen S. et al. study, hospitalization patterns among patients with Alzheimer's disease (AD) and Parkinson's disease (PD) varied markedly. For hospitalized patients with AD and PD, it is crucial to apply alternative management, and distinct priorities should be set when developing primary preventive programs, identifying care needs, and allocating healthcare resources.

Peng et al. investigated cognition and physical frailty in older persons and found that sleep quality partially mediates the association between cognitive impairment and physical frailty.

Jiao et al. reported that there are notable regional and national differences in the illness burden of atrial fibrillation (AF). In terms of incident cases [818,493 (562,871–1,128,695)], deaths [39,970 (33,722–46,387)], and disability-adjusted life years (DALYs) [1,383,674 (1,047,540–1,802,516)] at the national level, China topped among the list of nations.

Patients with mild cognitive impairment (MCI) benefit significantly from Tai Chi in addition to transcranial direct current stimulation (tDCS) for improved global cognitive performance, memory, execution function, and attention (Xu et al.). These results point to the possible application of Tai Chi and tDCS as a non-invasive brain stimulation regimen and physical exercise to enhance cognitive function in older persons with MCI.

Using a multi-state population model, Elamin and Ansah estimated the prevalence of periodontal diseases and dental caries in the adult population in the United Kingdom. This model gives policymakers a realistic, evidence-based estimate of future demand for oral health issues. Due to the considerable time lag in the education and training of oral health professionals, these forecasts allow policymakers to anticipate future capacity demands proactively rather than reactively.

The nature of sarcopenia transitions and estimations of life expectancy with and without sarcopenia are addressed by Ye et al.. Their results underscore the significance of early detection and treatment for sarcopenia among older Chinese people, enhancing our knowledge of the connection between sarcopenia and life expectancy, and offering targeted health education. They noted that sarcopenia is more common in women, older adults with low education, single people, those with an agriculture hukou, and smokers, both current and past. Targeted interventions are needed to increase the number of older people in western China's impoverished and rural areas who do not have sarcopenia.

Chen J. et al. reviewed factors that influence older persons' medical expenses. The medical costs of older persons need to be evaluated more thoroughly since they are more likely to develop chronic illnesses. Financing strategies, multidimensional comparisons, and factor investigations should all be used to analyse the medical costs incurred by older persons. Furthermore, research should be done on how rising medical expenses affect Medicare 'financing for older adults, healthcare services, and medical insurance support programs. In order to lessen the burden on older persons, policy makers should focus more on the medical costs of these individuals and the factors that influence them and develop relevant policies in a multifaceted and all-encompassing manner.

According to a network meta-analysis by Gao et al., middle-aged and older persons can significantly lower their blood pressure with both static and aerobic exercise. Both exercise modalities had a considerable impact on systolic blood pressure, but not diastolic blood pressure. The SUCRA ranking results indicate that for middle-aged and older persons, static exercise lowers blood pressure more effectively than aerobic exercise, and for those with hypertension, appropriate exercise can lower blood pressure to some extent.

In a meta-analysis by Dai et al., providing traditional Chinese exercises (TCEs) to patients with chronic heart failure (CHF) had a positive impact on their recovery, primarily by improving LVEF, VO_2max, anaerobic threshold, quality of life, and single-item traditional Chinese medicine scores (fatigue, palpitations, floating limbs, and shortness of breath).

According to Li et al. meta-analysis, lifestyle modification (LSM) is advised as a long-term BP (blod pressure) control regimen; additionally, TCD bubble is suggested for lowering SBP and RE as a potential means of lowering BP. Aerobic exercise on its own or combined with resistance exercise and dietary approaches to stop hypertension (DASH) are recommended for the Prehypertension (PHT) population with moderate to high quality evidence for BP lowering.

According to Zhou et al., pharmacological interventions can minimize the incidence of potentially inappropriate medications (PIMs), the number of PIMs per person, the amount of pharmaceuticals used, and the 30-day readmission rate, all of which can enhance the prognosis of older patients.

De Cola et al. claim that the establishment of a hub-and-spoke network for intense neuro-rehabilitation has improved regional care services for neuro-rehabilitation while also facilitating the management of neurological patients by preventing needless long-distance travel.

To promote system-wide solutions, Ansah et al.'s research discusses the elements that either facilitate or impede hip fracture recovery. They do this by adopting a feedback perspective. Their study report that recovering from a hip fracture-related loss of function is largely dependent on two factors: (a) identifying the difference between one's pre-fracture and current physical functions; and (b) using psychological resilience to act quickly to address a functional loss through rehabilitation services.

According to the results of the (Phi et al.) study, a large number of older Vietnamese individuals had functional impairments. Those not marital (divorced, separated, single) had the highest percentage of unmet demands but the lowest rate of care needs among this group. Unmet needs were more common among rural people with poorer health than among those who lived in cities and had normal or fair health.

Conclusion

The past decade has seen increased research on aging, driven by scientific breakthroughs and a growing aging population. Clinical trials have made progress in targeting aging mechanisms, but a more holistic approach is needed. There is a growing interest in observational studies and real-world data. This editorial recognizes the need to adopt "Complexity in Aging Research," and hence we call for more interdisciplinary collaboration and public engagement. A shift toward more innovative research methodologies that integrate diverse disciplines is required. This change presents significant challenges, such as ethical considerations and interdisciplinary collaboration. The research institutions must champion this critical transition by supporting innovative clinical trial designs and fostering interdisciplinary collaboration. Encouraging partnerships between biologists,

gerontologists, social scientists, data scientists, and ethicists will be crucial for designing and implementing comprehensive aging research programs. Late-life learning programs can help target age-related diseases such as dementia and cognitive decline. These programs are cost-effective, scalable, and suitable for use in low-resource settings.

Author contributions

BS: Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing. EvT: Conceptualization, Data curation, Methodology, Supervision, Writing – original draft, Writing – review & editing. PS: Methodology, Validation, Writing – review & editing. RK: Methodology, Validation, Writing – review & editing. HA: Methodology, Supervision, Validation, Writing – review & editing.

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Conflict of interest

BS and HA were employed by Hamad Medical Corporation.

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Effects of traditional Chinese exercises on the rehabilitation of patients with chronic heart failure: A meta-analysis

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Background: With the development of rehabilitation medicine, exercise therapy has gradually become one of the methods to prevent and treat cardiovascular diseases. It is widely used in clinic because it can further reduce the mortality rate, improve clinical symptoms, restore the activity ability of the body, improve the quality of life of patients and reduce the hospitalization rate. Traditional Chinese exercises have developed rapidly in recent years, which mainly include Baduanjin, Tai Ji, etc. However, meta-analyses of all types of exercises are not well characterized.

Objectives: To evaluate the effect of traditional Chinese exercises (TCEs) on the rehabilitation of patients with chronic heart failure (CHF) using a meta-analysis.

Methods: A systematic search of randomized controlled trials (RCTs) on TCEs for patients with CHF in 13 databases (PubMed, China National Knowledge Infrastructure, etc.). Meta-analysis was performed using Review Manager software (version 5.3) after two investigators independently screened the studies, assessed the quality of the studies, and extracted the data.

Results: Meta-analysis of 21 randomized controlled trials which involved 1,665 patients with chronic heart failure showed that practicing TCEs was effective in improving patients' physiological outcomes such as VO_2max [MD = 2.14, 95% CI (1.02, 3.26), $P < 0.001$], AT [MD = 1.61, 95% CI (1.06, 2.16), $P < 0.001$], and left ventricular ejection fraction [MD = 2.60, 95% CI (1.17, 4.02), $P < 0.001$]. Non-physiological outcomes benefited from the application of TCEs: 6-min walking distance [MD = 38.55, 95% CI (36.67, 40.42), $P < 0.001$], quality of life [MD = 5.52, 95% CI (3.17, 7.88), $P < 0.001$], and single-item TCM symptom scores in CHF patients: tiredness and fatigue [MD = 0.78, 95% CI (0.03, 1.53), $P = 0.04$], shortness of breath [MD = 0.44,95% CI (0.26, 0.62), $P < 0.0001$], facial puffiness and limb swelling [MD = 0.44,95% CI (0.12, 0.76), $P = 0.007$], palpitations [MD = 0.68,95% CI (0.14, 1.21), $P = 0.01$] were improved.

Conclusions: TCEs improved several recovery indicators, heart failure-related clinical symptoms, quality of life, and physiological indicators in patients with CHF. It is worthwhile to expand the participants for practical application in clinical practice, but the existing evidence is insufficient and the heterogeneity of outcome is large. Therefore, more high-quality clinical trials are needed to support these results.

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KEYWORDS

traditional Chinese exercises, Tai Chi, chronic heart failure, rehabilitation, meta

1. Introduction

Chronic heart failure (CHF) is the end stage of many cardiovascular diseases. It is a complex syndrome that causes high hospitalization and mortality rates and places a significant burden on the public health system (1, 2). Studies show (3) that the absolute number of people with heart failure has nearly doubled since 1990. With the development of modern medicine, exercise rehabilitation has become one of the most important aspects of cardiac rehabilitation as one of the core elements of cardiac rehabilitation, enabling patients to improve their disease status through active exercise (4). The relevant guidelines (5)[1] strongly recommend cardiac rehabilitation.

Traditional Chinese exercises (TCEs) combine internal and external training, rigidity, and flexibility, including Ba Duan Jin, Six-character formula, Taijiquan, Five mimic-animal exercises, and Zhan Zhuang. China's traditional exercises are based on traditional Chinese medicine, Yin and Yang, the theory of five elements, the science of channels and collaterals and the theory of Zang and fu, and China's traditional philosophic thinking and regimen concept are the upper concepts (6, 7). TCEs emphasize the harmony of the body and mind, and promote the operation of one's qi, blood, and fluids. After thousands of years of exploration and renewal, TCEs have evolved into the core of the idea of "adjusting the body, breath and mind," through conscious inhaling and exhaling, relaxing body and mind, concentrating the mind to achieve the effect of disease prevention and cure, and consequently prolonging life. The good implementation effect of traditional Chinese exercises has been verified by meta-analysis in patients with hypertension (8), stroke (9), sleep disorder (10) and other chronic diseases. Practicing traditional Chinese exercises, for example, can effectively improve the gait of stroke patients, the pain symptoms of patients with chronic low back pain, the mood and symptoms of patients with sleep disorders etc. Studies have shown that traditional Chinese exercises as a sort of rhythmic and moderate-intensity aerobic exercises can promote physical ability, quality of life and health level (8). But the existing research on the rehabilitation effect of patients with chronic heart failure is lacking.

TCEs, as a non-pharmacological therapy with great cultural implications in China, have been used in the rehabilitation of patients with CHF because of their advantages of safety, economy, and not being restricted by venue and time (11). There are few studies on the intervention of chronic heart failure patients by traditional methods such as Baduanjin, Yijinjing, and Wuqinxi in China, and their universality and effectiveness need to be further tested. At present, there is a lack of a clear understanding of the regulatory variables (content, cycle, etc.) that affect the intervention effect of China's traditional exercises on patients with chronic heart failure.

However, the results of these clinical studies have varied widely. Some studies have shown that TCEs can effectively improve left ventricular ejection fraction (LVEF) (12–22), 6-min walking distance (6MWD) (13, 14, 16–19, 21–25), quality of life (QOL) (14–16), and other outcomes. Some related studies have shown that TCEs did not effectively affect patients' LVEF (15), 6WMD (17), and QOL (18, 19) compared with conventional medication or care, which was not statistically significant. However, caregivers need systematic scientific advice and guidelines to support them in developing relevant plans for their patients. Systematic evaluation of the effect of TCEs on the rehabilitation of patients with CHF is lacking.

At present, there is no best practice plan about different traditional Chinese exercises for the rehabilitation of CHF patients. This study evaluated the effect of TCEs on the rehabilitation of patients with CHF through meta-analysis to provide a reliable basis for clinical practice. This study also fills the gap in the current meta-analysis of related topics and provides an in-depth design idea for related clinical trials in the future. At the same time provides an effective practical path for the implementation of the "Key Project Planning for the Inheritance and Development of Chinese Excellent Traditional Culture."

2. Methods

2.1. Search strategy

Randomized controlled trials (RCTs) on TCEs for patients with CHF were searched using a computerized retrieval system in the Chinese full-text journal database, VIP database, Wan Fang database, China National Knowledge Infrastructure (CNKI), WeiPu, WanFang, China Biology Medicine disc, National Medical Journal of China, PubMed, Cochrane Library, Web of Science, EBSCO, and Embase databases from the time of database construction to 25 November 2022. Chinese database mainly uses keywords such as "Ba Duan Jin," "Taijiquan," "Five mimic-animal exercises," "Six-character formula," "Qigong," and "Yi Jin Jing," "Five Elements Palm," "Zhan Zhuang," "Hui Chun Gong," "Heart Failure," "Chronic Heart Failure," "cardiac insufficiency" for searching, and the specific search strategy is presented in Appendix. Thus, the search for the retrieval strategy for non-Chinese databases could be finalized (the concrete retrieval formula of the database is shown in Appendix). The reference lists of the relevant articles were screened and checked to identify more eligible studies.

2.2. Study inclusion and exclusion criteria

The inclusion criteria for studies were applied as follows. Study's participants: (1) Patients aged ≥18 years. (2) Recognized or authoritative guideline criteria confirmed the diagnosis of CHF. (3) Patients with NYHA cardiac function class I to III. (4) The patient does not have other serious complications. (5) The patient does not have physical activity disorder or cognitive impairment.

Abbreviations: LVEF, left ventricular ejection fraction; MLHFQ, Minnesota Living with Heart Failure Questionnaire; 6MWD, 6 min walking distance; CHF, chronic heart failure; RCTs, randomized controlled trials; QOL, quality of life; TCEs, traditional Chinese exercises.

1 Available online at: https://www.researchgate.net/publication/358352812_Guidelines_for_Cardiac_Rehabilitation_Programs_AACVPR.

Interventions: (1) Patients in the experimental group were given a single traditional Chinese exercise (e.g., Ba Duan Jin, Yi Jin Jing, Five mimic-animal exercises, Six-character formula, etc.). Study design: randomized controlled trial (RCT). Study language: Chinese or English.

The exclusion criteria for studies were applied as follows. (1) The intervention did not match or combined with the other instruments. (2) The intervention participants do not meet the inclusion criteria or is not clear. (3) Book or conference study. (4) Unavailability of the complete study.

2.3. Data extraction and quality assessment

The title and abstract of each retrieved study were read by two independent reviewers (MengQiao Dai and ZiYan Luo) who had undergone an evidence-based nursing course. The study was initially screened manually, while it was imported into EndNoteX9 for duplication. The remaining studies were again read in their entirety, and those that did not meet the criteria were removed according to the exclusion criteria. Two reviewers independently extracted and checked the information about the study, including author characteristics, year of publication, participants, type of study design, specific measures of the control and intervention groups, duration of the intervention, outcomes (LVEF, VO_2max, AT, QOL, 6MWD, single-item TCM symptom scores), and the evaluation tool used for the outcome indicator. In case of disagreements between the two reviewers in the above steps, a third reviewer with the same qualifications was asked to discuss the decision.

Two reviewers performed an independent quality assessment of all the included studies. The Cochrane 5.1.0 quality evaluation criteria were used which consisted of seven items, and the reviewers made "low risk," "high risk," and "unclear" classifications for each item. If a study fully satisfied the criteria, the study was considered to have a low possibility of bias i.e., was classified as grade A; partially satisfied as grade B, the study was considered to have a moderate possibility of bias; completely unsatisfied as grade C; the study was considered to have a high possibility of bias.

2.4. Statistical analyses

Meta-analysis was performed using RevMan 5.3 software, and the count data were expressed as relative risk (RR) with 95% CI; continuous variables, such as maximal oxygen uptake (VO_2max), anaerobic threshold (AT), LVEF, 6WMD, QOL, and traditional Chinese medicine (TCM) evidence alone scores, were expressed as mean difference (MD) or standardized mean difference (SMD) with 95% CI. If $P > 0.05$, $I^2 < 50\%$, there was no significant statistical heterogeneity among the studies, and a meta-analysis was performed using a fixed-effects model. If $P < 0.05$, $I^2 > 50\%$, there was greater heterogeneity among the studies, and a random-effects model was used to calculate the combined effect size. A subgroup analysis was conducted to further explore the sources of heterogeneity. Statistical significance was set at $P < 0.05$.

3. Results

3.1. Results of literature retrieval

A total of 2,539 documents were obtained by computer and manual search, including 1,827 documents in English and 712 documents in Chinese, and a total of 853 duplicate documents were removed using Endnote software manually. After reading the titles and abstracts of the remaining studies, 1,558 irrelevant pieces of study were removed. The full text of the remaining 128 papers was read according to the inclusion and exclusion criteria of the study, and 21 papers were finally included in the final statistical analysis. A flow diagram of the search and selection of the studies is shown in Figure 1.

3.2. Study characteristics

The 21 included papers (12–32) were sorted by article. A total of 1,665 patients with CHF were included. In this study, the sample size ranged from 18 to 150. The time span for literature publication was from 2016 to 2022. Among them, 17 were Chinese studies and four were English studies. The basic characteristics of the included studies are presented in Supplementary Table 1.

3.3. Risk of bias assessment

The quality of the study was evaluated using Review Manager version 5.3. We assessed the risk of bias in all the included studies. All 21 (12–32) included studies mentioned "randomization," of which four mentioned allocation concealment. Participants could not be blinded due to the intervention; therefore, all articles were at a high risk of blinding of participants and personnel. Six mentioned the blind method of outcome assessment. The risk of incomplete outcome data was low in all trials. All studies had an unclear risk of bias in selective reporting. The detailed results of the bias risk assessment are summarized in Figures 2, 3.

4. Meta-analysis results

4.1. Left ventricular ejection fraction

LVEF values in patients with CHF were reported in 13 studies (12–22, 25, 26), which showed that LVEF values were higher in the trial group than in the control group. Meta-analysis showed a statistically significant difference in LVEF values in the trial group compared with the control group [MD = 2.60, 95% CI (1.17, 4.02), $P < 0.001$] due to high heterogeneity between studies ($I^2 = 94\%$, $P < 0.001$) (Figure 4).

Because of the large bias in LVEF results across studies, subgroup analyses were performed with different types of gong methods, whether instructions other than drugs and gong methods

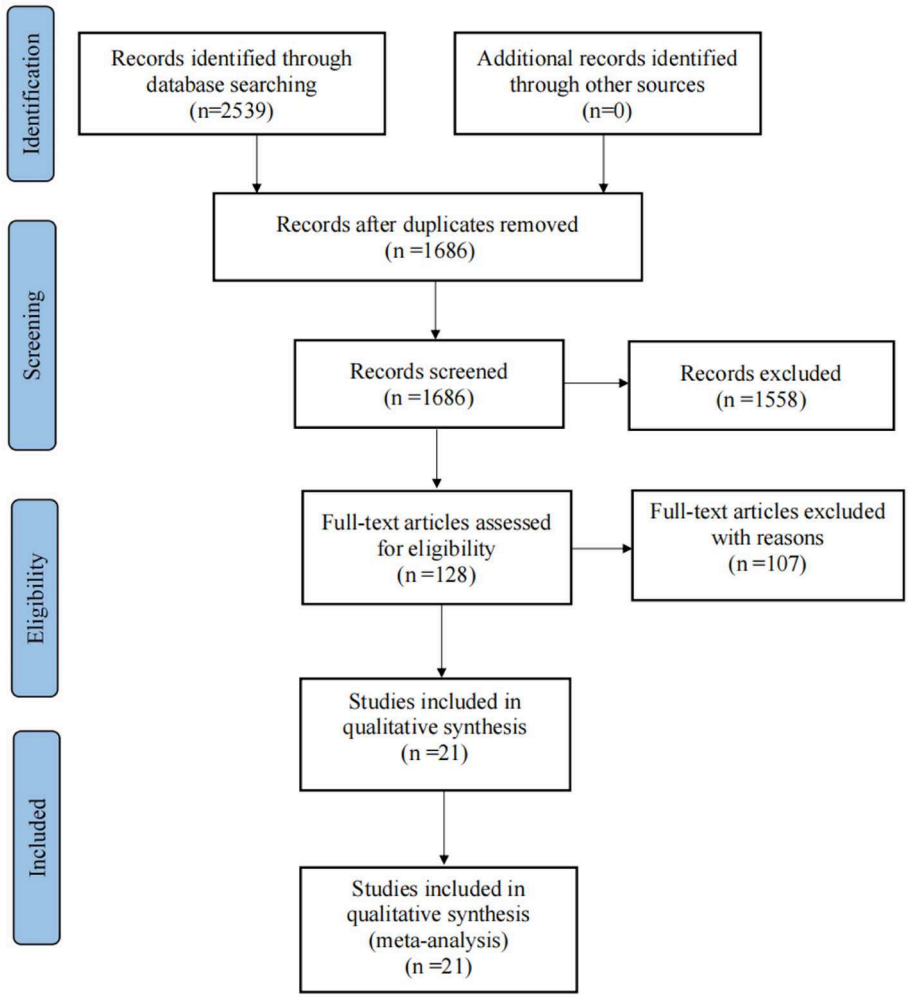

FIGURE 1
Flow diagram of search and selection of studies.

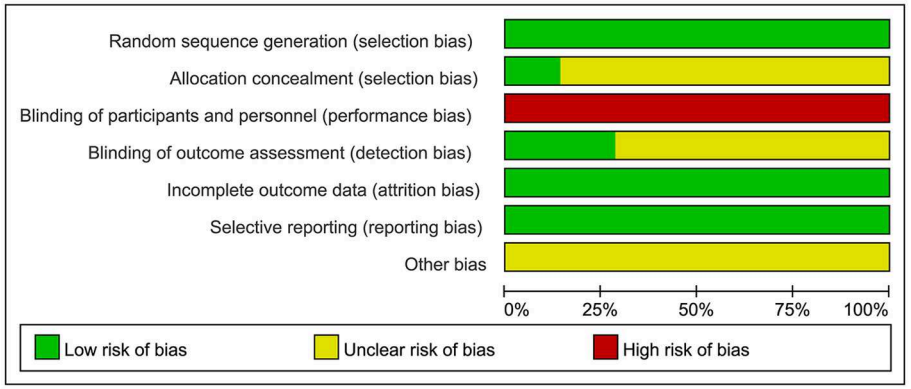

FIGURE 2
Bias risk diagram: judgment of risk of bias expressed as a percentage of all included studies.

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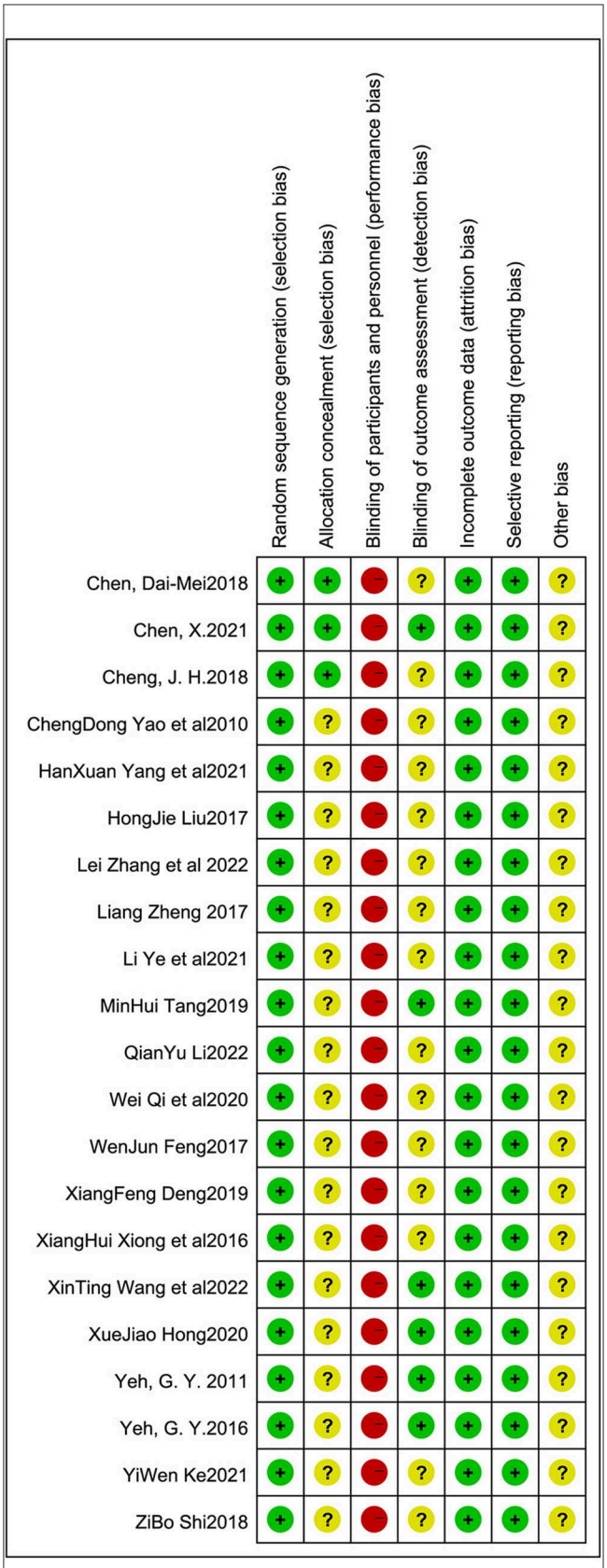


FIGURE 3
Bias risk summary: judgment of risk of bias and items with bias included in the studies; "+", low risk; "−", high risk; "?", unclear.

were given, length of intervention (≤3; >3 months), and length of single intervention (≤30; >30 min) as subgroup variables (Figure 5).

In the subgroup analysis with an intervention using different types of exercises as subgroup variables, in which Bada Duan Jin and Taijiquan were used in five studies each [14–17, 19–21, 23, 27, respectively], the analysis was performed using a random effects model. The results showed that the LVEF values in the studies with Bada Duan Jin experimental group was statistically significant ($P = 0.03$) compared with the control group. However, in the studies in which the intervention exercises were combined using different gong methods, results showed that there was no statistically significant difference between the groups ($P = 0.23$) (Figure 5A).

In the subgroup analysis with the subgroup variable of whether or not to give instructions other than drugs and exercises, seven studies (13, 16, 17, 19, 21, 22) mentioned administering drugs and exercise interventions, while five studies (14, 18, 20, 25, 26) additional instructions were given to patients such as health education and emotional guidance ($P = 0.19$ and $P = 0.10$, respectively) (Figure 5B).

In a subgroup analysis with intervention duration as a subgroup variable, eight studies (13, 15, 17–20, 22, 25) with intervention duration ≤3 months and four studies (14, 16, 21, 26) with intervention duration >3 months were analyzed using a random effects model. The results showed that the LVEF values were not statistically significant in the experimental group compared to the intervention group for intervention lengths of < or > 3 months ($P = 0.14$, $P = 0.16$) (Figure 5C).

In a subgroup analysis with a single intervention duration as a subgroup variable, it was shown that nine studies (13–17, 19, 21, 22, 25, 26) had a single intervention duration of ≤30 min, and three studies (16, 18, 20) had a single intervention duration >30 min, which were analyzed using a random effects model. The results showed that the LVEF values were not statistically significant in the experimental group compared to the control group for single intervention durations of < or > 30 min ($P = 0.05$ and $P = 0.14$, respectively) (Figure 5D).

4.3. Maximum oxygen uptake (VO_2max)

Four studies (21, 26, 27, 29) reported patient VO_2max, which is an indicator of aerobic exercise capacity in humans. Owing to the large heterogeneity of the included studies ($P < 0.001$, $I^2 = 94\%$), meta-analysis using a random effects model showed that the VO_2max levels in the group using TCEs were greater than those in the control group, and the difference between the two groups was statistically significant [MD = 2.14, 95% CI (1.02, 3.26), $P < 0.001$] (Figure 6).

4.4. Anaerobic threshold

Four studies (19, 24, 27, 29) reported patient AT levels, which are indicators of the ability to perform daily activities, and are

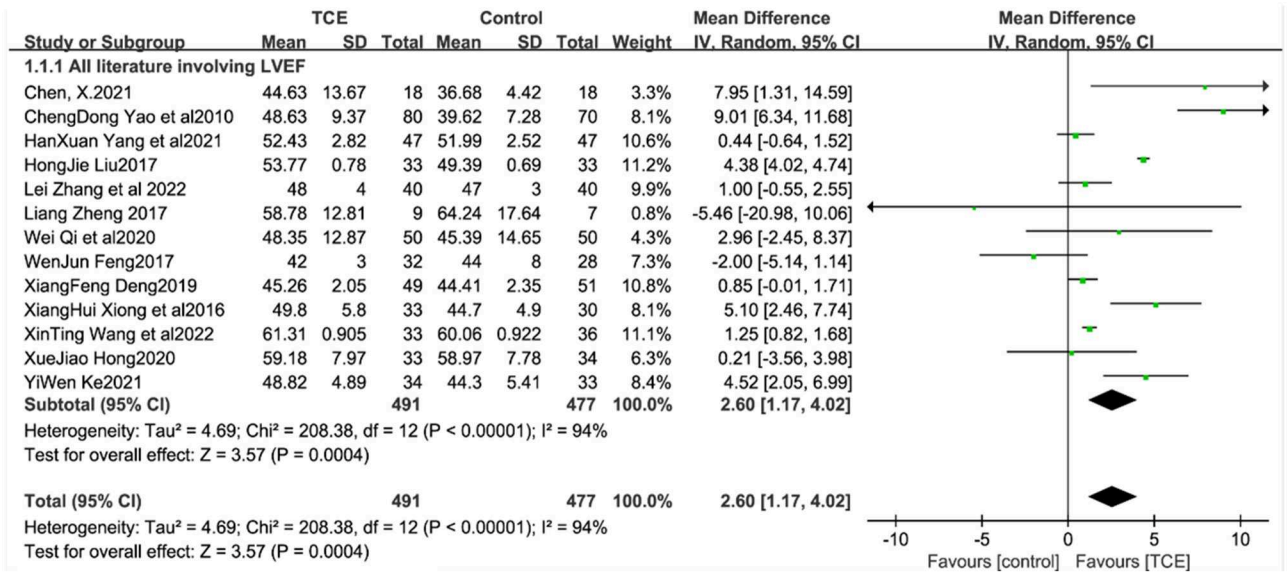


FIGURE 4
The effect of Traditional Chinese exercises on patients' LVEF.

closely related to cardiac function classification. Due to the large heterogeneity of the included studies ($P < 0.001$, $I^2 = 83\%$), a meta-analysis using a random-effects model showed that AT levels were greater in the TCE group than in the control group, and the difference between the two groups was statistically significant [MD = 1.61, 95% CI (1.06, 2.16), $P < 0.001$] (Figure 7).

4.5. Quality of life

Seventeen studies (12–14, 17–27, 29, 30, 32) reported quality of life scores in patients with CHF. All the included study used the uniform Minnesota Malfunctional Heart Quality of Life Scale (MLHFQ) for scoring. Due to the high heterogeneity of the included studies ($I^2 = 95\%$, $P < 0.001$), a random-effects model was used for the analysis. The results of the meta-analysis showed that the test group had a statistically significant difference from the control group in terms of QOL scores [MD = 5.52, 95% CI (3.17, 7.88), $P < 0.001$]. Subgroup analyses were performed using the subgroup indicator of intervention duration (≤3 and >3 months). Of the subgroup analyses with intervention duration, five studies (14, 21, 26, 27, 30) had intervention duration >3 months, and 12 studies (12, 14, 17–20, 22–25, 29, 32) had intervention durations ≤3 months. The heterogeneity of the included studies was high and a meta-analysis with a random-effects model was used. The results showed that the quality of life was statistically significant in the experimental group of different time studies of intervention feats, compared to the intervention group ($P < 0.001$ and $P = 0.007$, respectively) (Figure 8).

4.6. 6MWD

Twelve studies (13, 14, 16–19, 21–24, 28) reported 6MWD in patients with CHF, and all 6MWD were higher in the trial group than in the control group. Due to the high heterogeneity of the included studies ($I^2 = 86\%$, $P < 0.001$), a random-effects model was used for the analysis. The results of the meta-analysis showed that the test group differed significantly from the control group in terms of QOL scores [MD = 36.83, 95% CI (29.11, 44.56), $P < 0.001$]. In the subgroup analysis of interventions by intervention duration, three studies (14, 16, 21) and (13, 17, 19, 22–25, 28) had an intervention duration greater than and ≤3 months, respectively. The heterogeneity of the included studies was high and a meta-analysis with a random-effects model was used. The results showed that the QOL was statistically significant in the experimental group of different time studies of intervention feats, compared to the intervention group ($P < 0.001$ and $P = 0.007$, respectively) (Figure 9).

4.7. Single-item TCM symptom scores in CHF patients

4.7.1. Tiredness and fatigue

Three studies (17, 20, 22) reported the level of fatigue and weakness in the single-item TCM score of patients. Owing to the large heterogeneity of the included studies ($P < 0.001$, $I^2 = 94\%$), meta-analysis using a random-effects model showed that the level of fatigue and weakness in the group using TCEs was better than that in the control group, and the difference was statistically significant when comparing the two groups [MD = 0.78, 95% CI (0.03, 1.53), $P = 0.04$] (Figure 10).

4.7.2. Shortness of breath

Three studies (17, 20, 22) reported the level of shortness of breath in the single-item TCM score of patients. Due to the small heterogeneity of the included studies ($P = 0.45$, $I^2 = 0\%$), meta-analysis using a fixed-effects model showed that the level of

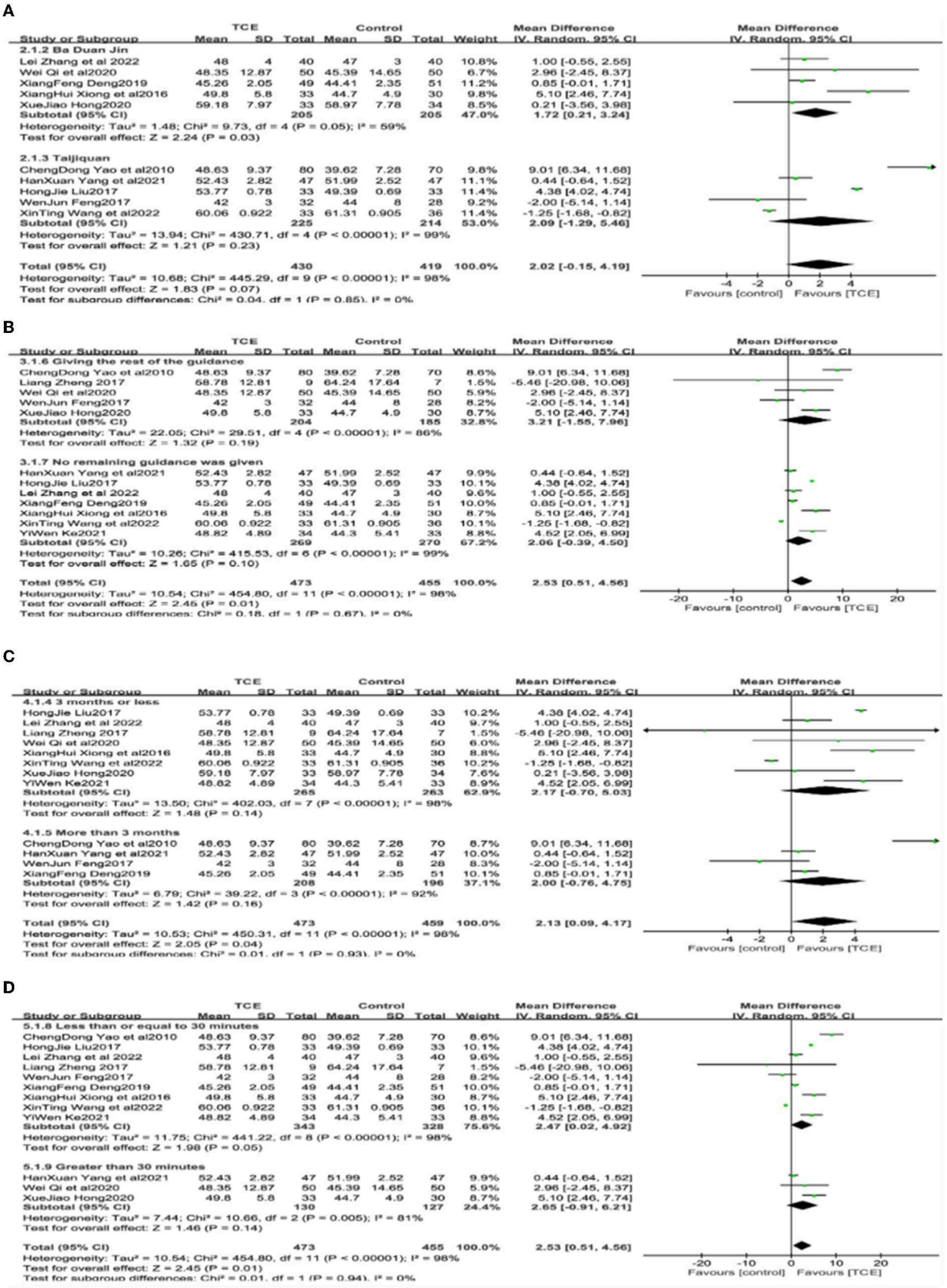


FIGURE 5
(A–D) Subgroup of the effect of Traditional Chinese exercises on patients' LVEF.

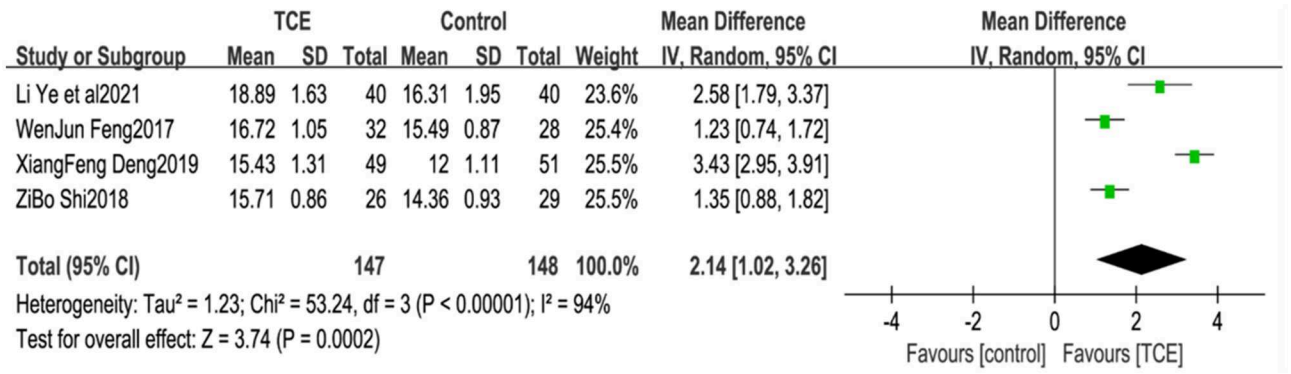


FIGURE 6
The effect of Traditional Chinese exercises on patients' VO2max.

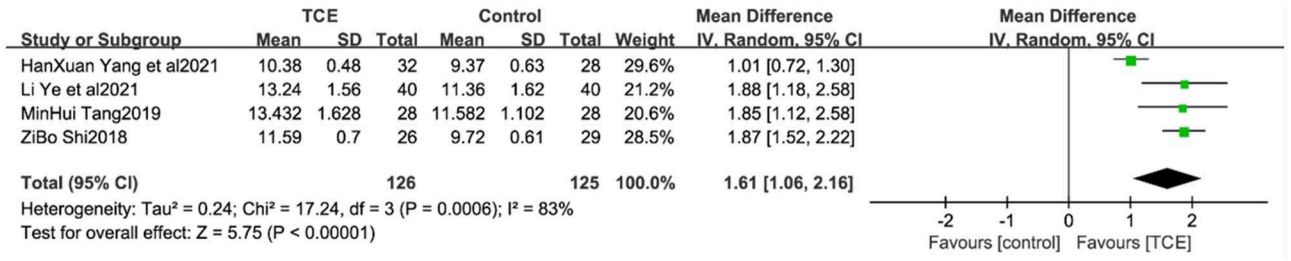


FIGURE 7
The effect of Traditional Chinese exercises on patients' AT.

shortness of breath in the group using TCEs was better than that in the control group, and the difference was statistically significant when comparing the two groups [MD = 0.44, 95% CI (0.26, 0.62), $P < 0.0001$] (Figure 10).

4.7.3. Facial puffiness and limb swelling

Three studies (17, 20, 22) reported the level of facial puffiness and limb swelling in the single-item TCM score of patients. Owing to the large heterogeneity of the included studies ($P = 0.11$, $I^2 = 55\%$), meta-analysis using a random-effects model showed that the level of fatigue and weakness in the group using TCEs was better than that in the control group, and the difference was statistically significant when comparing the two groups [MD = 0.44, 95% CI (0.12, 0.76), $P = 0.007$] (Figure 10).

4.7.4. Palpitations

Three studies (17, 20, 22) reported the level of palpitations in the single-item TCM score of patients. Owing to the large heterogeneity of the included studies ($P = 0.006$, $I^2 = 80\%$), meta-analysis using a random-effects model showed that the level of fatigue and weakness in the group using TCEs was better than that in the control group, and the difference was statistically significant when comparing the two groups [MD = 0.68, 95% CI (0.14, 1.21), $P = 0.01$] (Figure 10).

5. Publication bias and sensitivity analysis

Funnel plots were used for the analysis when the number of studies in the meta-analysis was ≥10. The results showed partial asymmetry, suggesting the possibility of a publication bias. Sensitivity analysis was performed by comparing the differences between the effect sizes obtained from the different combined models and comparing the changes in the total effect sizes after excluding each study individually.

6. Discussion

6.1. Improving cardiac function and prognosis

The LVEF is an index related to the myocardial contractility. The stronger the myocardial contractility, the more the stroke volume and the higher the LVEF. A meta-analysis showed that TCEs can effectively improve the LVEF of patients, which is consistent with a previous study by Ren et al. (33). The benefits of TCEs, such as Taijiquan, for patients with chronic heart failure have been included in relevant guidelines[2]. This is due to the fact that

2 Available online at: https://www.moh.gov.my/moh/resources/penerbitan/CPG/CPG%20Heart%20Failure%202019.pdf.

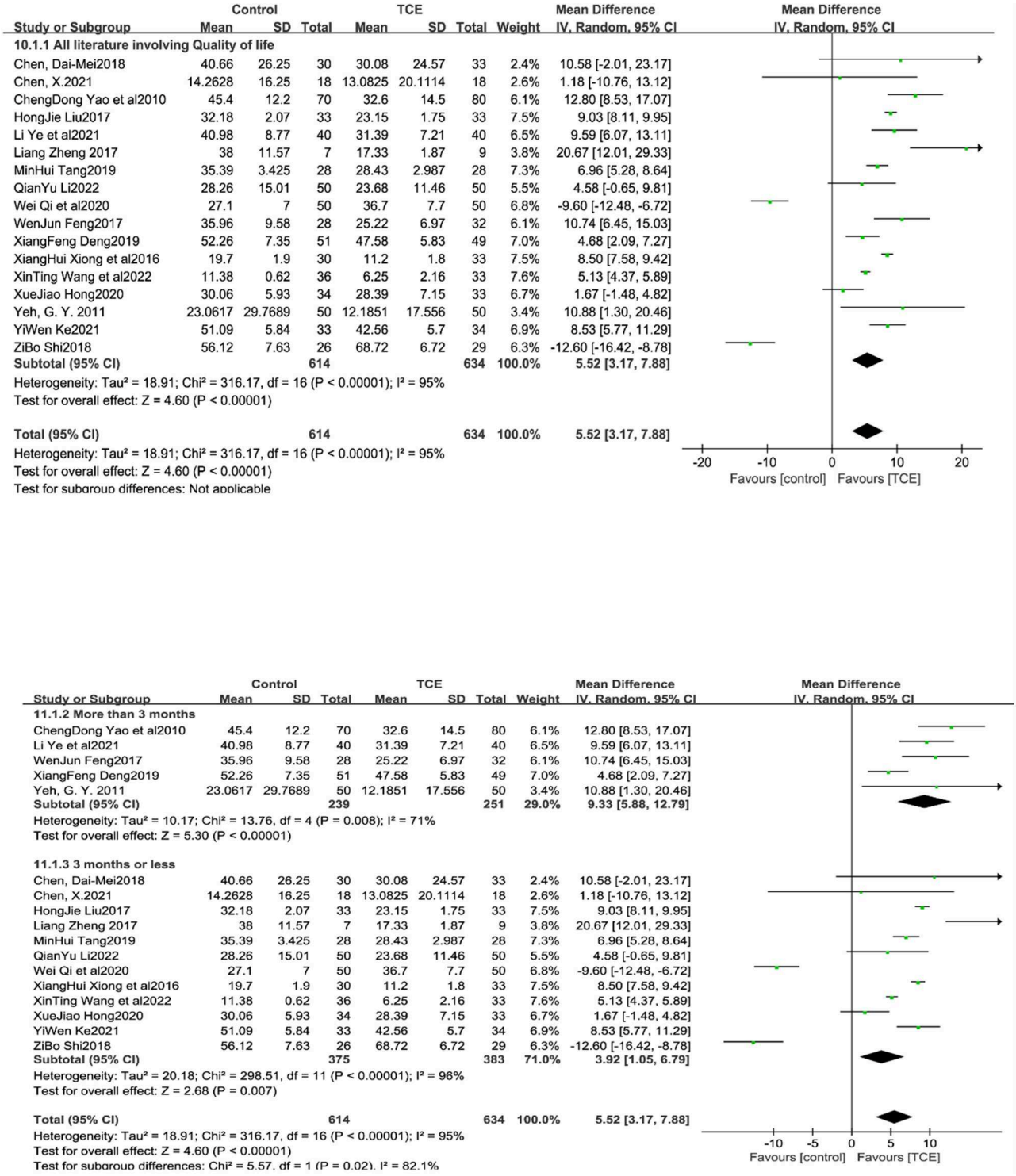


FIGURE 8
The effect of Traditional Chinese exercises on patients' quality of life (included subgroup analysis).

traditional exercises such as Taijiquan can make cardiomyocytes compensately thickened, resulting in the overall enhancement of myocardial contractility, so that the stroke volume and ejection fraction are correspondingly increased (34). In a subgroup analysis of LVEF, a possible source of heterogeneity was found in the study (15, 18–21), and the reason for this was that the TCEs used in the study were Ba Duan Jin, whereas the exercises used in the other included studies were Taijiquan, Yi Jin Jing, and Liu Zi Jue. The reasons for this need to be discussed further. In terms of improving myocardial contractility in heart failure patients, the use

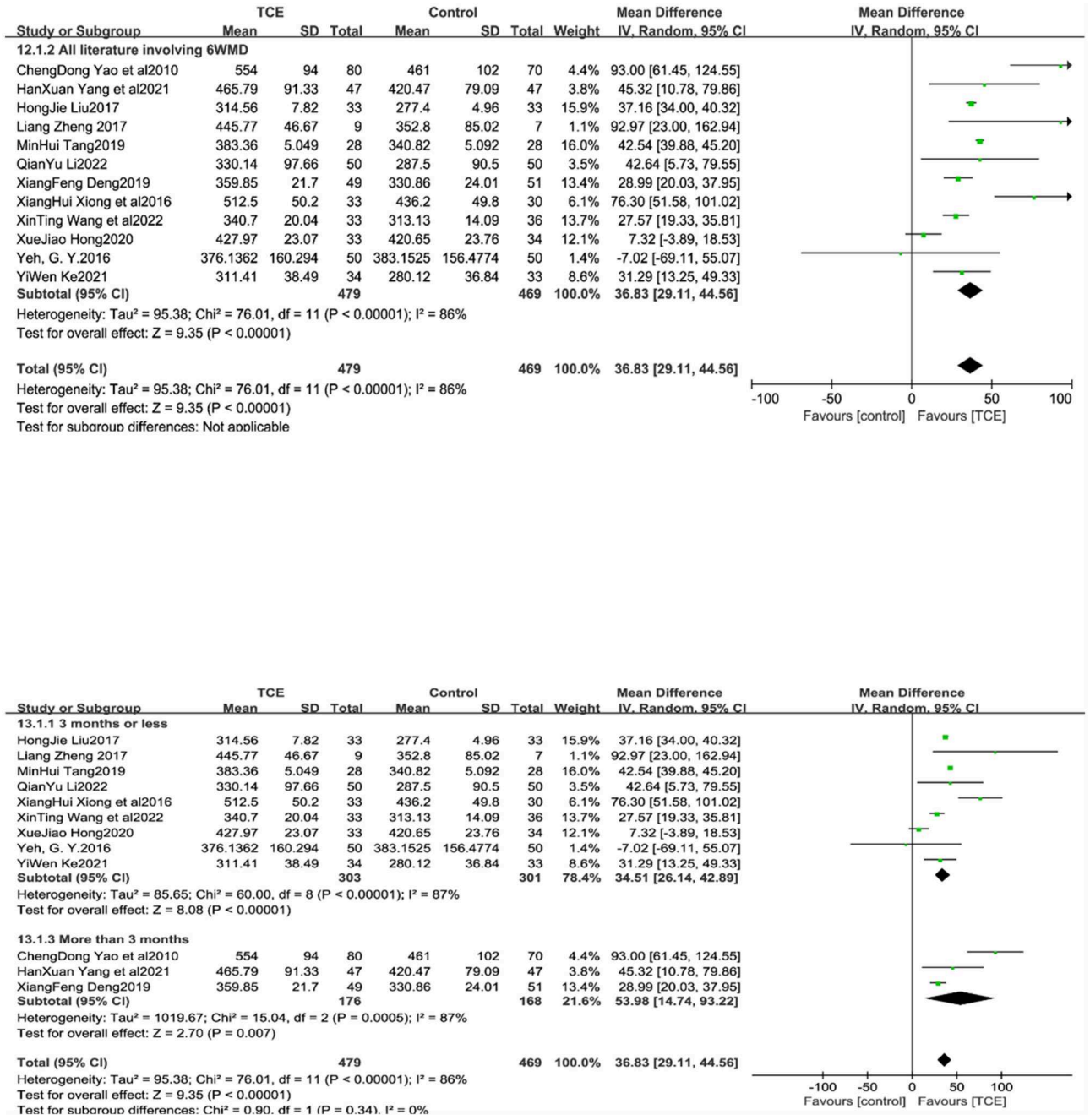
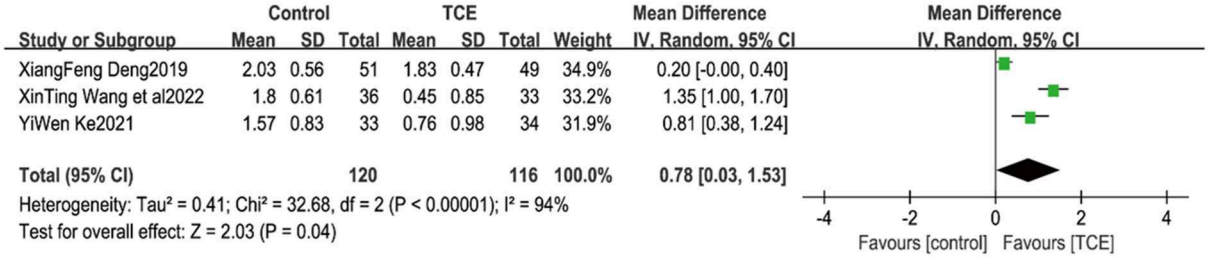


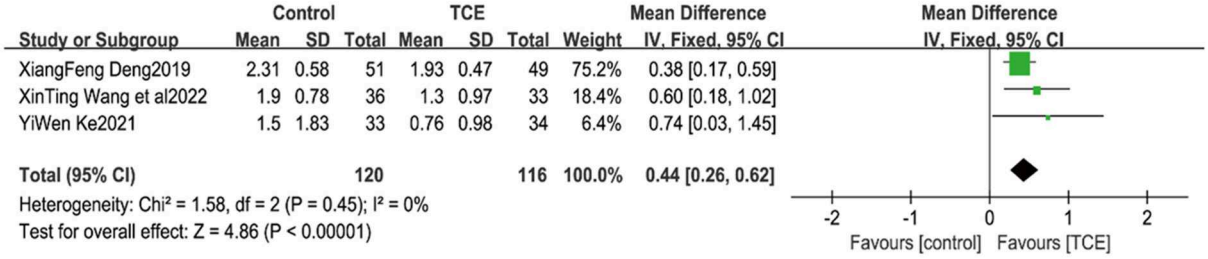
FIGURE 9
The effect of Traditional Chinese exercises on patients' 6MWD (included subgroup analysis).

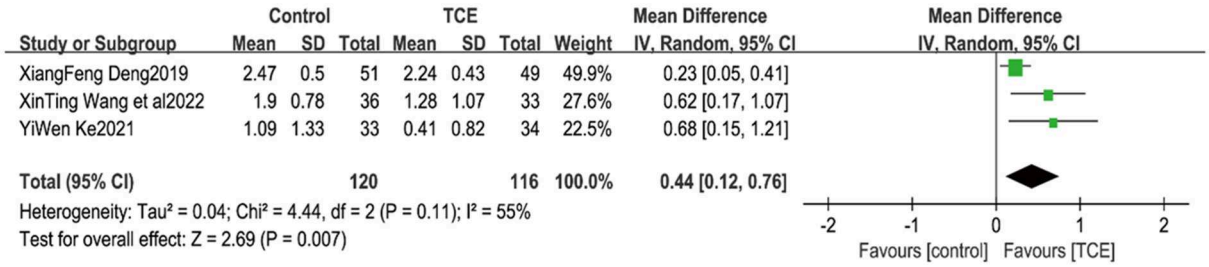
of Bada Duan Jin may be superior to Taijiquan, and more clinical studies are needed to prove the specific mechanism. Ba Duan-jin emphasized keeping gentle and steady lower limb movements, which increased the endurance of lower limb skeletal muscles, enhanced the strength and strength of muscle fibers, improved muscle perfusion and metabolism, and increased the total volume density of mitochondria and the capacity density of cytochrome c oxidase in muscle fiber cells (35, 36). In future clinical practice, healthcare providers can carry out training of TCEs to improve myocardial contractility during the rehabilitation phase according to the condition of heart failure patients. However, owing to the small sample size and heterogeneity of the studies included in this analysis, more clinical trials are needed to corroborate the results in the future.

6.2. Enhancement of exercise capacity

Meta-analysis results showed that TCM methods could effectively enhance patients' maximal oxygen consumption,







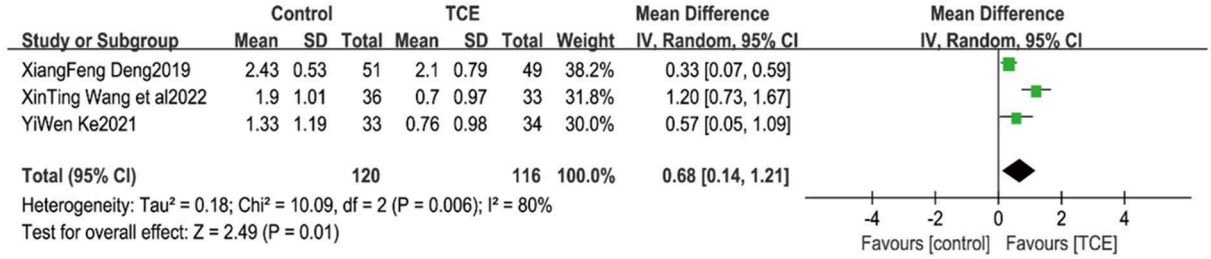


FIGURE 10
The effect of Traditional Chinese exercises on patients' single-item TCM symptom scores.

anaerobic threshold level, and 6MWD, both of which represented an increase in patients' exercise endurance and intensity. This may be because abdominal breathing in some movements of gong methods such as Yi Jin Jing and Taijiquan can regulate parasympathetic activity and heart rate variability, thus improving cardiopulmonary function (37). At the same time, abdominal breathing will increase the range of diaphragm movement, increase the maximum ventilation and reduce the residual volume, improve the hypoxia state during exercise and increase exercise endurance (38). Of interest is that in the subgroup analysis of 6MWD, the results showed that those with ≤3 months of intervention were more statistically significant compared to those with >3 months of intervention. However, since there were only three studies with an intervention period >3 months, there may be a bias in the results, and more long-period intervention trial studies are needed to support this result in the future.

6.3. Reducing symptom clusters and improving QOL

A previous study Huang et al. (39) has shown that patients' symptoms and quality of life are closely related. Meta-analysis results showed that fatigue, shortness of breath, swelling of the face and limbs, and palpitations improved in the individual TCM symptom scores of patients; however, since only three studies were included for each outcome, there may be false negatives. TCEs can stimulate yang, regulate qi and blood, regulate vital qi of human meridians and viscera, reduce heart burden, improve the ability of transporting and utilizing oxygen in human blood circulation, thus reducing oxygen consumption of myocardium, alleviating dyspnea symptoms of heart failure and improving quality of life (40). TCEs like Tai Ji can effectively promote the excitement of the right hemisphere, inhibit the activity of the left hemisphere, increase the α brain waves, endorphins and catecholamines of practitioners, make practitioners feel pleasant and enhance their quality of life (41, 42). The results suggest that TCEs can be effective in improving the QOL, and the timing of the intervention may be a source of heterogeneity; however, further discussion is needed.

7. Limitations of the study

Slight differences in the intervention protocols and sample population characteristics due to the included studies may lead to increased heterogeneity of the results. In the case of physiological index measurements, the use of different instruments may lead to differences in the results and bias in measurement. In terms of QOL, single TCM symptom scores and subjective research instruments were mostly used, and the lack of uniform criteria may have affected the reliability of the results. In addition, flaws in the included studies, such as the inability to perform hidden allocation, failure to elaborate on whether measurement bias was performed, and follow-up bias may have affected the reliability of the results.

8. Summary

The present study clarified the beneficial effects of subjecting patients with CHF to TCEs on their recovery, mainly by enhancing LVEF, VO_2max, anaerobic threshold, quality of life, and single-item TCM scores (fatigue, shortness of breath, floating limbs, and palpitations) in patients with CHF. However, the source of heterogeneity in the quality of life is unclear. Future research can be compared according to patients' different cardiac function grades, so as to provide more specific exercise recommendations for patients with heart failure. Also more high-quality, large-sample RCTs are needed to specifically analyse the above outcome indicators for further quantitative clinical promotion of TCEs in the rehabilitation of patients with CHF.

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

MD and ZL: conceptualization and methodology. MD: data curation and analysis and original writing. SH and HC: review and editing. JY, DG, and WL: data curation and validation. All authors have made substantive contributions to this study in regard to design and implementation, 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.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1139483/full#supplementary-material

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Interventions for reducing blood pressure in prehypertension: A meta-analysis

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Background: We aimed to address which interventions best control blood pressure (BP) and delay disease progression in prehypertension and to give recommendations for the best option following a quality rating.

Methods: A Bayesian network meta-analysis was used to assess the effect of the intervention on BP reduction, delaying hypertension progression and final outcome, with subgroup analyses for time and ethnicity. Recommendations for interventions were finally based on cumulative ranking probabilities and CINeMA.

Results: From 22,559 relevant articles, 101 eligible randomized controlled trial articles (20,176 prehypertensive subjects) were included and 30 pharmacological and non-pharmacological interventions were evaluated. Moderate-quality evidence demonstrated that angiotensin II receptor blockers, aerobic exercise (AE), and dietary approaches to stop hypertension (DASH) lowered systolic blood pressure (SBP). For lowering diastolic blood pressure (DBP), AE combined with resistance exercise (RE) or AE alone provided high quality evidence, with calcium channel blockers, lifestyle modification (LSM) combined with drug providing moderate quality evidence. LSM produced the best BP lowering effect at 12 months and beyond of intervention. In Asians, TCD bubble was moderate quality evidence for lowering SBP and RE may have had a BP lowering effect in Caucasians. No recommendation can be given for delaying the progression of hypertension and reducing mortality outcomes because of low to very low quality of evidence.

Conclusion: AE combined RE are preferentially recommended for BP control in prehypertension, followed by DASH. Long-term BP control is preferred to LSM. Asians and Caucasians add TCD bubble and RE to this list as potentially effective interventions.

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KEYWORDS

prehypertension, hypertension, meta-analysis, aerobic exercise, dietary approaches to stop hypertension (DASH)

1. Introduction

Hypertension is one of the strongest risk factors for cardiovascular disease (CVD) and stroke affecting the global population (1). Prehypertension (PHT), as a transitional stage from ideal blood pressure (BP) to hypertension, with typical threshold values of 120–139 mmHg systolic or 80–89 mmHg diastolic (2, 3), provides clinicians with criteria for the need for BP management and treatment to control its progression to hypertension (HT) and to prevent subclinical damage to cardiovascular target organs (4).

Non-pharmacological treatment is mostly recommended for PHT compared to the first-line pharmacological management recommended for HT. Secondary prevention with a single BP-lowering medication is only recommended when the patient has diabetes, is at an increased risk of CVD (5) or is approaching a threshold (140/90 mmHg) (3). Recent trials (6), meta-analyses (7), and additions to the guidelines (8) have added important information for these questions on the intervention thresholds and protocols for PHT, with people across different levels of BP being able to take medication for BP-lowering management. The risk of major adverse cardiovascular events is reduced by ∼10% when SBP is reduced by 5 mmHg, benefitting people with PHT with or without CVD risk.

Overall, the results of the 2015 SPRINT study (9) have led to the development of a more enhanced concept of BP. With this in mind, BP control needs to be tailored to the characteristics of the PHT population. A large number of studies have provided ample evidence to support the effectiveness of lifestyle modification (LSM) (10, 11) such as increasing physical activity and modifying dietary habits, in reducing BP in people with PHT. However, it is the high calorie food consumption and sedentary lifestyle habits that conflict with LSM and affect adherence to implementation in people with PHT. A number of studies are now emerging that provide evidence for pharmacological treatment, but long-term drug use places a financial burden on the healthcare system and families (12). Previous studies have included BP across both PHT and HT populations, and fewer studies have discussed pharmacological and non-pharmacological interventions together. Therefore, a reasonable measure of the effectiveness of different interventions in lowering BP in the PHT population warrants detailed consideration to arrive at the most reasonable BP-lowering regimen.

This study is the first network meta-analysis (NMA) to include PHT as a study population and this paper will systematically review all randomized controlled trials (RCTs) of pharmacological and non-pharmacological interventions in the PHT population. In addition to examining the effect of BP lowering, this article specifically examines HT progression rates and cardiac, cerebral, renal and mortality outcomes. Exploring the optimal intervention options as an important part of evidence synthesis and decision making in healthcare provides clinicians with recommendations for the best interventions.

2. Methods

This article is registered on the Prospero website (CRD42022356302, https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=356302) and follows the PRISMA checklist (Supplementary Table 1).

2.1. Search strategy

A search formula was developed based on the research strategy (Supplementary Table 2). Seven electronic databases—PubMed, The Cochrane Library, SCOPUS, Web of Science, CNKI, Wanfang Data, VIP were searched from the inception of the databases to 5 October 2022, a process that did not restrict the language of the original articles. In addition, references to the included literature are reviewed to avoid article omissions.

The screening process was carried out independently by two researchers (Wj L, Xa W) and a third independent reviewer (Hao L) was consulted in case of disagreement.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) The article is a randomized controlled trial; (2) participants with prehypertension between 120 and 139 mmHg systolic and/or 80–89 mmHg diastolic were included; (3) the intervention group was given at least 4 week and more of intervention; (4) outcomes included BP values before and after the intervention.

Exclusion criteria: (1) Participants with co-morbid diabetes or cardiovascular disease; (2) participants were children/adolescents or pregnant women; (3) incomplete data from the trial were not available to extract the required data; (4) articles in which participants were taking anti-hypertensive medication other than the RCT in which the pharmacological intervention was performed; (5) duplicate articles, systematic reviews, conference papers, and animal studies.

2.3. Data extraction

A standardized extraction form was used to extract article information, study population information, intervention protocol, and outcomes (increased clinical incidence of hypertension progression and adverse outcomes compared to the original protocol). Data were extracted and cross-checked against the records to verify the consistency of the data.

When the results of a study were unclear or incomplete, we contacted the author by email to obtain relevant information. If data were still not available, the study was excluded.

2.4. Quality assessment

Two reviewers (Wj L and Cq W) independently identified the risk of bias using the Cochrane Risk of Bias tool. Articles were considered low risk of bias when the number assessed as low except for the "Blinding of participants and personnel" section (13) was ≤3, high when there was a high bias rating, and uncertain risk of bias in the remaining cases. In case of disagreement, the decision was made after discussion with a third investigator (Yx W).

Funnel plot analysis was used when the outcome indicator contained 10 or more trials and quantitative estimates were made using egger tests to determine whether there was potential publication bias and small sample effects in the articles.

2.5. Data analysis

The results were analyzed using Stata 17.0 software and R 4.2.2 software. The code used is publicly available. For continuous

variables outcome indicators, the mean deviation (MD) and standard deviation (SD) before and after the intervention were used as effect sizes, and when mean and interquartile data were available, they were converted in accordance with guidelines (14). For the count data the odds ratio (OR) and its 95% confidence interval (CI) were used as the effect analysis statistic.

Heterogeneity was assessed using the Cochran Q test and the I^2 heterogeneity test, and data with $I^2 > 50\%$ heterogeneity were subjected to subgroup or sensitivity analysis. A random effects model and a fixed effects model were fitted separately for statistical analysis, and the degree of fit of the models was judged according to the deviance information criterion (DIC) values to select an appropriate model.

Forest plots of outcome indicators were drawn and two-by-two comparisons of the efficacy of each intervention were made. To ensure consistency of evidence for direct and indirect comparisons, inconsistency tests were performed using nodal splitting. The area under the cumulative probability ranking curve under the Bayesian model was calculated in R language to visually estimate the treatment rank of each intervention (15), with SUCRA expressed as a percentage between 0 (when the treatment was determined to be the worst) and 100% (16) (when the treatment was determined to be the best), presenting the likelihood of each intervention being the best.

Subgroup analyses were also conducted to differentiate between interventions, for interventions longer than 12 months, and for populations from different ethnic and cultural backgrounds, to address the heterogeneity of the study and to make targeted recommendations for the population.

2.6. Certainty of evidence

The quality of evidence for the NMA analysis was graded using the CINeMA program, an online mesh Meta-analysis based on the GRADE method developed by Salanti et al. (17). The quality rating was assessed by the "netmeta" package of the R software and the calculation of the contribution matrix of the NMA (18). The results of the NMA were assessed overall and the quality of evidence was rated as high, moderate, low, and very low.

3. Data synthesis and analysis

A total of 22,559 articles were generated by searching the database, 4,419 duplicate studies were first removed, 17,896 studies that were not relevant to the article were excluded after reading the title and abstract, and 101 studies were included for meta-analysis after assessing full-text article eligibility (Figure 1), reporting on SBP (99 articles), DBP (97 articles), progression of hypertension (22 articles), and cardiovascular outcomes (five articles). This included 49 English articles, 51 Chinese articles, and one Spanish article.

3.1. Characteristics of the included literature

The data from the included studies, summarized in this paper (Supplementary Table 3), show the main characteristics relevant to the purpose of this review. The 101 articles included 108 studies from Asia ($n = 75$), North America ($n = 15$), Europe ($n = 6$), South America ($n = 3$), and Oceania ($n = 2$). A total of 20,176 participants were included whose mean age was 47.21 years, of which 54.70% were male. The majority of RCTs used the JNC7 definition of prehypertension ($n = 83$), including SBP of 120–139 mmHg and/or DBP of 80–89 mmHg. Of the included RCTs, all were two-arm studies, except for 17 three-arm trials, 2 four-arm trials, and 1 five-arm trial. The median duration of intervention was 12 weeks (range 4 weeks to 6 years) and 32 studies were ≥12 months in length.

3.2. Model examination

Under the fixed effects model, DIC = 430.6918, $I^2 = 0\%$ for SBP, and DIC = 420.5391, $I^2 = 0.3\%$ for DBP. Under the random effects model, DIC for SBP = 2,980.4307, DIC for DBP = 1,795.0285. The fixed effects model with smaller DIC values and better fit was used as the model for data analysis (Supplementary Table 4).

3.3. Risk of bias

The risk of bias was assessed using the Cochrane assessment tool (Supplementary Table 5) and 81 articles were classified as "low bias," 4 as "moderate bias," and 16 as "high bias." The risk of bias was mainly due to the lack of random sequence generation during randomization ($n = 51$) and the inability to achieve complete double-blindness ($n = 74$) due to the majority of LSM in this paper, and the inevitable degree of dislocation and progression of patients from prehypertension to hypertension ($n = 26$) as the duration of interventions was extended in the included studies.

Studies containing both BP and hypertension progression outcome indicators were above 10 and publication bias was assessed using funnel plots. The results showed more symmetry (Supplementary Figure 1) and further quantitative analysis using the Egger test showed better results without significant publication bias (Supplementary Table 6).

3.4. Results

There were 106, 104, 26, and five trials respectively that provided available studies that included SBP, DBP, hypertension progression and cardiac, cerebral, renal, and mortality outcomes (Figure 2), forming a triangular closed loop indicating both direct, and indirect evidence in the comparison of efficacy. Figure 2, Supplementary Figure 2, and Supplementary Tables 7–13 show the antihypertensive efficacy, priority and quality of evidence for each intervention, respectively.

Twelve measures with moderate to very low quality evidence were likely to reduce SBP compared with controls (Table 1). In direct vs. indirect comparisons, the best efficacy was obtained with calcium channel blockers (CCB), followed by the angiotensin II receptor antagonist (ARB; WMD −12.5, 95% CrI −17.59, −7.54; moderate quality). TCD bubble, high-intensity intermittent exercise (HIIT), lifestyle modification

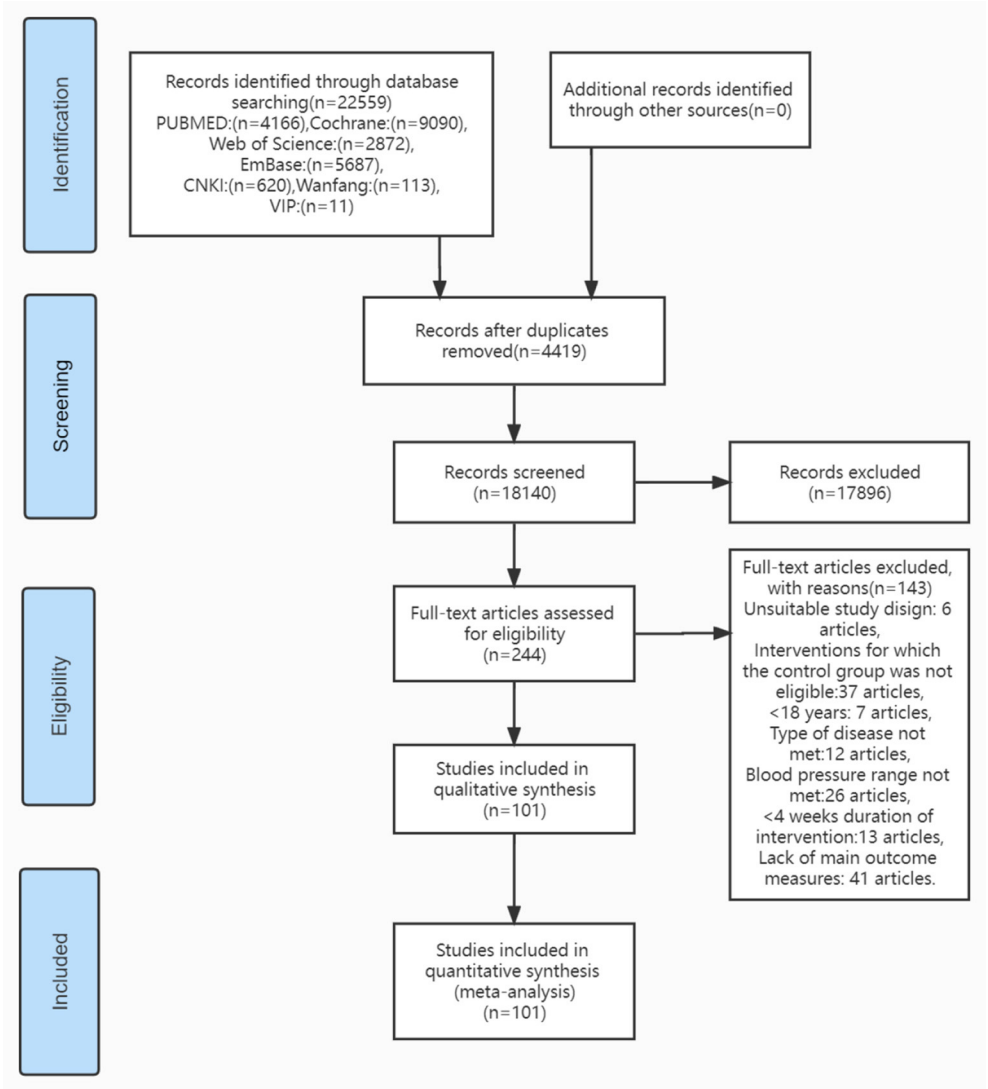

FIGURE 1
Database search and selection process.

(LSM) combined with medication, aerobic exercise (AE; WMD −10.65, 95% CrI −17.12, −4.32; moderate quality) also have some hypotensive effect.

Interventions with high quality evidence for DBP reduction emerged in the comparison (Table 2), such as AE combined with resistance exercise (RE; WMD −11.02, 95% CrI −16.73, −5.21; high quality) and AE (WMD −8.03, 95% CrI −12.25, −3.69; high quality) achieving good BP reduction with credible results. The remaining interventions with moderate to low quality evidence were CCB (WMD −12.44, 95% CrI −20.81, −4.04; moderate quality), LSM+drug (WMD −10.08, 95% CrI −14.93, −5.28; moderate quality), HIIT (WMD −7.46, 95% CrI −14.89, −0.13; moderate quality), ARB, RE, DASH, TCD bubble, and Food extract.

Analysis of the 27 trials that included HT progression (Supplementary Table 14) yielded ARB (OR 0.13, 95% CrI 0.03, 0.45; low quality), Acupoint therapy (OR 0.15, 95% CrI 0.03, 0.78; low quality), LSM (OR 0.25, 95% CrI 0.06, 0.94; low quality), and DASH (OR 0.5, 95% CrI 0.04, 5.83; low quality) were effective interventions but were not recommended due to the low quality of evidence.

Only five studies included data on cardiorenal and mortality outcomes (Supplementary Table 15) and statistical analysis failed to produce meaningful data and no recommendation was made in this area.

3.5. Sensitivity analysis and subgroup analysis

The large variety of studies included in this paper produced a more pronounced heterogeneity. The heterogeneity of EMG, AE combined with RE decreased when subgroup analyses were performed according to interventions (Supplementary Table 16); excluding studies of low to moderate quality on this basis did

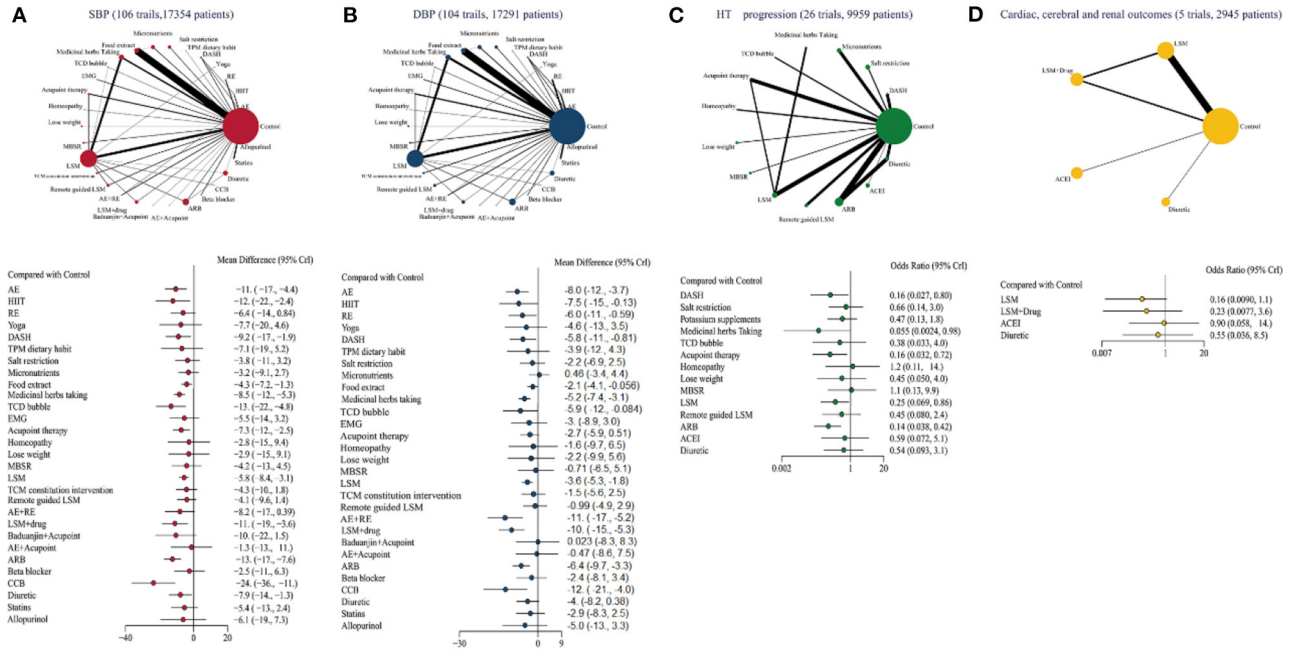

FIGURE 2
Network geometry and forest plot in PHT with four outcomes. **(A)** SBP (106 trails, 17,354 patients), **(B)** DBP (104 trails, 17,291 patients), **(C)** HT progression (26 trails, 9,959 patients), **(D)** Cardiac, cerebral, renal, and mortality outcomes (five trails, 2,945 patients). The difference among each comparison is visualized with forest plot, and the effect size is labeled on the right-hand side. AE, aerobic exercise; HIIT, high-intensity interval training; RE, resistance exercise; DASH, dietary approaches to stop hypertension; TPM, Traditional Persian Medicine; TCD, traditional Chinese drug; EMG, electromyographic; MBSR, mindfulness-based stress reduction; LSM, lifestyle modification; TCM, Traditional Chinese Medicine; ARB, angiotensin II receptor blockers; ACE, angiotensin-converting enzyme inhibitors; CCB, calcium channel blockers.

not change the heterogeneity significantly and the results were more stable.

A subgroup analysis was performed on 32 studies over 12 months (Table 3). Of a total of 15 interventions, only LSM achieved reductions in SBP and DBP control; the quality of evidence for the remaining interventions was too low. In the absence of original literature on prolonged interventions, only long-term BP lowering is currently recommended for LSM.

Based on differences in the ethnic and cultural backgrounds of the included populations, 72 studies from yellow and 29 studies from white populations were analyzed by subgroup (Table 3) and sensitivity analysis (Supplementary Table 17), including BP indicators (the three studies based on black populations could not be subjected to NMA construction). Analysis of 23 studies from Asian-based data showed that the TCD bubble was significant in reducing SBP; AE combined with RE, and LSM combined with drug were significant in reducing DBP. A total of 12 interventions in Caucasians, Medicinal herbs taking and RE had reduced SBP and DBP significantly. Food extract was effective in reducing DBP.

3.6. Inconsistency tests

There is a closed loop of outcome indicators for BP and HT progression in this paper, and inconsistency analysis was performed using the node-splitting method (Supplementary Figure 3). As the control group included in the literature included LSM, usual care and no intervention, some inconsistency ($p<0.05$) emerged between direct and indirect comparisons of medicinal herbs taking, LSM and emote-guided LSM in the analysis of SBP; and medicinal herbs taking and LSM in the analysis of DBP. This result will be explained in CINeMA and in the discussion. Otherwise, the difference between the direct and indirect evidence results for the intervention programmes was not statistically significant, indicating good agreement between the direct and indirect comparisons.

3.7. CINeMA quality of evidence grading results

The quality of evidence for the primary outcomes measured by CINeMA ranged from high to very low (Supplementary Tables 8–11), with the quality of evidence obtained for intervention programmes with SBP as an outcome ranging from moderate to very low, for intervention programmes involving a reduction in DBP ranging from high to very low, and for all HT progression and cardio-renal death outcomes being low or very low. The lower overall quality of the body of evidence is mainly due to problems with the Imprecision and Heterogeneity of the studies. To ensure the credibility of the results, only high or moderate quality evidence is recommended for analysis in this paper.

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TABLE 1 Summary of findings on the efficacy of various interventions to reduce SBP.

Intervention	Direct comparisons/ participant	Relative effect (95% CI)	Certainty of evidence (CINEMA)	SUCRA
CCB	1 RCTs; 68 participants	**−23.67 (−36.34, −11)**	⨁⨁OO	97.76%
ARB	6 RCTs; 3,044 participants	**−12.5 (−17.59, −7.54)**	⨁⨁⨁O	82.88%
TCD bubble	2 RCTs; 220 participants	**−13.44 (−22, −4.64)**	⨁⨁OO	82.37%
HIIT	2 RCTs; 44 participants	**−12.46 (−22.42, −2.39)**	⨁⨁OO	77.58%
LSM + drug	2 RCTs; 924 participants	**−11.07 (−18.5, −3.49)**	⨁⨁OO	74.03%
AE	2 RCTs; 138 participants	**−10.65 (−17.12, −4.32)**	⨁⨁⨁O	73.01%
Baduanjin + Acupoint	1 RCTs; 118 participants	−10.48 (−22.33, 1.6)	⨁OOO	67.10%
DASH	2 RCTs; 332 participants	**−9.21 (−16.47, −1.67)**	⨁⨁⨁O	64.40%
Medicinal herbs taking	17 RCTs; 1,890 participants	**−8.51 (−11.71, −5.33)**	⨁⨁OO	63.17%
AE + RE	2 RCTs; 70 participants	−8.23 (−16.72, 0.38)	⨁⨁⨁O	58.25%
Diuretic	1 RCTs; 730 participants	**−7.92 (−14.44, −1.24)**	⨁⨁OO	57.27%
Yoga	1 RCTs; 100 participants	−7.73 (−20.29, 4.44)	⨁OOO	54.43%
Acupoint therapy	7 RCTs; 513 participants	**−7.3 (−12.1, −2.57)**	⨁OOO	54.16%
TPM dietary habit	1 RCTs; 84 participants	−7.13(−19.32, 5.19)	⨁OOO	51.52%
RE	3 RCTs; 70 participants	−6.54 (−13.87, 0.71)	⨁OOO	48.80%
Allopurinol	1 RCTs; 72 participants	−5.95 (−19.53, 7.46)	⨁OOO	45.96%
EMG	2 RCTs; 71 participants	−5.6 (−14.46, 3.32)	⨁OOO	43.29%
LSM	9 RCTs; 2,856 participants	**−5.77 (−8.44, −3.12)**	⨁OOO	43.18%
Statins	3 RCTs; 203 participants	−5.32 (−13.06, 2.41)	⨁OOO	41.44%
MBSR	2 RCTs; 592 participants	−4.23 (−12.9, 4.44)	⨁OOO	35.54%
TCM constitution intervention	4 RCTs; 617 participants	−4.27 (−10.44, 1.8)	⨁OOO	34.39%
Remote guided LSM	5 RCTs; 1,035 participants	−4.1 (−9.67, 1.35)	⨁OOO	33.11%
Food extract	19 RCTs; 1,561 participants	**−4.27 (−7.24, −1.31)**	⨁⨁⨁O	32.79%
Salt restriction	3 RCTs; 1,177 participants	−3.86 (−10.95, 3.15)	⨁OOO	32.63%
Lose weight	1 RCTs; 564 participants	−2.82 (−14.79, 9.11)	⨁OOO	31.11%
Homeopathy	1 RCTs; 84 participants	−2.72 (−14.95, 9.27)	⨁OOO	30.77%
Micronutrients	3 RCTs; 734 participants	−3.27 (−8.99, 2.61)	⨁⨁OO	28.08%
Beta blocker	2 RCTs; 115 participants	−2.56 (−11.32, 6.31)	⨁OOO	26.76%
AE + Acupoint	1 RCTs; 100 participants	−1.42 (−13.45, 10.76)	⨁OOO	24.93%
Control				9.31%

CI, confidence interval; RR, risk ratio; SUCRA, surface under the cumulative ranking; AE, aerobic exercise; HIIT, high-intensity interval training; RE, resistance exercise; DASH, dietary approaches to stop hypertension; TPM, Traditional Persian Medicine; TCD, traditional Chinese drug; EMG, electromyographic; MBSR, mindfulness-based stress reduction; LSM, lifestyle modification; TCM, Traditional Chinese Medicine; ARB, angiotensin II receptor blockers; ACE, angiotensin-converting enzyme inhibitors; CCB, calcium channel blockers.
⨁⨁⨁O, moderate quality.
⨁⨁OO, low quality.
⨁OOO, very low quality.

4. Discussion

This study used the NMA to summarize the effectiveness of 30 pharmacological and non-pharmacological interventions in reducing BP and delaying progression to adverse outcomes such as HT and cardiac, cerebral, renal and mortality outcomes in people with PHT to make recommendations for interventions, with a combination of SUCRA ranking and CINeMA evidence quality.

In terms of BP reduction, ARB, AE, DASH, and food extracts reduce SBP with moderate quality evidence support; in terms of DBP reduction, AE combined with RE and exercise measures for AE are preferentially recommended with high quality evidence levels. When the length of intervention was extended beyond 12 months, only LSM retained a moderate quality of evidence for BP reduction in terms of SBP and DBP reduction. At the same time, there were significant differences in priority interventions based on ethnicity. For Asians, TCD bubble, AE combined with RE and LSM

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TABLE 2 Summary of findings on the efficacy of various interventions to reduce DBP.

Intervention	Direct comparisons/ participant	Relative effect (95% CI)	Certainty of evidence (CINEMA)	SUCRA
CCB	1 RCTs; 68 participants	**−12.44 (−20.81, −4.04)**	⊕⊕⊕O	92.78%
AE + RE	2 RCTs; 70 participants	**−11.02 (−16.73, −5.21)**	⊕⊕⊕⊕	91.89%
LSM + drug	2 RCTs; 924 participants	**−10.08 (−14.93, −5.28)**	⊕⊕⊕O	89.70%
AE	2 RCTs; 138 participants	**−8.03 (−12.25, −3.69)**	⊕⊕⊕⊕	82.95%
HIIT	2 RCTs; 44 participants	**−7.46 (−14.89, −0.13)**	⊕⊕⊕O	74.14%
ARB	6 RCTs; 3,044 participants	**−6.42 (−9.69, −3.26)**	⊕⊕OO	72.83%
RE	3 RCTs; 70 participants	**−6 (−11.24, −0.59)**	⊕⊕⊕O	67.47%
DASH	2 RCTs; 332 participants	**−5.81 (−10.8, −0.81)**	⊕⊕⊕O	66.09%
TCD bubble	2 RCTs; 220 participants	**−5.87 (−11.7, −0.08)**	⊕⊕⊕O	66.01%
Medicinal herbs taking	17 RCTs; 1,890 participants	**−5.24 (−7.42, −3.09)**	⊕⊕OO	64.51%
Allopurinol	1 RCTs; 72 participants	−5.03 (−13.31, 3.32)	⊕OOO	57.75%
Yoga	1 RCTs; 100 participants	−4.6 (−12.63, 3.52)	⊕⊕OO	54.91%
Diuretic	1 RCTs; 730 participants	−3.95 (−8.24, 0.38)	⊕⊕OO	51.59%
TPM dietary habit	1 RCTs; 84 participants	−3.9 (−12.01, 4.29)	⊕OOO	49.91%
LSM	9 RCTs; 2,856 participants	−3.56 (−5.33, −1.79)	⊕OOO	48.42%
EMG	2 RCTs; 71 participants	−2.98 (−8.93, 3)	⊕OOO	43.29%
Statins	3 RCTs; 203 participants	−2.85 (−8.27, 2.53)	⊕⊕OO	42.25%
Acupoint therapy	7 RCTs; 513 participants	−2.69 (−5.86, 0.51)	⊕OOO	40.09%
Beta blocker	2 RCTs; 115 participants	−2.42 (−8.09, 3.44)	⊕OOO	38.80%
Lose weight	1 RCTs; 564 participants	−2.2 (−9.9, 5.64)	⊕⊕OO	38.15%
Salt restriction	3 RCTs; 1,177 participants	−2.18 (−6.91, 2.46)	⊕⊕OO	36.34%
Food extract	18 RCTs; 1,521 participants	**−2.06 (−4.08, −0.06)**	⊕⊕⊕O	34.16%
Homeopathy	1 RCTs; 84 participants	−1.58 (−9.68, 6.49)	⊕⊕OO	34.11%
TCM constitution intervention	4 RCTs; 617 participants	−1.54 (−5.56, 2.46)	⊕OOO	30.40%
AE + Acupoint	1 RCTs; 100 participants	−0.47 (−8.58, 7.51)	⊕⊕OO	26.97%
Remote guided LSM	4 RCTs; 1,012 participants	−0.99 (−4.92, 2.91)	⊕⊕OO	25.77%
MBSR	2 RCTs; 592 participants	−0.71 (−6.49, 5.07)	⊕⊕OO	25.74%
Baduanjin + Acupoint	1 RCTs; 118 participants	0.02 (−8.28, 8.35)	⊕OOO	24.22%
Micronutrients	3 RCTs; 734 participants	0.46 (−3.41, 4.37)	⊕⊕OO	15.21%
Control				15.18%

CI, confidence interval; RR, risk ratio; SUCRA, surface under the cumulative ranking; AE, aerobic exercise; HIIT, high-intensity interval training; RE, resistance exercise; DASH, dietary approaches to stop hypertension; TPM, Traditional Persian Medicine; TCD, traditional Chinese drug; EMG, electromyographic; MBSR, mindfulness-based stress reduction; LSM, lifestyle modification; TCM, Traditional Chinese Medicine; ARB, angiotensin II receptor blockers; ACE, angiotensin-converting enzyme inhibitors; CCB, calcium channel blockers.
⊕⊕⊕⊕, high quality.
⊕⊕⊕O, moderate quality.
⊕⊕OO, low quality.
⊕OOO, very low quality.

combined with drug are first recommended to reduce SBP and DBP respectively; for Caucasians, RE, Medicinal herbs taking to reduce BP, or Food extract to reduce SBP are recommended. No measures are recommended for slowing the progression of HT, prevention of all organ lesions and mortality outcomes, because of the low to very low quality level of evidence.

ARBs (candesartan, irbesartan, and telmisartan), one of the first-line antihypertensive drugs for initial use (19), have been shown to be less effective in the HT population (20), but have shown better efficacy in the PHT population. ARB also has a lower incidence of adverse events after discontinuation than all antihypertensive drugs and has the advantage of maintaining stable BP (21), preventing cardiovascular events caused by rapid changes in BP. Experimental data suggest that ARBs are better at improving arterial stiffness (22) and that administration early in the course of the disease results in a

TABLE 3 Subgroups analysis of SBP and DBP based on prolonged intervention and different ethnic and cultural backgrounds (Asian, Caucasian).

Comparison	SBP				DBP			
	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)
AE								
Overall analysis	3	−10.65 (−17.12, −4.32)	⊕⊕⊕O	6	3	−8.03 (−12.25, −3.69)	⊕⊕⊕⊕	4
12 months and above	0				0			
Asians	3	−10.62 (−17.39, −3.85)	⊕⊕OO	6	3	−7.84 (−12.53, −3.1)	⊕⊕OO	5
CaucAsianss	0				0			
HIIT								
Overall analysis	0	−12.46 (−22.42, −2.39)	⊕⊕OO	4	0	−7.46 (−14.89, −0.13)	⊕⊕⊕O	5
12 months and above	0				0			
Asians	0	−13.19 (−26.05, −0.39)	⊕OOO	4	0	−9.03 (−18.16, 0.33)	⊕⊕OO	4
CaucAsianss	0				0			
RE								
Overall analysis	3	−6.54 (−13.87, 0.71)	⊕OOO	15	3	−6 (−11.24, −0.59)	⊕⊕⊕O	7
12 months and above	1	−8.58 (−26.54, 9.56)	⊕OOO	6	1	−7.84 (−19.66, 3.92)	⊕OOO	3
Asians	1	−1.49 (−15.31, 12.57)	⊕OOO	21	1	0.73 (−10.94, 12.52)	⊕OOO	22
CaucAsianss	2	−8.74 (−14.66, −2.83)		2	2	−7.92 (−12.43, −3.47)		2
Yoga								
Overall analysis	1	−7.73 (−20.29, 4.44)	⊕OOO	12	1	−4.6 (−12.63, 3.52)	⊕⊕OO	12
12 months and above	0				0			
Asians	0	−7.73 (−20.92, 5.64)	⊕OOO	13	0	−4.21 (−13.13, 4.58)	⊕OOO	11
CaucAsianss	0				0			
DASH								
Overall analysis	2	−9.21 (−16.47, −1.67)	⊕⊕⊕O	8	2	−5.81 (−10.8, −0.81)	⊕⊕⊕O	8
12 months and above	1	−17.38 (−35.14, 0.23)	⊕⊕⊕O	1	1	−8.8 (−19.6, 1.98)	⊕⊕OO	2
Asians	2	−9.36 (−17.28, −1.32)	⊕⊕OO	9	2	−6.06 (−11.51, −0.6)	⊕⊕OO	7
CaucAsianss	0				0			
TPM dietary habit								
Overall analysis	1	−7.13(−19.32, 5.19)	⊕OOO	14	1	−3.9 (−12.01, 4.29)	⊕OOO	14
12 months and above	0				0			

(Continued)

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TABLE 3 (Continued)

Comparison	SBP				DBP			
	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)
Asians	0				0			
CaucAsianss	1	−7.06 (−15.18, 1.05)		3	1	−3.85 (−9.8, 2.07)		3
Salt restriction								
Overall analysis	3	−3.86 (−10.95, 3.15)	⨁OOO	24	3	−2.18 (−6.91, 2.46)	⨁⨁OO	21
12 months and above	1	0.3 (−17.18, 17.57)	⨁⨁OO	13	1	0.07 (−10.11, 10.43)	⨁⨁OO	13
Asians	0				0			
CaucAsianss	3	−3.16 (−8.01, 1.15)		6	3	−1.66 (−5.33, 1.52)		9
Micronutrients								
Overall analysis	3	−3.27 (−8.99, 2.61)	⨁⨁OO	27	3	0.46 (−3.41, 4.37)	⨁⨁OO	29
12 months and above	2	−0.32 (−12.67, 12.14)	⨁OOO	14	2	0.01 (−7.15, 7.36)	⨁OOO	14
Asians	0				0			
CaucAsianss	1	−0.31 (−5.68, 5.03)		11	1	0.07 (−3.82, 3.95)		12
Food extract								
Overall analysis	19	−4.27 (−7.24, −1.31)	⨁⨁⨁O	23	18	−2.06 (−4.08, −0.06)	⨁⨁⨁O	22
12 months and above	0				0			
Asians	7	−5.12 (−10.58, 0.22)	⨁⨁OO	18	7	−3.31 (−6.99, 0.39)	⨁⨁OO	12
CaucAsianss	10	−3.96 (−6.47, −1.51)		4	9	−1.88 (−3.78, 0.05)		8
Medicinal herbs Taking								
Overall analysis	17	−8.51 (−11.71, −5.33)	⨁⨁OO	9	17	−5.24 (−7.42, −3.09)	⨁⨁OO	10
12 months and above	3	−6.62 (−16.75, 3.45)	⨁OOO	9	3	−3.35 (−9.18, 2.8)	⨁OOO	7
Asians	8	−7.74 (−11.37, −4.12)	⨁OOO	12	8	−4.69 (−7.13, −2.23)	⨁OOO	10
CaucAsianss	1	−21.71 (−29.82, −13.61)		1	1	−10.68 (−16.55, −4.88)		1
TCD bubble								
Overall analysis	2	−13.44 (−22, −4.64)	⨁⨁OO	3	2	−5.87 (−11.7, −0.08)	⨁⨁⨁O	9
12 months and above	0				0			
Asians	1	−13.52 (−22.63, −4.11)	⨁⨁⨁O	3	1	−5.65 (−11.89, 0.81)	⨁⨁OO	8
CaucAsianss	0				0			

(Continued)

TABLE 3 (Continued)

Comparison	SBP				DBP			
	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)
EMG								
Overall analysis	2	−5.6 (−14.46, 3.32)	⨁ OOO	17	2	−2.98 (−8.93, 3)	⨁ OOO	16
12 months and above	0				0			
Asians	2	−5.59 (−14.94, 3.83)	⨁ OOO	15	2	−2.96 (−9.57, 3.51)	⨁ OOO	14
CaucAsianss	0				0			
Acupoint therapy								
Overall analysis	7	−7.3 (−12.1, −2.57)	⨁ OOO	13	7	−2.69 (−5.86, 0.51)	⨁ OOO	18
12 months and above	1	−13.45 (−32.2, 5.09)	⨁ OOO	2	1	−6.74 (−17.42, 4.26)	⨁ OOO	4
Asians	4	−7.29 (−12.48, −2.21)	⨁⨁ OO	14	4	−2.5 (−5.98, 0.96)	⨁ OOO	16
CaucAsianss	0				0			
Homeopathy								
Overall analysis	1	−2.72 (−14.95, 9.27)	⨁ OOO	26	1	−1.58 (−9.68, 6.49)	⨁⨁ OO	23
12 months and above	0				0			
Asians	1	−2.73 (−16.08, 10.5)	⨁ OOO	20	1	−1.58 (−10.46, 7.31)	⨁ OOO	17
CaucAsianss	0				0			
Lose weight								
Overall analysis	1	−2.82 (−14.79, 9.11)	⨁ OOO	25	1	−2.2 (−9.9, 5.64)	⨁⨁ OO	20
12 months and above	1	−2.76 (−20.19, 14.68)	⨁ OOO	11	1	−2.27 (−12.65, 8.08)	⨁ OOO	9
Asians	0				0			
CaucAsianss	1	−2.96 (−10.46, 4.59)		8	1	−2.24 (−7.7, 3.22)		7
MBSR								
Overall analysis	2	−4.23 (−12.9, 4.44)	⨁ OOO	20	2	−0.71 (−6.49, 5.07)	⨁⨁ OO	27
12 months and above	0				0			
Asians	1	−8.46 (−22.21, 5.27)	⨁ OOO	10	1	−0.63 (−10.25, 8.96)	⨁ OOO	19
CaucAsianss	1	−0.51 (−8.1, 6.95)		10	1	−0.82 (−6.33, 4.72)		10
LSM								
Overall analysis	9	−5.77 (−8.44, −3.12)	⨁ OOO	18	9	−3.56 (−5.33, −1.79)	⨁ OOO	15
12 months and above	7	−7.36 (−12.59, −2.12)	⨁⨁⨁ O	7	7	−4.18 (−7.27, −1.07)	⨁⨁⨁ O	6

(Continued)

TABLE 3 (Continued)

Comparison	SBP				DBP			
	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)
Asians	8	−5.79 (−8.81, −2.75)	⨁ OOO	17	8	−3.18 (−5.2, −1.14)	⨁ OOO	13
CaucAsianss	0	7.45 (−2.98, 17.93)		12	0	−2.7 (−12.1, 6.83)		6
TCM constitution intervention								
Overall analysis	4	−4.27 (−10.44, 1.8)	⨁ OOO	21	4	−1.54 (−5.56, 2.46)	⨁ OOO	24
12 months and above	3	−3.88 (−13.91, 5.98)	⨁ OOO	10	3	−0.8 (−6.71, 5.01)	⨁ OOO	11
Asians	4	−4.33 (−10.77, 2.23)	⨁ OOO	19	4	−1.54 (−5.91, 2.76)	⨁ OOO	18
CaucAsianss	0				0			
Remote guided LSM								
Overall analysis	5	−4.1 (−9.67, 1.35)	⨁ OOO	22	4	−0.99 (−4.92, 2.91)	⨁⨁ OO	26
12 months and above	3	−0.32 (−10.25, 10.03)	⨁ OOO	15	3	0.46 (−6.81, 7.76)	⨁ OOO	15
Asians	1	1.37 (−11.69, 14.3)	⨁ OOO	23	1	1.73 (−6.7, 10.45)	⨁ OOO	23
CaucAsianss	3	−2.72 (−7.17, 1.81)		9	3	−2.86 (−6.76, 1.23)		4
AE + RE								
Overall analysis	2	−8.23 (−16.72, 0.38)	⨁⨁⨁ O	10	2	−11.02 (−16.73, −5.21)	⨁⨁⨁⨁	2
12 months and above	0				0			
Asians	2	−8.22 (−17.43, 0.88)	⨁⨁ OO	11	2	−10.81 (−17.11, −4.58)	⨁⨁⨁⨁	2
CaucAsianss	0				0			
LSM + drug								
Overall analysis	2	−11.07 (−18.5, −3.49)	⨁⨁ OO	5	2	−10.08 (−14.93, −5.28)	⨁⨁⨁ O	3
12 months and above	2	−11.92 (−22.79, −0.81)	⨁⨁ OO	3	2	−10.44 (−16.77, −3.92)	⨁⨁ OO	1
Asians	2	−11.09 (−19.17, −2.9)	⨁⨁ OO	5	2	−9.95 (−15.32, −4.68)	⨁⨁⨁ O	3
CaucAsianss	0				0			
Baduanjin + Acupoint								
Overall analysis	1	−10.48 (−22.33, 1.6)	⨁ OOO	7	1	0.02 (−8.28, 8.35)	⨁ OOO	28
12 months and above	0	−10.55 (−28.24, 6.87)	⨁ OOO	5	0	−0.02 (−10.56, 10.67)	⨁ OOO	12
Asians	1	−10.58 (−23.65, 2.35)	⨁ OOO	7	1	−0.02 (−8.94, 8.96)	⨁ OOO	21
CaucAsianss	0				0			

(Continued)

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TABLE 3 (Continued)

Comparison	SBP				DBP			
	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)
AE + Acupoint								
Overall analysis	1	−1.42 (−13.45, 10.76)	⨁OOO	29	1	−0.47 (−8.58, 7.51)	⨁⨁OO	25
12 months and above	1	−1.29 (−18.71, 15.65)	⨁⨁OO	12	1	−0.44 (−11.14, 10.12)	⨁⨁OO	10
Asians	1	−1.37 (−14.46, 11.64)	⨁⨁OO	22	1	−0.47 (−9.41, 8.3)	⨁⨁OO	20
CaucAsianss	0				0			
ARB								
Overall analysis	6	−12.5 (−17.59, −7.54)	⨁⨁⨁O	2	6	−6.42 (−9.69, −3.26)	⨁⨁OO	6
12 months and above	5	−10.13 (−17.65, −2.47)	⨁⨁OO	4	5	−4.45 (−8.95, 0.05)	⨁⨁OO	5
Asians	3	−12.86 (−18.45, −7.48)	⨁⨁OO	2	3	−6.56 (−10.24, −2.92)	⨁⨁OO	6
CaucAsianss	0				0			
Beta blocker								
Overall analysis	2	−2.56 (−11.32, 6.31)	⨁OOO	28	2	−2.42 (−8.09, 3.44)	⨁OOO	19
12 months and above	0				0			
Asians	0				0			
CaucAsianss	2	−3.01 (−8.66, 3.07)		7	2	−2.89 (−6.86, 1.48)		5
CCB								
Overall analysis	1	−23.67 (−36.34, −11)	⨁⨁OO	1	1	−12.44 (−20.81, −4.04)	⨁⨁⨁O	1
12 months and above	0				0			
Asians	0	−23.63 (−37.4, −10.02)	⨁⨁OO	1	0	−12.06 (−21.5, −2.95)	⨁⨁OO	1
CaucAsianss	0				0			
Diuretic								
Overall analysis	2	−7.92 (−14.44, −1.24)	⨁⨁OO	11	2	−3.95 (−8.24, 0.38)	⨁⨁OO	13
12 months and above	1	−7.02 (−18.91, 4.82)	⨁OOO	8	1	−3.11 (−10.22, 3.84)	⨁OOO	8
Asians	1	−9.81 (−18.31, −1.41)	⨁OOO	8	1	−5.13 (−10.68, 0.44)	⨁⨁OO	9
CaucAsianss	1	−3.4 (−11.12, 4.28)		5	1	−0.59 (−6.01, 4.84)		11
Statins								
Overall analysis	3	−5.32 (−13.06, 2.41)	⨁OOO	19	3	−2.85 (−8.27, 2.53)	⨁⨁OO	17
12 months and above	0	−7.02 (−18.91, 4.82)	⨁OOO	8	0	−3.11 (−10.22, 3.84)	⨁OOO	8

(Continued)

TABLE 3 (Continued)

Comparison	SBP				DBP			
	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)	No. of study	Weighted mean difference (95% CrI)	Certainty of evidence (CINEMA)	SUCRA (efficacy ranking)
Asians	3	−5.35 (−13.64, 2.97)	⨁⨁OO	16	3	−2.87 (−8.66, 2.93)	⨁OOO	15
CaucAsianss	0				0			
Allopurinol								
Overall analysis	1	−5.95 (−19.53, 7.46)	⨁OOO	16	1	−5.03 (−13.31, 3.32)	⨁OOO	11
12 months and above	0				0			
Asians	0				0			
CaucAsianss	0				0			

CI, confidence interval; RR, risk ratio; SUCRA, surface under the cumulative ranking; AE, aerobic exercise; HIIT, high-intensity interval training; RE, resistance exercise; DASH, dietary approaches to stop hypertension; TPM, Traditional Persian Medicine; TCD, traditional Chinese drug; EMG, electromyographic; MBSR, mindfulness-based stress reduction; LSM, lifestyle modification; TCM, Traditional Chinese Medicine; ARB, angiotensin II receptor blockers; ACE, angiotensin-converting enzyme inhibitors; CCB, calcium channel blockers.
⨁⨁⨁O, moderate quality.
⨁⨁OO, low quality.
⨁OOO, very low quality.

stronger effect of this vascular change-mediated hypotension (23). CCB (amlodipine) also achieved good results due to its sodium-independent antihypertensive effect in response to the high salt intake dietary preferences of East Asian populations (24). In the overall analysis, drugs achieved better efficacy and preferred treatment ranking, but their antihypertensive effect became unclear when treatment was prolonged or when analyzed across ethnic groups. Drug regimens are not recommended for people with no other co-morbidities and whose BP is not close to the threshold, and when PHT requires drug treatment, treatment with ARBs may be preferred or, in Asian populations, with CCBs.

LSM is a comprehensive non-pharmacological intervention to change physically and mentally unhealthy behaviors and habits (25) and is mostly considered in this paper in terms of dietary modification (DASH, salt restriction), management of tobacco, alcohol and increased activity. It was not recommended in the mixed comparison because of the low quality of the evidence, but as the duration of the intervention increased and the number of interventions with LSM as a control group decreased, LSM became the only intervention effective in reducing BP. And it may also have a positive effect in slowing progression to HT. This is consistent with the results of the current guidelines.

Recently the use of remote based tools (26) (telephone, SMS, and web) for LSM interventions has been gaining ground, improving patient compliance while being less time and location dependent. The remote LSM interventions included in this paper also need to be of sufficient duration (12 months) and intensity (27) to increase their appeal and thus produce meaningful outcomes.

Guidelines and studies in a range of regions have demonstrated the antihypertensive effect of physical activity (28, 29). The same positive efficacy was obtained in the PHT patients in this paper. AE, AE combined with RE have moderate to high quality levels of evidence in reducing SBP and DBP, making them the best interventions recommended here. Meanwhile, RE and HIIT have good evidence for reducing DBP. However, due to the lack of support from trials >12 months, this paper cannot explore the long-term pressure control effects of exercise therapy, which is an important part of the next step that needs to be urgently achieved. Moreover, AE combined with RE had moderate quality evidence of DBP reduction in Asian populations, and RE may also have an effect in reducing BP in Caucasians. The cumulative effects of physical activity, as perceived through its effects on sympathetic activity, enhancement of endothelial function and reduction of oxidative stress, contribute to the prevention and treatment of hypertension (30).

The benefits of AE in modulating cardiovascular risk factors are widely recognized, and the moderate to high intensity AE (over 20 min three times a week to achieve 50–85% HRmax) included in this paper resulted in a −10.65/−8.03 mmHg reduction in BP over the course of 5–24 weeks of exercise. The remaining exercise modalities yielded more definite gains in DBP reduction, with RE as a complementary therapy to AE having the best BP reduction in combination with AE and, to a lesser extent, alone. HIIT has the advantage of being more time efficient in lowering BP and is suitable for young people who are short of time (31). In addition to its effectiveness in controlling BP, another potential benefit of physical activity is weight loss (29), which is often the other non-pharmacological intervention recommended for PHT (32). With a weight loss of 10 kg, BP can be reduced by 5–20 mmHg. The combined benefits of lowering BP and weight loss after physical activity may help to further reduce or prevent elevated levels of pressure (33).

Data from the Global Burden of Disease Group (34) suggests that an unhealthy diet is a major risk factor for premature death and disability. To control BP, the guidelines suggest dietary recommendations that should be adopted by people with

hypertension: increase the intake of fresh fruit and vegetables, low-fat dairy products and reduce the intake of sodium. The DASH intervention fits the above components and has shown promising BP-lowering effects in the analysis and is supported by evidence in Asians. The lack of efficacy of salt restriction as a stand-alone intervention is consistent with previous studies in the PHT population (35, 36) and may also be related to the different criteria in this paper, whereas increases in other micronutrients (potassium and magnesium) may reduce SBP. Foods containing flavanols, polyphenols, and anthocyanins promote vasodilation by increasing nitric oxide utilization (37, 38) (grape seed, and cocoa) and reducing oxidative stress (39, 40) (green tea and roselle). However, the short duration of intervention (4–24 weeks) and the small sample size of each individual extract, combined with access and economic costs can only be used as a complementary programme.

Traditional medicine in various countries has been shown to be effective in reducing BP. TCD bubble produces moderate quality evidence recommendations in reducing DBP through a decoction of one or more herbal formulations that allow the medicine to be absorbed through the skin of the foot and stimulate acupuncture points on the foot through a warming effect.

5. Strengths and limitations

This is the first NMA analysis of a PHT population that uses direct vs. indirect comparisons to provide reliable estimates of outcome indicators. This paper provides an extensive search of the database and does not restrict interventions or language to include more RCTs for comparison. Moreover, intervention studies of more than 4 weeks were included, with an overall considerable sample size to interpret on the four outcome indicators. At the same time, a subgroup analysis of BP indicators in people from different ethnic and cultural backgrounds, over 12 months of intervention, provides more targeted advice.

The main limitation comes from the protocols and number of studies included in the literature. Studies in subgroup analyses need to be conducted over a longer period of time and in different ethnic contexts to produce more relevant results.

6. Conclusions

The main findings of this study suggest that AE, an exercise regimen of AE combined with RE and DASH are preferentially recommended for the PHT population as moderate to high quality evidence for BP lowering, and LSM is recommended as a long-term BP control regimen for intervention; on top of this, the addition of TCD bubble for SBP lowering in yellow populations and RE as a possible means of BP lowering in the Caucasian population. Long-term interventions in different cultural contexts will also need to be added in the future, with attention to the impact of interventions on final outcome indicators.

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

WL contributed to the conception of the article, searched and analyzed the data, and wrote the original article. XW contributed in analyzing and checking the data and revising the original article. HL contributed to conceiving the article, analyzing the data, and revising the original text. CW and YW provide suggestions for screening the literature and extracting data. HX and JL made key suggestions and gave important input in revising the original article. All authors contributed to the critical revision of important intellectual content of the article and read and approved the final version of this article.

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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.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1139617/full#supplementary-material

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Analyses of hospitalization in Alzheimer's disease and Parkinson's disease in a tertiary hospital

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Background: To characterize the pattern of hospitalization in patients with Alzheimer's disease (AD) or Parkinson's disease (PD), and compare the differences to see whether AD patients and PD patients have a different picture of hospitalization.

Methods: The clinical features of all consecutive patients from January 2017 to December 2020 were reviewed. We identified AD patients and PD patients from an electronic database in a tertiary medical center.

Results: The study group comprised 995 AD patients and 2,298 PD patients who were admitted to the hospital for the first time, and re-hospitalized 231 AD patients and 371 PD patients were also included. AD patients were older than PD patients when they were hospitalized ($p < 0.001$). AD patients had longer lengths of stay, higher re-hospitalization rates, and higher intrahospital mortality rates than PD patients during hospitalization even after adjusting age and gender. PD patients had higher levels of total cost than AD patients due to the cost of the deep brain stimulation (DBS) insertion. Hospitalizations for AD patients occurred most often in the department of geriatrics, while most PD patients were admitted to the department of neurology. Hospitalization due to the presence of comorbid conditions was much higher in AD patients, but a larger proportion of PD patients were hospitalized due to PD disease itself.

Conclusions: The present study found that AD patients and PD patients have a significantly different picture of hospitalization. It is important to implement different management for hospitalized AD and PD, and different emphasis should be given when establishing primary prevention strategies, informing care needs, and guiding healthcare resource planning.

KEYWORDS

Alzheimer's disease, Parkinson's disease, hospitalization, a tertiary hospital, analyses

Introduction

Alzheimer's disease (AD) is the most common age-related neurodegenerative disease, and Parkinson's disease (PD) is the second most common neurodegenerative disorder. Over the past decades, AD and PD have become a heavy public health burden in China. From 1990 to 2016 in China, the age-adjusted prevalence of dementia reached 5.6%, while the global prevalence increased by 1·7% (1). In 2020 China, it was estimated that 9.83 million had AD, out of the 249.49 million people aged ≥60 years old (2). From 1990

to 2016 in China, the age-adjusted prevalence rates of PD more than doubled, which is the largest increase worldwide (3). It is estimated that the number of PD patients in China will rise to 4.94 million in 2030, accounting for 57% of the total number (4). The hospitalization of AD patients and PD patients influences healthcare utilization and life expectancy. Besides disease-related conditions, respiratory diseases, cardio-cerebrovascular disorders, infection, falls, and bone fractures complaints are the common causes of hospital admission. Despite the importance of hospitalizations in AD and PD, there are as yet no studies to address these issues and to allow direct comparison. Here, we describe the features of the hospital admissions of a geographically defined population of AD and PD patients over 4 years (January 2017-December 2020). The aims of the present study are: (1). to show the characteristics of hospitalization in AD and PD patients in Southwest China; (2). to detect the impact of comorbid conditions in AD and PD patients; (3). to compare the differences in hospitalization between AD patients and PD patients; (4). to identify possible preventive strategies targeting differently to AD and PD.

Methods

West China Hospital (WCH) is a tertiary medical center located in Chengdu city, Sichuan Province, China, with about 300,000 patients discharged from inpatient departments annually. WCH has 4,300 beds and covers an area of more than 470,000 m^2. All clinical records of patients with the diagnosis of AD or PD discharged from January 2017 to December 2020 were consecutively reviewed by two clinicians trained in neurodegenerative disorders. Medical records of patients with a discharge diagnosis of AD or PD were collected from the computer patient administration system. Other types of dementia, including vascular dementia, frontotemporal dementia, Lewy body dementia, and other extrapyramidal disorders, including Parkinsonism-plus, and vascular or drug-induced Parkinsonism were excluded. We excluded patients diagnosed with both PD and AD (or dementia) at the time of initial screening. Admissions for dialysis and inpatient rehabilitation were also excluded from this analysis. The screening flow was shown in Figure 1. Ethics approval of data collection protocol received from the Ethical Committee of West China Hospital of Sichuan University.

Demographic data, including age at first hospitalization, gender, reasons for hospital admission, admission ward, mean days of hospital stay, surgical procedures and outcomes, were collected in all the AD patients and PD patients. The cause of hospitalization was informed as the main diagnosis, defined as what caused the hospitalization. The main diagnosis was categorized as AD or PD, neuropsychiatric disorders, immune-related disorders, cerebrovascular disease, other neurological diseases (dizziness, headache, encephalitis, hydrocephalus, etc.,), pulmonary infection, urinary infection, sepsis, other infectious diseases (skin infection, digestive tract infection, etc.,), respiratory disease, vascular disorder, gastrointestinal disorders, urological disorders, endocrine and metabolic diseases, tumors, others medical diseases, head trauma, fracture, others trauma. The common reasons for hospital admission were recorded, and the differences in the cause of hospitalization were analyzed between AD and PD patients. Mean days hospitalized were calculated using the following formula: the total in-hospital days of all hospitalizations/the number of hospital admissions during the 4 years. Hospitalization duration was calculated based on the length of hospitalization from admission to discharge. The total costs during the hospitalization were recorded, composed of care services, medical expenses, examination/laboratory test charges, and surgery costs. Reasons for in-hospital deaths were obtained by reviewing medical records.

Between-group differences in proportions for categorical variables were assessed using Wilcoxon rank-sum, Chi-square, or Fisher's exact tests, and Student's t-test was used to compare continuous variables. An analysis of covariance (ANCOVA) was used to compare differences between AD and PD patients in total costs, care services, medical expenses, examination/laboratory test charges, surgery costs, and mean hospital days, with age and sex as covariates. Bonferroni correction was applied to optimize for multiple tests.

Logistic regression analyses were performed to assess associations of in-hospital deaths or re-hospitalizations with the main diagnosis while adjusting for potential confounding variables. These analyses resulted in odds ratios (OR) with 95% confidence intervals (CI). Two-sided p-values < 0.05 were considered statistically significant.

Results

Admission distribution

During the study period, there were 3,293 first admissions involving 995 AD patients and 2,298 PD patients (Figure 2). The mean age at first hospitalization was 80.78 $\pm$ 0.30 years in AD patients, and 68.36 $\pm$ 0.24 years in PD patients; AD patients were significantly older than PD patients when first admitted to the hospital ($p < 0.001$). The female/male ratio was 464/531 in AD patients and 1,025/1,273 in PD patients, and there were no significant differences in gender ratio between AD and PD patients ($\chi^2 = 1.154$, $P = 0.283$). We only found that the gender ratio was significantly different in those patients aged between 75 to 84 years ($\chi^2 = 15.53$, $p < 0.001$), and this finding was shown in Figure 2 (Supplementary Table S1). In AD patients, 79.1% were aged $\geq$75 years old when they were first hospitalized, while in PD patients, 33.8% were aged between 65 to 74 years old, and 26.5% were aged between 75 to 84 years old. When sex and age were added as covariates, the results of ANCOVA analysis showed that the difference in mean hospitalization duration of the first admission between AD patients and PD patients was still significant (19.18 $\pm$ 0.80 vs.11.01 $\pm$ 0.27, $F = 71.71$, $p < 0.01$).

Admission wards

Admission wards of the first admission for AD patients and PD patients were listed in Figure 3. In AD patients, 42.7% were admitted to the department of geriatrics, while in PD patients, 60.7% were admitted to the department of

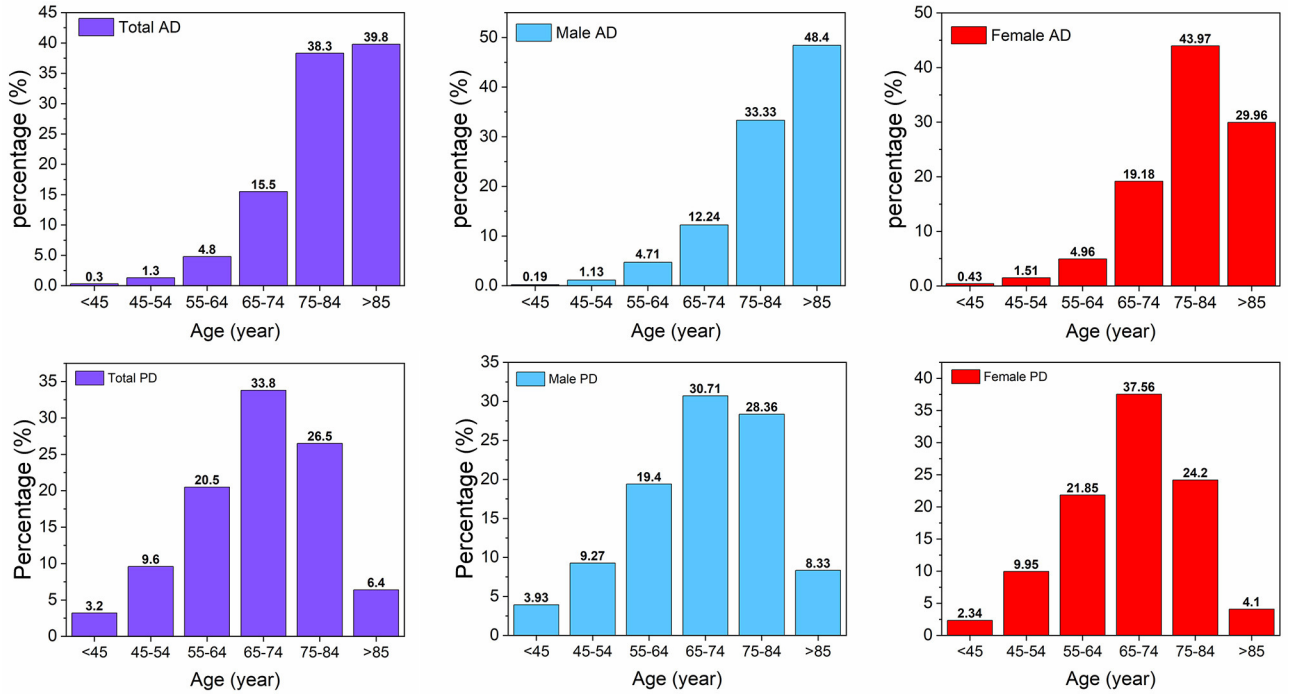

FIGURE 1
Screening process of AD patients and PD patients. AD, Alzheimer's disease; PD, Parkinson's disease.

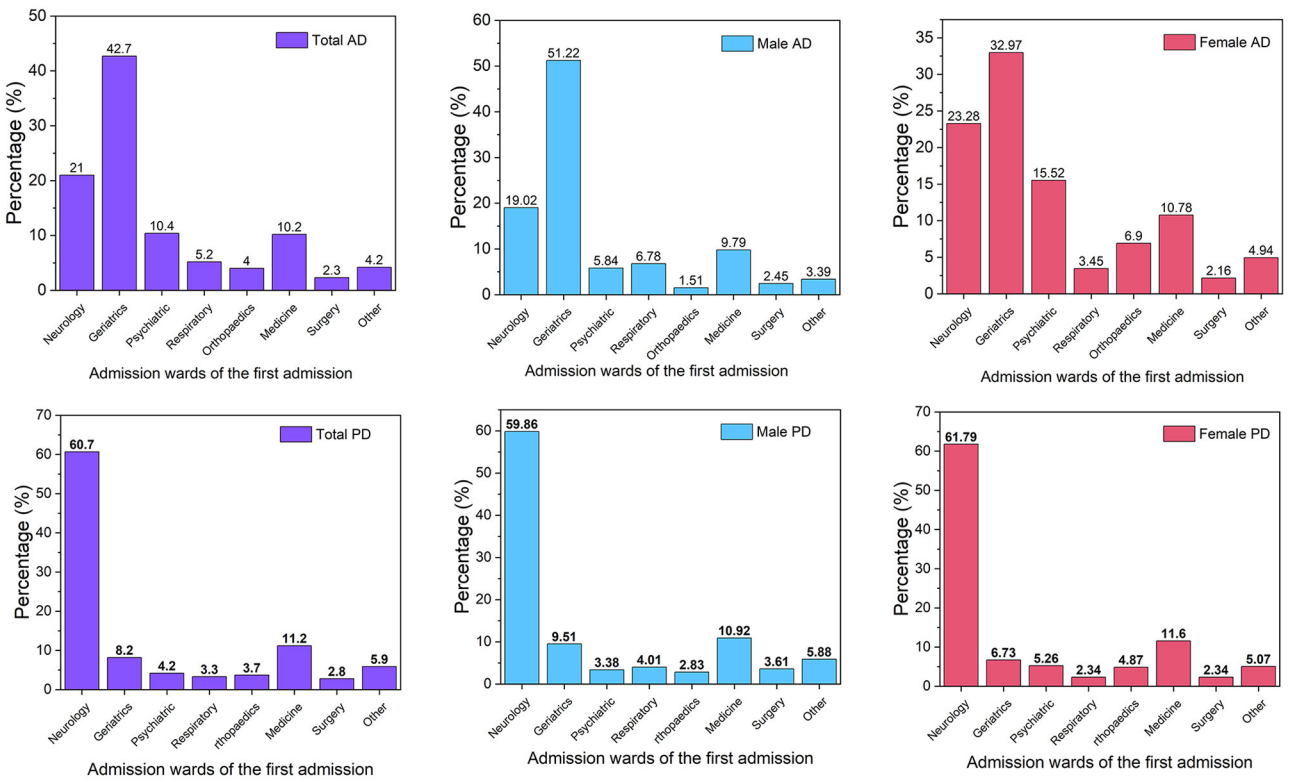

FIGURE 2
Age distribution of AD and PD on first admission. AD, Alzheimer's disease; PD, Parkinson's disease.

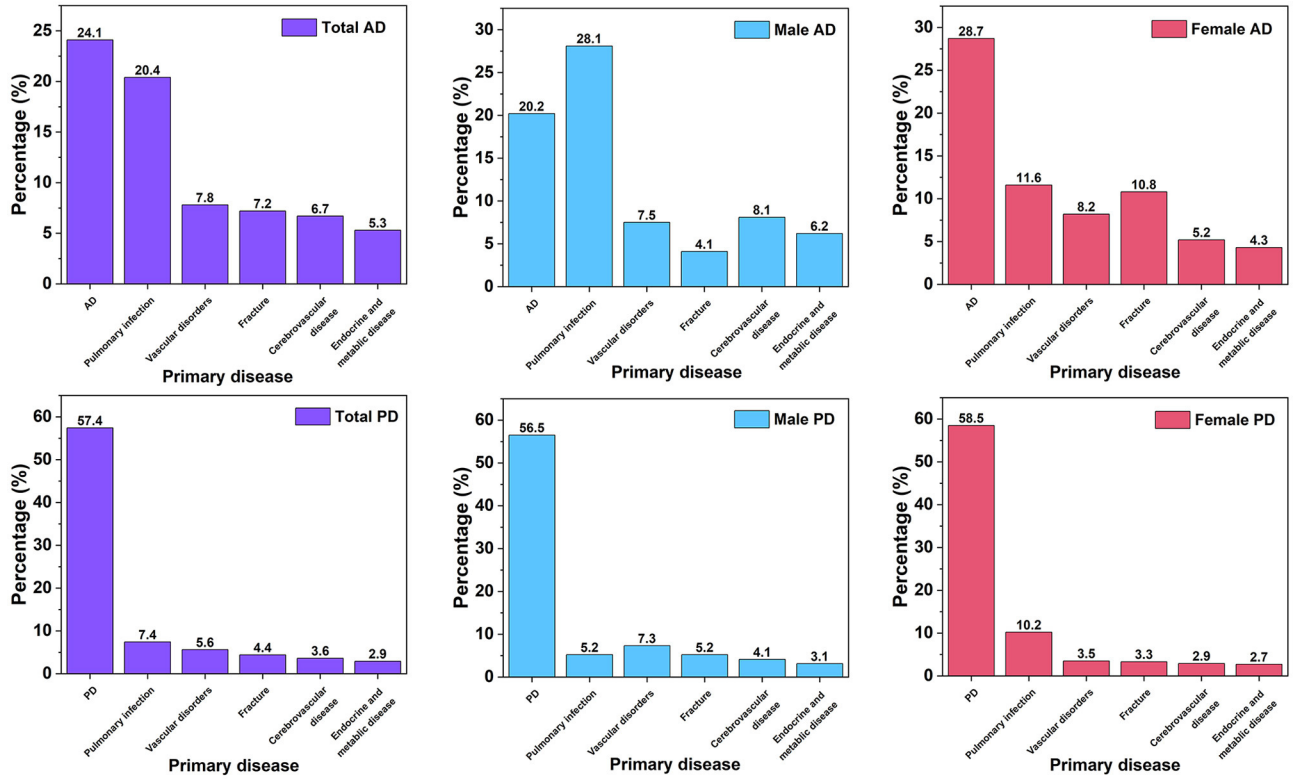

FIGURE 3
First admission department distribution of AD and PD. AD, Alzheimer's disease; PD, Parkinson's disease.

neurology (Supplementary Table S2). Both AD and PD patients with different gender had similar distributions in the admission ward (Supplementary Table S1).

Admission reason

The primary diagnosis for the first admission in AD patients and PD patients was listed in Supplementary Table S3, and the top six main reasons for hospital admission were shown in Figure 4. In AD patients, the presence of comorbid conditions caused 755 out of 995 admissions (75.9%), while the remaining AD patients were admitted due to the main diagnosis of AD. The most common cause of the first hospitalization in AD patients was AD disease itself (24.1%); the following main causes were pulmonary infection (20.4%), vascular disorder (7.8%), and fracture (7.2%). In female AD patients, 28.7% were caused by AD disease itself, followed by pulmonary infection (11.6%), fracture (10.8%), and vascular disorder (8.2%). In male AD patients, 28.1% had the main diagnosis of pulmonary infection, followed by AD itself (20.2%), cerebrovascular disease (8.1%), and vascular disorder (7.5%). In PD patients, 979 out of 2,298 admissions (42.6%) were caused by the presence of comorbid conditions, while the remaining PD patients were admitted for a diagnosis of PD or a complication directly related to PD (motor fluctuation or dyskinesia). The most common cause of the first hospitalization was PD disease itself (57.4%); the following main causes were fracture (7.4%), pulmonary infection (5.6%), and neuropsychiatric disorders (4.7%). Of male PD patients, 56.5% were caused by PD disease itself (56.5%), followed by pulmonary infection (7.3%), fracture (5.2%), and vascular disorder (5.2%). In female PD patients, 58.5% had the main diagnosis of PD, followed by fracture (10.2%), neuropsychiatric disorders (6.1%), and pulmonary infection (3.5%). Hospitalization due to the presence of comorbid conditions was much higher in AD patients compared with PD patients ($\chi^2 = 308.43$, $p < 0.001$). A larger proportion of PD patients were hospitalized due to PD disease itself, while AD patients had a higher proportion of pulmonary infection and vascular disease than PD patients while hospitalized (Supplementary Table S3).

Hospitalization costs

The total costs from the first admission were 29,090.36 ± 1,923.21 and 62,427.70 ± 2,125.80 Yuan in AD patients and PD patients, respectively. The total cost of the first admission was significantly higher in PD patients than that in AD patients, even after adjusting for age and sex ($F = 18.11$, $p < 0.001$) (Figure 5 and Supplementary Table S4). ANCOVA analysis also showed that AD patients had higher expenses in care services ($F = 24.63$, $p < 0.001$), medicine ($F = 15.88$, $p < 0.001$), and examination/laboratory tests ($F = 335.24$, $p < 0.001$) than PD patients. In addition, 422 out of 2,298 PD patients (18.40%) were admitted for DBS insertion. Therefore, the surgery cost was significantly higher in PD patients

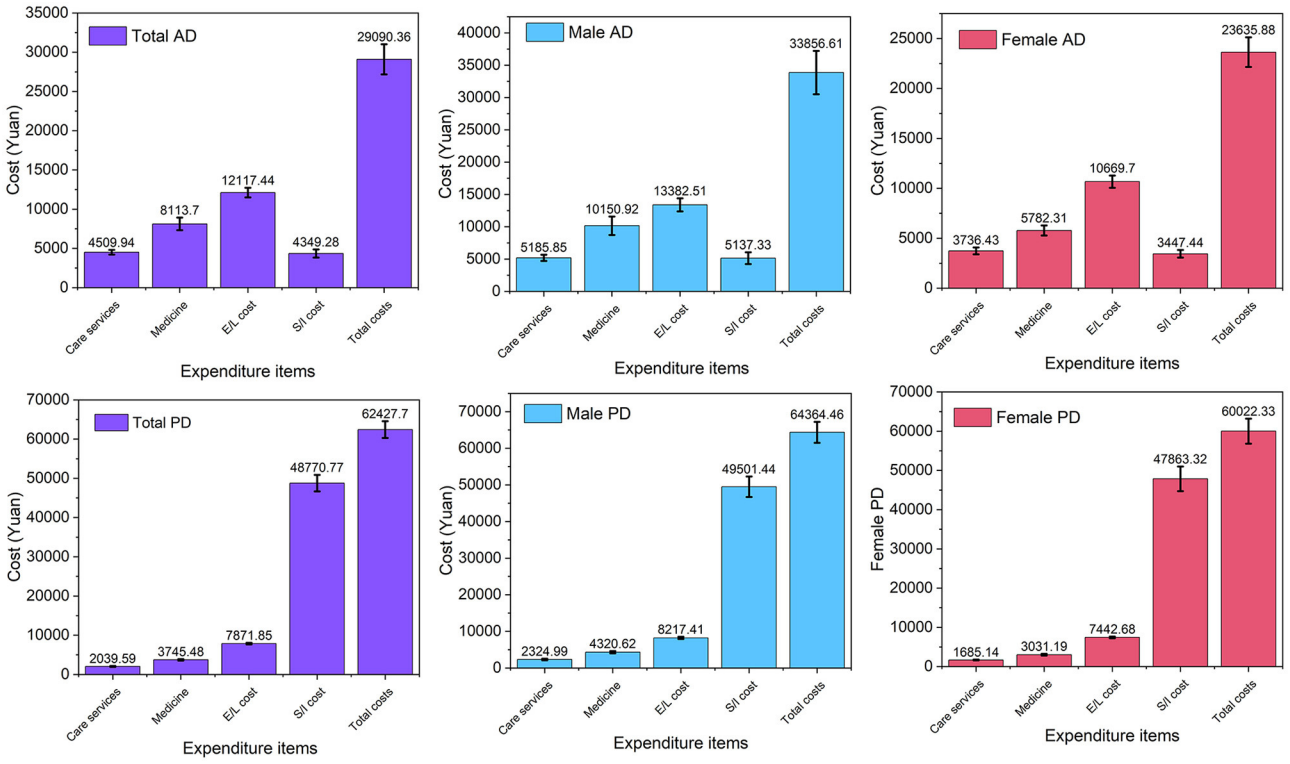

FIGURE 4
The main diagnostic distribution of AD and PD on first admission. AD, Alzheimer's disease; PD, Parkinson's disease; OND, Other neurological diseases; OID, Other infectious diseases; OMS, Other medical disorders; OT, Other trauma.

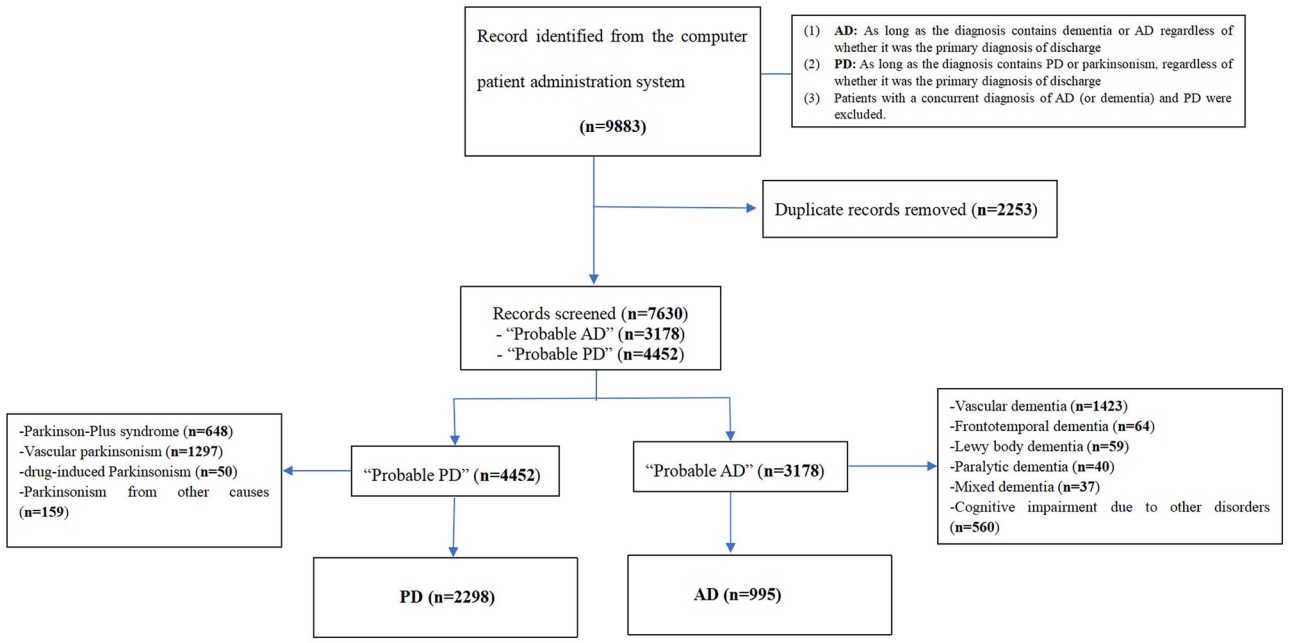

FIGURE 5
Comparison of total first-admission costs between AD and PD. AD, Alzheimer's disease; PD, Parkinson's disease; E/I cost, examination/laboratory tests; S/I cost, surgery/inventory cost.

than in AD patients ($F = 16.81$, $p < 0.001$). When PD patients who received DBS insertion were removed, there was no significant difference in the cost of surgery service for AD patients and PD patients (4,349.28 ± 523.13 vs. 4,628.65 ± 316.06, $F = 0.40$, $p = 0.526$).

Outcomes

Re-hospitalization

During the study period, 231 out of 995 AD patients (23.2%) and 371 out of 2,298 PD patients (16.1%) were re-hospitalized, and AD patients had a statistically higher re-hospitalization rate than PD patients ($\chi^2 = 23.24$, $p < 0.001$). This difference in re-hospitalization was also significant in male patients ($\chi^2 = 141.77$, $p < 0.001$), but was not significant in female patients ($\chi^2 = 3.47$, $p = 0.063$). The mean re-hospitalization duration was 25.06 ± 1.72 days in AD patients and 11.97 ± 0.48 days in PD patients, and AD patients had a significantly longer duration of re-hospitalization than PD patients even after adjustment for age and sex ($F = 33.07$, $p < 0.001$).

The distribution of re-hospitalization for AD patients and PD patients by age and sex was listed in Supplementary Table S5. The age at re-hospitalized for AD patients was significantly older than that for PD patients (86.06 ± 7.30 vs. 72.05 ± 11.87, $p < 0.001$). Among AD patients, 67.5% were aged ≥85 years, but among PD patients, only 14.6% were older than 85 years ($p < 0.01$). The most common re-hospitalized department for AD patients was the department of geriatric (74.9%), while in PD patients the most common re-admitted department was the department of neurology (38.0%). Admission wards of re-hospitalization for AD patients and PD patients were all listed in Supplementary Table S6. Comorbidities were present in 85.3% (179/231) of AD patients, and 63.9% (237/371) of PD patients when re-admitted, and a significantly higher comorbidity rate was found in AD patients ($\chi^2 = 12.347$, $p < 0.001$). The most common cause of re-hospitalization was pulmonary infection (32.0%), followed by AD itself (14.7%), vascular disorder (8.7%), and fracture (8.2%). In re-hospitalized PD patients, the most common cause was the PD disease itself (36.1%), followed by fracture (12.1%), pulmonary infection (11.9%), and tumors (7.8%). The main diagnosis for re-hospitalization in AD patients and PD patients was listed in Supplementary Table S7. The total re-hospitalization costs were 30,911.96 ± 2,453.11 and 43,112.32 ± 4,196.12 Yuan in AD and PD patients, respectively. The total cost of re-hospitalization was significantly higher in PD patients than that in AD patients ($p < 0.001$), but this difference was not statistically significant after we adjusted sex and age ($F = 0.777$, $p = 0.379$). There were 37 out of 371 PD patients (9.97%) re-admitted for DBS insertion. Therefore, the surgery costs were significantly higher in PD patients than in AD patients ($p < 0.05$), and this difference was more pronounced in male patients ($p < 0.01$). Interestingly, there was no significant difference between first admission and re-hospitalization costs in AD patients ($p > 0.05$). However, in PD patients, the cost for the first admission was significantly higher than the cost of re-hospitalization ($p < 0.01$), and more PD patients received DBS surgery at first hospitalization compared to re-admission (18.40% vs. 9.97%, $\chi^2 = 15.79$, $p < 0.001$). The hospitalization costs for re-hospitalization in AD patients and PD patients were listed in Supplementary Table S8. The mean length of hospital stay for the re-admissions in AD patients was significantly longer than that in PD patients (18.79 ± 0.70 vs. 10.87 ± 0.24, $p < 0.001$), and the difference remained statistically significant after adjusting for age and sex in ANCOVA analysis ($F = 25.76$, $p < 0.001$).

Intrahospital mortality

Concerning intrahospital mortality, 48 out of 995 (4.82%) AD patients died, and 42 out of 2,298 (1.80%) PD patients were deceased. The mortality rate was significantly higher in AD patients than that in PD patients ($\chi^2 = 23.452$, $P < 0.001$). The top three causes of death in AD patients included AD itself (17/48, 35.42%), pulmonary infection (10/48, 20.83%), and fracture (9/48, 18.75%). In PD patients, the top three causes of death were pulmonary infection (21/42, 50%), gastrointestinal disorders (5/42, 11.90%), and PD itself (4/42, 9.50%). There was no significant difference in the proportion of the most common in-hospital causes of death between the two groups ($\chi^2 = 1.953$, $p = 0.162$). The gender-specific analyses found that the most common cause of death in male AD patients was pulmonary infection (9/25, 36.00%) and AD itself (9/25, 36.00%), but in female AD patients, it was AD itself (8/23, 34.78%) and fracture (8/23, 34.78%). However, pulmonary infection rather than PD itself was the most common cause of death in both male and female PD patients (17/29, 58.60% vs. 4/13, 30.80%).

Logistic regression models were developed to evaluate the variables affecting re-hospitalization (Supplementary Table S9) and intrahospital mortality in AD patients and PD patients (Supplementary Table S10). The result showed that re-hospitalization of AD and PD patients was associated with age, hospitalization duration, neurological hospitalization, and surgical procedures in the first admission. The intrahospital death of PD patients was found to be correlated to age, comorbidity in the hospital, neurological hospitalization, and repeated hospitalization.

Discussion

Several studies have demonstrated the pattern of hospitalization in AD or PD patients. However, knowledge about hospitalized AD and PD patients and comparing the differences has been limited. The present study described the hospitalization of patients with AD and PD discharged from January 2017 to December 2020 in a tertiary medical center and found that AD patients and PD patients have a significantly different picture of hospitalization.

Admission distribution

We found the mean age at first admission was 80.78 years in AD patients, which was older than that in PD patients (68.36 years). A retrospective study from the United Kingdom found that the mean age at primary hospitalization was 84.5 years in dementia patients (5). AD is predominantly a disease of older

adults, and most of the reasons for hospital admission might have been related to age, AD and its associated comorbidities. Therefore, it is important to focus attention on the age at admission that is specifically associated with hospital admission in AD patients. One reason is that the true level of awareness and knowledge about AD in China is likely to be far lower. In China, dementia continues to be seen by many as an inevitable and natural part of the aging process. Therefore, knowledge about AD can bring about earlier assessment and diagnosis, particularly around addressing modifiable risk factors and the potential for dementia prevention. In PD patients, we noticed that 3.2% were aged ≤45 years old when they were first hospitalized, and 9.6% were aged between 45 to 54 years old. Studies have shown that young-onset PD (YOPD in adults under 40 years of age) has been estimated to account for up to 10% of PD patients (6, 7). YOPD is an important subgroup of PD patients, and PD patients are significantly younger when admitted to the hospital.

One study found that the mean duration of stay was 9.7 for PD patients and 9.2 days for controls; the difference was not significant (8). A previous study looked at admissions of PD patients to a general hospital and found that the average length of stay was 11.7 days in PD patients, compared to 8.7 for other adults (9). A prospective cohort study found that the mean length of stay per admission was 10 days in PD patients and 10.5 days in controls, and it was also found that the mean duration of stay in PD patients was seven days, which was longer than that in control patients (10). A systematic review found that PD patients were generally 2–14 days longer hospitalized than non-PD patients (11). For dementia patients, one study found that the mean duration of the hospital stay was longer in patients with dementia (13.4 vs. 10.7 days) (12). In our study, the mean length of stay was longer in AD patients than that in PD patients (18.79 vs. 10.87 days), and this finding may be related to the higher presence of comorbid conditions in AD patients.

Admission wards

A 4-year hospital discharge database record in Spain showed that internal medicine departments discharged 44% of identified patients with dementia, neurology departments 22%, and psychiatry departments 21% (12). In the present study, we found that 42.7% of AD patients were admitted to the department of geriatrics, followed by neurology departments (21%) and psychiatry departments (10.4%). We also found that most AD patients were not admitted to the hospital for dementia but for other reasons, and that the impact of comorbidity was higher in AD patients than in PD patients. AD patients were hospitalized primarily for medical reasons, including pulmonary infection, vascular disorder, and fracture. Therefore, they are more often admitted to the geriatrics department because the target population of the geriatrics department is older adults with multi-comorbid conditions. When AD patients are admitted to the hospital, their conditions are not limited exclusively to the AD disease itself, and their diseases were progressed to a certain stage. Hospital admissions of AD patients are often problematic, especially when patients are admitted to non-neurological wards. As most non-neurologically educated healthcare personnel are not professionals in AD diagnosis and treatment, protocols would be helpful to improve the care of AD patients in such environments. Guidelines to guide physicians in the hospital environment could be helpful. Hospitals should implement specific programs to identify AD patients earlier and integrated treatment to the comorbidities. In addition, specific care plans should be designed to manage those AD patients who are admitted to the department of geriatrics, which is not specialized in managing AD patients. However, PD patients have less comorbidity than AD patients when they are hospitalized. A systematic review analyzed the factors that lead to hospitalization in PD patients and found that PD-related problems were the most common cause of admission to a neurological ward due to worsening motor or non-motor symptoms (13). This finding contributes to our understanding of the different approaches to the management of AD patients and PD patients in a hospital setting.

Admission reason

The included AD patients had more hospitalizations caused by comorbid conditions than PD patients. Previous studies have shown that comorbidity and higher age were associated with an increased risk of hospitalization in patients with dementia (14, 15). The incidence rates of falls, injury, and infection were higher in subjects with AD than in those without AD (16). A recent meta-analysis found that there was strong evidence that admission of people with dementia was strongly associated with older age, and was moderately associated with multimorbidity, but dementia severity alone was not associated with admission (17). A retrospective 6-year study identified the most common cause of admission in dementia patients was severe respiratory disorder (respiratory failure and complicated infections) (12). Similarly, a retrospective study found that acute lower respiratory tract infection, pneumonia, and fractured neck of femur diagnoses were more prevalent in AD patients compared to controls when they were admitted (5). A cohort study also found that the most common hospitalization discharge diagnoses among patients with dementia were urinary system disorders, pneumonia, and fracture of the femur (18). An earlier systematic review of reasons for admissions for people with dementia also found that people with dementia were more likely to have been admitted to hospitals for respiratory and urological infections, falls, and fractures than inpatients without dementia (19). The high proportion of pulmonary infections in hospital admission for AD patients may be due to a lack of physical exercise, mobility, and self-neglect, and perhaps also impaired swallowing function in these patients, which increases the risk of aspiration pneumonia (20). An Italian hospital-based study obtained data from 51,838 consecutive computerized discharge records and found a higher prevalence of cerebrovascular disease, pneumonia, and hip fracture among the primary diagnoses in dementia patients (21). Dementia patients also had more acute cardiac events than non-dementia cases (22). These findings suggested a greater load of comorbidity in AD patients. Therefore, early recognition and management of respiratory infections and meticulous fall prevention are valuable future intervention strategies in AD patients. Obviously, a large

proportion of hospital admissions caused by muti-comorbidity of advanced AD may be avoidable by early intervention.

The present study found that the proportion of patients admitted for PD disease as their primary diagnosis was larger than AD patients. A prospective cohort study also found that the most common cause of admissions to the hospital was PD disease itself, followed by vascular disease, trauma/fracture, and pulmonary infection, and a retrospective study analyzed the precipitants for admission to a large teaching hospital in PD patients and found that the most common primary diagnosis was PD disease itself, followed by falls and fractures, pneumonia, and gastrointestinal complications (23, 24). PD and its related problems appear responsible for about 25% of acute hospitalizations in PD patients (13). Exacerbation of PD-related symptoms can be avoided by frequent review of PD patients and appropriate adjustment of their medications to improve motor and non-motor function and manage drug-related side effects. Furthermore, poor motor control is associated with hospital admission, and optimizing PD symptom control through medication compliance may help reduce hospital admissions. A systematic review aiming to identify interventions to reduce hospitalization in PD found that frequent neurologist consultation and compliance with PD medication may reduce hospital admissions (25). When PD patients are admitted to the hospital due to PD disease itself, professional neurological consultations and treatments should be provided for medication adjustments, earlier detection, and management of complications. Therefore, in PD patients, frequent outpatient reviews with an emphasis on medication adjustment to maintain good mobility may help reduce hospitalization.

The present study found that besides PD disease, fracture, pulmonary infection, and neuropsychiatric disorders were common reasons for hospitalization. A systematic review confirmed that PD-related motor complications, psychiatric problems, infections, and falls were the top four main reasons for admission to a neurological ward (13). Another systematic review also summarized the causes for admission, and the leading causes included injuries (many with fractures), infections (mainly pneumonia and urinary tract infections), and poor control of PD (11). Compared to controls, admission for aspiration pneumonia, trauma/fracture, and psychosis were found to be higher in PD patients (26). Similarly, a previous study identified falls, fractures, infections, and cognitive and motor decline as risk factors for unplanned hospital admissions in patients with PD (27). Normally, falls and fractures can occur in PD due to postural instability, poor motor symptom control, and drug-related side effects. Therefore, early recognition and management of respiratory infections and meticulous fall prevention are valuable future intervention strategies in PD patients. Reducing the number of admissions might be achieved by extra attention to fall prevention, adequate drug regulation with acuity for side effects, and preventing and recognizing early symptoms of infections.

Hospitalization costs

A previous study found that the average daily cost per PD patient in 2005 was NOK 4500 (EUR 548) (28). The present study's average daily cost for each PD patient was RMB 5,675 YUAN (EUR 832). However, it should be noted that PD patients included in the present study represented a select group of people with PD attending specialist centers of care, as reflected by the rate of DBS (18.40%). Thus, this cohort may have had more advanced diseases and more complex medical issues. Therefore, the surgery costs of PD patients were higher in PD than in AD due to the higher cost of DBS devices. However, AD patients had higher expenses in care services, medicine, and examination/laboratory tests than PD patients, and the differences in these hospitalization costs could be explained by the longer length of stay and higher presence of comorbidities of patients with AD compared to those with PD.

Outcomes

A previous study analyzed the hospital-based discharge database records and found that the intrahospital mortality in dementia patients was 19.3%, which was higher than that in patients without dementia (8.7%) (12). Another study also found that the intrahospital mortality rate in dementia patients was higher than that in non-demented patients (10.5 vs. 8.7%) (21). Dementia was associated with a higher rate of admissions to hospitals, and dementia was an independent risk factor for intrahospital death (12, 21). A Meta-analysis of hospital administrative database studies showed that the mortality in dementia patients was 15.3% as compared to 8.7% in non-dementia cases (22). In the present study, we found that intrahospital mortality in AD patients was 4.82%, significantly higher than in PD patients (1.80%). Our samples of patients reflected that AD patients tended to be older, and were diagnosed at a later stage than PD patients. Our AD patients also had higher levels of comorbid conditions and a longer hospital stay, which may have influenced their higher levels of intrahospital death. Proper diagnosis and timely treatment should be available for AD patients (29, 30). However, a previous study evaluated the status of dementia diagnosis and treatment in China and found that a tremendous number of dementia patients were being overlooked (31). According to the "**World Alzheimer Report 2019. Attitudes to dementia"**, 95% of the public believe that they will develop dementia in their lifetime, and 2/3 of the people believe that dementia is a normal aging process. Therefore, there is an urgent need first to raise public awareness of AD. Second, it is important to implement a dementia training program to enhance the capacity of neurologists to manage AD patients (16). Third, setting up memory clinics to screen dementia at general hospitals could be useful to dementia practice in China (16, 32). Fourth, establish a multidisciplinary treatment (MDT) model and a one-stop clinic to develop personalized treatment plans for each AD patient."

In the present study, the re-hospitalization of PD patients was related to the surgical procedures during the first admission. Similarly, another study also suggested that DBS was a significant predictor of a new encounter with a hospital (26). According to previous research, intrahospital mortality ranged from 4 to 39% in PD patients (9, 10, 33, 34). A previous study reported that intrahospital mortality was 6% in both PD patients and matched controls (8). In our study, mortality was lower than those reported previously in other cohorts, which may be related to the standardized management of PD patients in our center, particularly in neurology hospitalizations. First, our hospital

took the lead in establishing the largest PD one-stop treatment center in Southwest China, which integrated multidisciplinary resources, and provided a number of cutting-edge treatments, including transcranial Doppler ultrasound, tremor gait analysis and DBS surgery. Second, we have built a database of PD patients, and conducted regular follow-up visits with each PD patient. During the follow-up visits, we assessed the motor function, as well as cognition, life skills, mental and emotional status, and caregiver burden. Through regular follow-up visits and standard assessments, we enhanced the doctor-patient interaction and promoted individualized treatment of the disease. Third, WCH also launched online clinics and teleconsultations to enable early intervention to reduce the admission for complications. In addition, this difference also depends on the different hospital facilities and the level of medical treatment.

Strengths and limitations

Considering limitations, despite a large number of the study population, the present analysis is based on electronic records from a single hospital. Thus, it needs to be replicated in different samples. Considering reasons for hospitalization, these data were derived from the discharge diagnoses recorded in the electronic medical records system. It was impossible to distinguish the complications that arose during the hospital stay from the reasons for the initial admission. Concerning comorbid conditions, newly diagnosed persons may have less disease-related comorbidity. The diagnosis of AD or PD can be challenging, and it is impossible to monitor the quality of each diagnosis; however, we know that each diagnosis is made by senior clinicians during hospital admission and reviewed carefully when the patient is discharged. Future studies with a multi-centered approach would allow comparison of a larger group of patients with AD or PD and make our results more generalizable.

Conclusions

In this study, we identified many clinically important issues that AD patients and PD patients experienced differently. AD patients were older than PD patients when they were hospitalized; AD patients had longer lengths of stay during hospitalization, higher re-hospitalization rate, and higher intrahospital mortality rate than PD patients. PD patients had higher levels of total cost than AD patients during hospitalization due to the cost of DBS insertion. Hospitalizations for AD patients occurred most often in the department of geriatrics, while most PD patients were admitted to the department of neurology. Hospitalization due to the presence of comorbid conditions was much higher in AD patients. AD Patients had a higher proportion of pulmonary infection and vascular disease than PD patients while hospitalized, but a larger proportion of PD patients were hospitalized due to PD disease. In AD patients, raising public awareness and knowledge about dementia, establishing memory clinics, developing a dementia training program, active anti-dementia treatment, and implementing preventative measures for comorbidity are important interventions to reduce the need for hospital admission and mortality. However, the most effective measure to reduce the hospitalization rate of PD patients is to maintain good mobility, manage drug side effects, and control motor complications. The results of the present study may be useful in establishing primary prevention strategies, informing care needs, and guiding future healthcare resource planning and allocation.

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 study was approved by the Ethics Committee of West China Hospital of Sichuan University.

Author contributions

SC, JF, and XL contributed to the compilation of articles and data analysis. YH and TB contributed to the selection and data entry. XC and HS contributed to the review, editing, and scientific research thinking and methods. 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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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1159110/full#supplementary-material

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Toward social-health integration in Sicily: description of the first hub and spoke model to improve the diagnostic therapeutic care paths for neurorehabilitation

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Introduction: The study describes a hub and spoke network for neuro-rehabilitation recently activated in Sicily, and evaluates the before-after changes yielded, in terms of integrated care.

Methods: A set of indicators based on data contained in the administrative database of inpatients of the Regional Health System are presented and discussed. Statistical analysis was conducted both globally and separately for the 9 Sicilian provinces (Agrigento, Caltanissetta, Catania, Enna, Messina, Palermo, Siracusa, Ragusa, and Trapani).

Results: Results showed an increase in admissions of people residing in the province where the Spokes have been opened: Trapani (+32.4%), Messina (+7.8%) and Palermo (+4.4%); besides a significant increase of patients from healthcare facilities proportion ($p = 0.001$) and from acute wards ($p = 0.029$). In addition, we found a decrease of discharge to protected healthcare facilities ($p = 0.001$) and to acute wards ($p < 0.001$), as well as an increase of discharges to home ($p = 0.018$).

Discussion: In conclusion, it would seem that the activation of this network has facilitated the management of these patients, avoiding unnecessary migrations to other provinces and/or regions, and improving the regional care service for neuro-rehabilitation. Future research will be direct to investigate this aspect, focusing on before-after variations in hospitalization rates and origin– destination patient flows.

KEYWORDS

hub and spoke, organization design, neuro-rehabilitation, quality indicators, robotic device

1. Introduction

According to the WHO principles of protecting worldwide population health, the Italian National Health Service (NHS) made social and health integration one of its pillars according to the Legislative Decree 229/1999. Since then, many steps forward have been made In Italy, both at national and local regional level. In Sicily a rehabilitation plan was designed in 2012 to deal with the lack of highly specialized rehabilitation services, as well as of an inadequate integration between hospital and territorial services (1). Indeed, the Sicilian government expressed its intention to requalify the rehabilitation facilities through the creation of a hub and spoke (HS) model, with the purpose of developing new guidelines, assistance protocols and recommendations on the rehabilitation pathway. A HS model includes a vertical organization with rules extending

from the hub to the spokes in order to maximize efficiencies and effectiveness (2), and in the last years, many integrated models designed as HS networks emerged in several health areas, including the organization and delivery of novel rehabilitation services (3–7).

In 2017 Sicily introduced the first Regional Socio-Health Plan, which defines an integrated system of rules that brings together health and social care (8). It is an interdisciplinary care plan designed to respond to the organizational fragmentation of health services. Thus, territorial services and home care programs can guarantee a continuity between care and rehabilitation, social inclusion and job reintegration. The challenge is to provide better health care with significant cost reduction, i.e., reducing hospitalization, improving the patient quality of life of older adults, disabled, patients suffering from chronic (often degenerative) and rare diseases.

In this scenario a new Diagnostic, Therapeutic and Care Pathway (DTCP) emerged, since it can be considered a tool of governance through which the Region defines guidelines for care processes centered on the patient's need, taking into account the resources available (9). Thus, health services delivered to citizens in a circular continuum approach can change the prognosis of certain diseases (10). DTCP for neurorehabilitation includes several healthcare professionals operating in different settings (primary, intermediate and hospital care) to provide better management by a multidisciplinary team in a redefinition of a model based on the continuity of care (11). An integrating neurorehabilitation service offers the opportunity to significantly improve patient outcomes, terms of residual disability and performance improvement (12). The DTCP for intensive and extensive neurorehabilitation is aimed at providing advice and guidelines about the management of neurological inpatients. In detail, intensive rehabilitation involves those patients in which the recovery could be maximized (e.g., those affected by stroke or traumatic brain injury), and then, if they do not have medical or psychiatric contraindications, the training should last at least 3 h per day whereas nursing assistance is provided on a 24 h basis. Extensive neurorehabilitation is instead provided 1–3 h per day, according to the patient's condition and potential recovery. Usually, patients with severe acquired brain injury are labeled as cod 75 and require the higher degree of care and cure; patients with spinal cord injury (cod 28) are provided with the same intensive care as cod 75, whereas patients with stroke, multiple sclerosis and other orthopedic and cardiopulmonary diseases are considered as cod 56, where rehabilitation and nursing are less intensive.

Many studies showed that a HS model can be included within a DTCP to manage different stages of neurological diseases from the acute phase or disease diagnosis (13, 14) to the rehabilitation (15) and return to normal life. The strong point of the HS network is the possibility of avoiding unnecessary travel (since the local spokes may provide nearly the same high-quality services than the hub), by reducing costs both from the healthcare system and patient's perspective, but improving the medical service offered (16, 17).

Thus, with the view of improving the social and health integration of the Sicilian DTCP for intensive neurorehabilitation within a territorial continuity path care, covering the unsatisfied demand for care and supporting the users within their own territory, a hub and spoke model was designed and has been tested for 5 years (since January 2017 to June 2022) by the IRCCS Centro Neurolesi "Bonino-Pulejo" of Messina, Sicily. The HS network defines the operating rules, the monitoring system, the quality and safety requirements of the processes and care paths, the qualification of professionals, and the ways of involving subjects. We assume that an integrated neurorehabilitation model might fully satisfy the patient care needs, providing interventions in compliance with the continuity of care process and clinical and organizational appropriateness.

The aim of this study is to describe in detail this Sicilian HS model and to evaluate the changes that occurred by its activation, especially in terms of integrated care. Indeed, we believe that a multidisciplinary and integrated care path dedicated to neurological patients, could led to better outcomes in terms of hospitalization and access to the rehabilitation network.

Thus, we compared the care paths of neurorehabilitation hospitalization patients in 2016 (i.e., before the introduction of the HS network) with the care paths of neurorehabilitation hospitalization patients in 2018 (after the introduction of the HS network and before the COVID-19 pandemic) through a set of suitably defined indicators.

2. The hub and spoke rehabilitation model

The IRCCS Centro Neurolesi "Bonino-Pulejo" of Messina is an experimental hub and spoke model to integrate the intensive neurorehabilitation process within a territorial DTCPs. This HS model derives from a regional project, designed in collaboration with the Ministry of Health and the Sicilian Government, which includes a network of Rehabilitation Units (Spokes) located throughout the Sicily, under the coordination of a Hub Centre (i.e., the IRCCS Centro Neurolesi). All patients treated in this HS presented neurological impairment due to stroke, spinal cord injury, brain injury and neurodegenerative diseases (e.g., Parkinson's disease or multiple sclerosis). To provide the best rehabilitation activities possible, each spoke center was equipped with innovative technologies for basic robotic rehabilitation (i.e., Lokomat, Erigo, Armeo power, VRRS, Pegaso Ciclo-FES), in addition to a gym where they performed conventional physiotherapy. Moreover, with the purpose to facilitate the empowerment of the disabled people, besides physiotherapy, any center provides speech therapy, neuropsychological rehabilitation, occupational therapy, psychological support to both patients and caregivers and social welfare assistance. Therefore, patients had access to the most modern treatments to recover functions, improve the quality of life, and facilitate the social reintegration at discharge.

Throughout 2017, the first three spoke centers were opened: one in Trapani (January) and two in Palermo (one in August and the other in November) leading to 56 new beds to supply the demand for neurological rehabilitation services in the west of the Region. In July 2018, the fourth center was placed in Catania with 25 new beds. Patients admitted to some spoke centers differ in severity, as well as in diagnosis, as shown in Figure 1.

2.1. Inpatient admission

Patients admission to each spoke was established by the hub center. Clinicians and or families in charge of the patients had to send a request for admission to the hub center by attaching the clinical discharge report from the acute department or the clinical report of a recent outpatient view. A specific hospital commission including neurologists and physiatrists evaluated the documentation and assigned a score based on

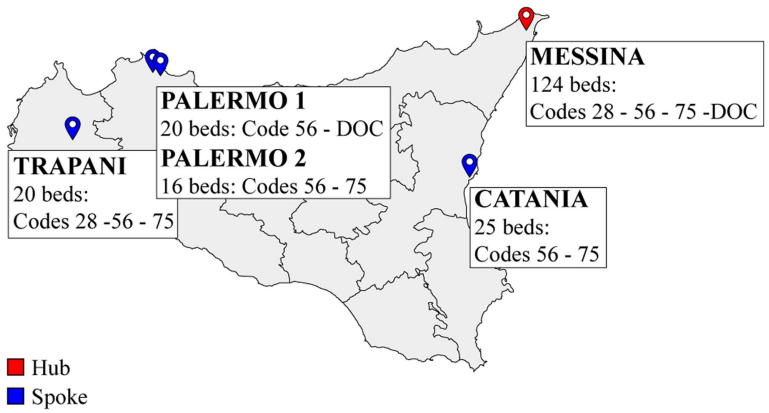

FIGURE 1
Geographical representation of the hub and spoke rehabilitation network in Sicily. DOC, disorder of consciousness.

individual clinical conditions, placing the patient in the ranking of the qualified spoke center. If the patient was not so severely affected, he/she was admitted to the spoke placed next to the residence area.

2.2. Supplies

The hub center has neurophysiology, neuroimaging and diagnostic labs, physiotherapy gym, advanced robotic and virtual reality devices, and telemedicine services after discharge (for more details see Table 1). On the contrary, the spoke centers only have physiotherapy gym and basic robotic devices and virtual reality. However, when necessary, neurorehabilitation specialists use telemedicine to improve services and provide a second opinion. Moreover, specialists of the hub center carried out interventions at each spoke center, such as pneumology, otorhinolaryngology, nutrition, endocrinology and neurophysiology. Other counseling activities, as well as neuroimaging and diagnostic evaluations, could be provided by the local healthcare services (ASP) whether necessary.

2.3. Staff training

The high-skilled personnel of the hub center trained the spoke's healthcare staff to apply the appropriate DTCP as well as correctly manage and use the robotic devices. Moreover, the hub center constantly supports the rehabilitation team of the spoke centers in order to ensure high standards of patient's management through the use of telemedicine. Indeed, the Virtual Reality Rehabilitation System (VRRS) can be also used real-time to help the Spokes's healthcare professionals providing rehabilitation to their inpatients (18, 19). A weekly evaluation of the individual rehabilitation plans and consultations about the current problems were also provided.

3. Methods

3.1. Data source

This study gathered information from the inpatient administrative database of the Regional Health System (RHS) from January 2016 to December 2018, including all discharges from rehabilitation/neurology wards in Sicily, as well as those of Sicilian residents that occurred in other Italian Regions. The hospitalizations studied for comparison were only those from the years 2016 and 2018; hospitalizations from the year 2017 were excluded. To identify hospitalizations, we used the version 24 of the diagnosis-related group codes (DRG) of the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) (20), and we selected only hospitalization with a DRG codes belonging to the Major Diagnostic Category 1 (Diseases and Disorders of the Nervous System - MDC 1). We also filtered for clinical specialty and hospital disciplines codes, defined by the Italian Health Ministry (21): code 28 (spinal cord unit), 56 (functional recovery and rehabilitation) and 75 (neurorehabilitation; DOC: disorder of consciousness) for rehabilitation wards, whereas 32 (neurology) and 49 (intensive unit) for acute wards were also evaluated to ascertain their transfer in a rehabilitation unit. Hospitalizations of non-Sicilian residents as well as pediatric patients were excluded. Voluntary discharge of the patient (against the advice of a doctor) were also excluded. To guarantee the quality of the data and the reliability of the results, we have selected from the database only complete records, i.e., records including patient's demographic characteristics, spatial variables (region and province), and information concerning the hospitalization.

3.2. Outcome measures

First of all, we examined the variation of the distribution of the hospitalizations within each province and the average length of stay (LOS), comparing the years 2016 and 2018. The proportion of hospitalizations in facilities placed within the patients' own province of residence (HwP), as well as the mean duration of these hospitalizations (LwP), have been considered a measure of demand satisfied by the province. Second, we sought changes in the demographic structure of the patients hospitalized. We then computed the average age, the percentage of patients over 75, and the percentage of women by province. Finally, to understand the role that the HS network could have on the DTCP, we observed: (i) variations in the access to hospital care by the proportion of patients coming from an acute ward (Acute in), from home (Home in), or

TABLE 1 Comparative analysis by citizen's province of residence - rehabilitation wards (units 28/56/75).

Province	Agrigento	Caltanissetta	Catania	Enna	Messina	Palermo	Ragusa	Siracusa	Trapani	Sicily
2016										
N. Hospitalizations	288	238	830	214	456	558	203	229	166	3,182
Length of stay (AVG)	56.6 ± 41.7	52.4 ± 49.6	50.2 ± 42.9	101.6 ± 90.9	56.5 ± 51.3	67.0 ± 59.2	47.8 ± 49.3	47.6 ± 34.9	65.8 ± 54.0	58.7 ± 54.2
HwP (%)	64.6	46.2	73.3	73.8	82.0	66.7	68.5	59.4	46.4	67.9
LwP (AVG)	34.9 ± 40.1	14.8 ± 19.1	31.3 ± 29.4	87.3 ± 99.0	42.1 ± 50.1	41.0 ± 54.2	23.7 ± 23.8	20.7 ± 21.5	21.4 ± 26.2	35.7 ± 47.9
Age (AVG)	61.1 ± 17.0	60.4 ± 18.6	65.6 ± 16.9	58.0 ± 16.7	63.1 ± 17.6	58.6 ± 17.1	64.4 ± 17.5	63.8 ± 16.8	64.5 ± 13.6	62.4 ± 17.2
Over 75 (%)	21.9	29.8	36.3	22.4	29.6	17.0	33.0	34.1	24.1	28.2
Women (%)	45.1	51.7	51.0	68.2	47.1	44.1	43.3	46.3	46.4	48.8
Acute in (%)	5.6	8.4	15.3	2.3	18.9	21.1	11.8	13.1	19.3	14.4
Home in (%)	74.3	74.8	38.9	77.6	66.2	62.5	56.2	36.2	62	57.6
Other in (%)	6.2	13.4	48.2	8.9	17.1	21.5	32.5	31.4	9.6	25.8
Waiting time (AVG)	20.6 ± 47.6	30.3 ± 63.9	15.7 ± 43.5	31.0 ± 55.9	21.7 ± 57.0	15.8 ± 46.6	18.0 ± 55.9	13.8 ± 47.8	11.5 ± 28.9	18.9 ± 49.9
Protected out (%)	18.8	5.9	9.8	7.5	8.6	10.4	10.8	20.5	15.7	11.2
Acute out (%)	5.6	6.7	12.8	4.7	11.6	9.7	14.3	7.4	7.2	9.8
Home out (%)	69.4	82.4	72.7	81.8	76.3	68.8	70.9	66.4	74.7	73.1
2018										
N. Hospitalizations	315	226	927	186	821	682	159	299	290	3,905
Length of stay (AVG)	60.8 ± 47.9	51.6 ± 49.5	52.9 ± 49.2	104.7 ± 100.5	56.2 ± 56.2	71.4 ± 65.8	48.1 ± 43.9	47.4 ± 45.4	62.2 ± 47.1	59.9 ± 57.9
HwP (%)	67.9	38.1	68.6*	69.9	88.9***	69.8	61.0	55.9	68.6***	70
LwP (AVG)	37.7 ± 41.4	12.4 ± 18.2	30.2 ± 32.4	86.2 ± 107.6	45.6 ± 52.4	48.6 ± 65.5*	21.8 ± 24.8	19.9 ± 21.9	35.7 ± 30.9***	38.2 ± 51.4*
Age (AVG)	61.7 ± 15.6	60.4 ± 18.0	65.8 ± 16.9	59.6 ± 16.6	65.7 ± 16.0**	59.4 ± 16.4	64.0 ± 17.0	63.2 ± 16.3	62.5 ± 14.9	63.2 ± 16.6
Over 75 (%)	20.6	23.5	35.5	23.7	32.3	18.0	32.7	25.4*	22.4	27.5
Women (%)	53	52.7	49	65.1	47.1	43	39	43.8	44.5	47.7
Acute in (%)	7.6	12.4	16.5	4.3	22.4	20.5	13.2	12.0	14.8	16.3*
Home in (%)	90.8***	71.7	35.9	78.0	69.5	59.1	45.3	42.8	59.3	58.2
Other in (%)	3.5	21.2*	52.8	12.4	18.3	24.8	42.8	33.1	30.0***	29.3**
Waiting time (AVG)	24.3 ± 47.7	23.1 ± 45.7	18.4 ± 51.5	22.2 ± 39.0	22.0 ± 57.9	24.6 ± 45.9***	19.4 ± 55.9	19.8 ± 51.0	24.7 ± 43.5***	21.8 ± 50.5*
Protected out (%)	20.3	9.7	13.5*	4.3	8.9	10.4	15.7	15.4	6.9**	11.6
Acute out (%)	6.0	4.0	11.8	2.2	3.8***	6.9	3.1***	5.0	7.2	6.7***
Home out (%)	69.5	79.2	70.9	84.4	82.0*	73.3	74.8	73.2	79.0	75.6*

Quantitative variables are expresses as mean ± standard deviation; HwP = Proportion of hospitalizations in facilities placed within the patients' own province of residence; LwP = Average length of stay in facilities placed within the patients' own province of residence.
*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

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from a different (public or private) healthcare facility (Other in), the average waiting time for hospitalization (Waiting time); (ii) variations in discharge outcomes by the proportion of discharges to home (Home out), protected discharges (Protected out), i.e., patients discharged to a nursing home or patients receiving home health care after being discharged, and transfers to an acute ward (Acute out).

3.3. Statistical analysis

The analysis was conducted both globally and separately by the 9 Sicilian provinces (Agrigento, Caltanissetta, Catania, Enna, Messina, Palermo, Siracusa, Ragusa, and Trapani).

We compared the above measures before and after the HS network activation, i.e., 2016 versus 2018. Statistical analysis was performed by using the 4.2.2 version of the open-source software R. A $p < 0.05$ was considered as statistically significant. Results for continuous variables were expressed in mean ± standard deviation, whereas categorical variables in frequencies and percentages. The Chi-square test with continuity correction was used to assess for statistical differences in proportions, whereas the unpaired Student's *t*-test was used to compare continuous variables.

4. Results

A total of 7,087 hospitalization records in rehabilitation units were included in this study. Table 1 reports results of the comparative analysis performed on the study outcome measures.

4.1. Demographic structure

The mean age of the patients hospitalized in 2016 was 62.4 ± 17.2 years, whereas in 2018 was 63.2 ± 16.6 years. Overall, no significant 2018-2016 changes in proportions for either gender or age (over 75) were found. However, the mean age resulted to be statistically increased ($t(341) = 2.18$, $p = 0.03$) in patients attending spinal cord unit (discipline code 28), with a higher proportion of over 75 in 2018 than in 2016 (+42.5%).

4.2. Hospitalizations and length of stay

There was no significant change in the overall mean length of stay between 2016 and 2018 ($t(6951) = 0.91$; $p = 0.362$). After the establishment of the HS network, we observed an increase in HwP in the provinces of Trapani (+32.4%), Messina (+7.8%) and Palermo (+4.4%). In the same provinces we also observed an increase in LwP: Trapani (+40.1%), Messina (+7.7%) and Palermo (+15.6%).

Figure 2 shows a detailed description of the LwP indicator by rehabilitation ward and province. Statistically significant changes between the 2 years were reported within the unit/code 28 and 56 in the province of Trapani ($t(19) = 4.5$, $p < 0.001$; $t(226) = 3.90$, $p < 0.001$, respectively), and also within the unit/code 75 in the province of Catania (+100%), Palermo (+55.8%) and Trapani (+100%).

4.3. Access to hospital care

Overall, we observed a significant increase of *Acute in* proportion (χ^2 (1) = 4.79, $p = 0.029$) from 2016 to 2018, whereas there was no significant change of *Home in* proportion (χ^2 (1) = 0.24, $p = 0.623$). In addition, we found a statistically significant increase of *Other in* proportion (χ^2 (1) = 10.5, $p = 0.001$) between 2016 and 2018. As shown in Figure 3, we observed a statistically significant increase of *Waiting time* in the provinces of Palermo ($t(1182) = 3.32$, $p = 0.001$) and Trapani ($t(444) = 3.86$, $p < 0.001$). On the contrary, in the provinces of Catania and Messina we observed an increase (from 15.7 ± 43.5 to 18.4 ± 51.5; from 21.7 ± 57.0 to 22.0 ± 57.9, respectively) that did not reach the statistical significance ($t(1748) = 1.21$, $p = 0.225$; $t(952) = 0.10$, $p = 0.919$, respectively).

4.4. Discharge outcomes

Overall, between 2016 and 2018, there was a statistically significant reduction of *Acute out* proportion (χ^2 (1) = 23.41, $p < 0.001$), and a significant increase of *Home out* (χ^2 (1) = 5.62, $p = 0.018$). On the contrary, there was no significant change in *Protected out* proportion (χ^2 (1) = 0.25, $p = 0.619$) from 2016 to 2018. We found similar results when performing 2018–2016 comparisons differencing by rehabilitation ward, as shown in Figure 4. Significant changes in *Acute out* emerged within the spinal unit (code 28) and the neurorehabilitation unit (code 75): χ^2 (1) = 8.33, $p = 0.004$; χ^2 (1) = 6.18, $p = 0.013$, respectively; as well as in *Home out*: χ^2 (1) = 6.93, $p = 0.008$; χ^2 (1) = 6.60, $p = 0.01$, respectively.

5. Discussion

This is the first Italian HS network for intensive neurorehabilitation that sought to improve quality of care and reduce patient migration (22). Indeed, to face the demand variation for care, the Sicilian government is heading toward a people-centered process of health services, reinforcing the existing DTCPs in order to support the clients in their own territory, and involving the general practitioners (GP) as consultants. After all, citizens identify their GP as the preferred point of access to local health services compared to other health professionals (23, 24). In this perspective, GP can collaborate with facilities of the RHS in an integrated network, giving a central role to the patient (25).

In this study, we focused on the evaluation of effects that this HS model had on the improvement of the health service and in hospitalization outcomes, as well as the integration and accessibility to the services, using a set of indicators specifically designed. Indeed, the integration of procedures among the various clinical settings requires careful monitoring of both the resources used and the results achieved in the different phases of the care process. Such monitoring, together with a critical assessment of the innovative health policies adopted can be a useful tool for supporting both the planning and the sustainability of the RHS. For example, a HS model can allow to avoid unnecessary migrations to other provinces and/or regions, with a consequent reduction of hospitalizations costs (26). This is exactly what we observed in our case: there has been an increase in admissions and average length of stay of people residing in the province where the Spokes have been opened. In addition, our findings show a significant increase in the spoke admission of patients from other care facilities

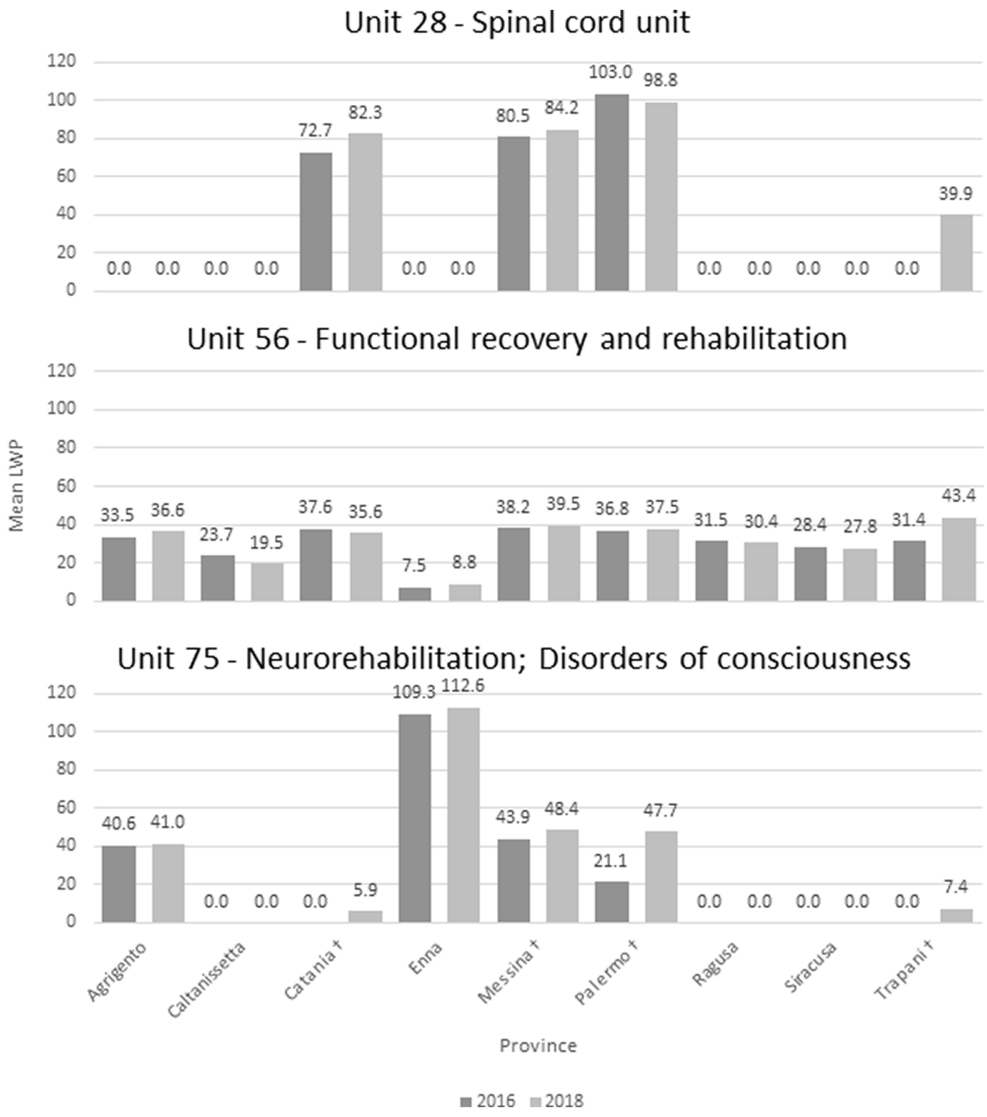

FIGURE 2
Mean LWP by rehabilitation ward (units 28/56/75) and province. †Province included in the HS network.

and from acute wards, which suggests that the opening of spokes could have (i) attracted a portion of patients who were previously served by private facilities and/or services, and (ii) improved RHS continuity of care service, with regard to the possibility for acute hospital wards to discharge to the new dedicated beds of the rehabilitation spokes facilities introduced in the provinces of Sicily (Acute in).

Indeed, before the application of our model, many patients were forced to move to other regions or out of Italy (e.g., Austria) where the rehabilitation pathway is more advanced and integrated to the territorial services. In Northern Italy, for example, patients with severe traumatic brain injury have a "continuity of care" network, called GRACER, for their complete management from the acute phase to the return home/to work. Patients and their caregivers are totally assisted since the admission to Intensive Care, during their stay in Neurorehabilitation Unit, their training as outpatients (Day-H and ambulatory clinics) and then also at home. Moreover, territorial services and No-profit associations help them (when the clinical condition allow this) in their social-economic life (e.g., to find job, practice a sport, etc.)

Results also show a decrease of discharge to protected healthcare facilities and to acute wards, as well as an increase of discharges to home. It could be hypothesized that the high quality of rehabilitation services provided by the Spokes (also thanks to the continuous supervision by the hub) may have led to better outcomes (although no specific clinical outcomes have been assessed) further improving the quality of the DTCP.

Therefore, to define a battery of indicators able to monitor the DTCP's outcomes in a standard way for all RHS facilities is becoming necessary, because of the recent growth of hospitalizations for intensive neurorehabilitation, especially for older adults (27). The increase of life expectancy makes the aging a risk factor for the development of multiple chronic diseases, including cardiovascular, cerebrovascular and neurodegenerative disorders (28), causing a significant economic burden for the healthcare system (29). Our findings report an increase of the mean age of the hospitalized patients, and of the over 75 proportion, concerning the spinal unit patients (code 28): this sustains the hypothesis that the opening of a

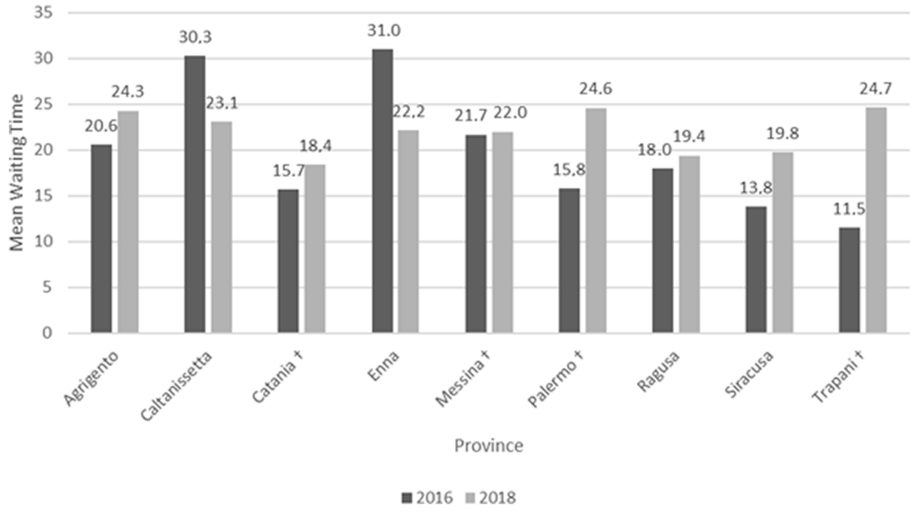

FIGURE 3
Mean waiting time for hospitalization by province. †Province included in the HS network.

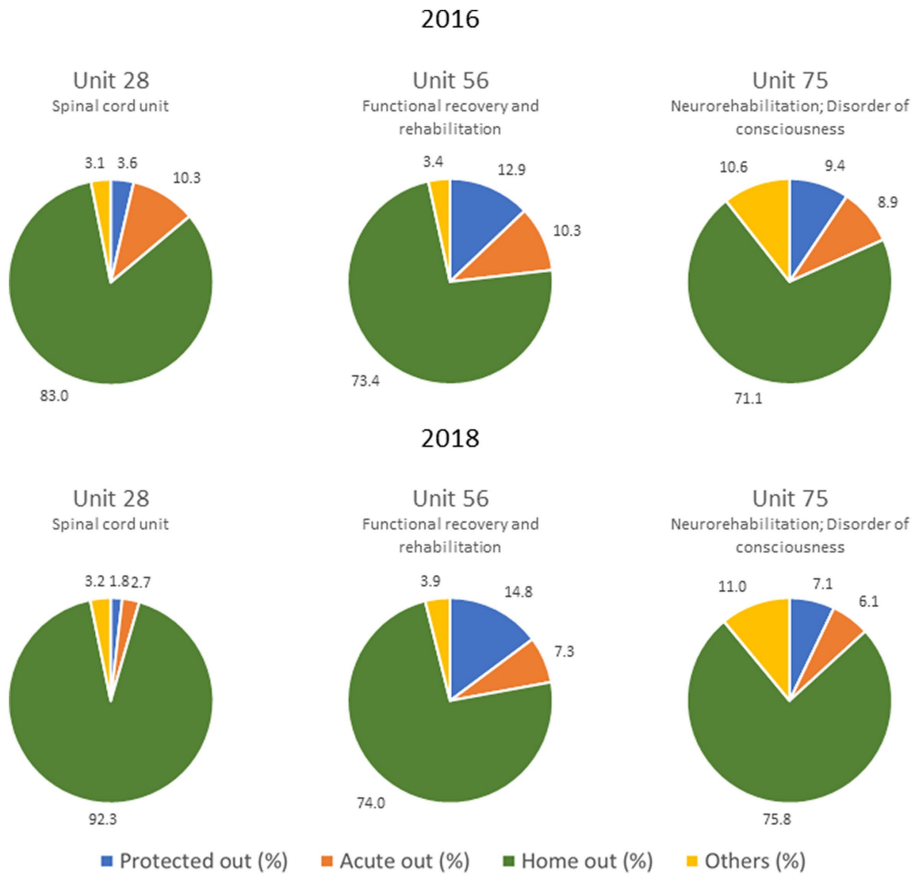

FIGURE 4
Discharge outcomes by rehabilitation wards and year.

spoke facilitates the management of these patients within the family, avoiding unnecessary displacement of these frail patients.

As a main strength, this model was conceived to properly address the issues related to neurorehabilitation in the main and underserved provinces of Sicily. Indeed, besides the specialistic rehabilitative management of acquired brain and spinal cord injury, the HS model provided rehabilitation also to neurodegenerative diseases, which are considered an emerging problem because of people aging.

6. Limitations and future research

The main limitation of this study is the lack of an economic evaluation of the H&S network, which could indicate whether the model provides cost savings for both local ASPs and RHS. Unfortunately, we do not have the economic information needed to carry it out. However, the H&P network has improved the existing health care supply and the ASPs located in Trapani and Palermo have already included the centers within their territorial network. Furthermore, some limitations could result from the fact that the study was carried out exclusively on inpatient administrative databases, without evaluating medical registers and patient satisfaction with the new organizational model implemented.

HS model could provide a means to better deal with the long-term pandemic sequelae. Indeed, neurological complications after SARS-CoV-2 infection (COVID-19) affecting the nervous system with associated muscular diseases have been reported (30, 31). COVID-19 related neurological symptoms are not limited to the motor (e.g., following stroke and encephalitis induced by the SARS-Cov2-infection) or the cardiopulmonary levels, but also include dysphagia, dysexecutive syndrome, apraxia, cognitive impairment, and psychiatric disorders such as depression, anxiety, and post-traumatic stress disorder, among others (32, 33). Thus, different organizational models were adopted in neurorehabilitation during the COVID-19 pandemic impacting the therapies time frame, the physical and mental health of healthcare professionals and the caregiver's workload. There is still uncertainty about the effectiveness of these new therapeutic strategies on the management of neurorehabilitation services and future studies should explore the effect on the patients' needs (34). Hence, this study could be extended in the future to examine the effects of the HS network considering a longer follow-up period.

Another important limitation is that we did not assess/investigate patients' functional outcomes at discharge from the spoke centers. Then, we are not able to state (but only suppose) if and to extent neurological patients were more likely to be independent with functional ambulation, self-care, activity of daily life, etc. Indeed, given that in our HB we have used different innovative technology that are known to further potentiate clinical outcomes, it is conceivable that people receiving this treatment could have better results than those treated with usual territorial care.

7. Conclusion

According to this study, the activation of a HS network for intensive neuro-rehabilitation has facilitated the management of neurological patients, avoiding unnecessary migrations to other provinces and/or regions, and improving the regional care service for neuro-rehabilitation. Future research will be direct to investigate this aspect, focusing on before-after variations in hospitalization rates and origin–destination patient flows. Finally, it would be beneficial to reinforce the role of the GP as a case manager, as well as train citizens in disease management at their own home.

Data availability statement

The data analyzed in this study were obtained from the Department of Health of the Sicilian Region, under the restrictions of non-public dissemination. Requests for access to these datasets should be addressed to Maria Cristina De Cola, mariacristina.decola@irccsme.it.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements.

Author contributions

MCDC and AI: conceptualization, methodology, and writing – original draft preparation. RSC: validation and writing – review and editing. MCDC: formal analysis and data curation. VLB: investigation. AQ: supervision. 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.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1141581/full#supplementary-material

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Estimates of the global, regional, and national burden of atrial fibrillation in older adults from 1990 to 2019: insights from the Global Burden of Disease study 2019

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Background: Atrial fibrill ation (AF) is a predominant public health concern in older adults. Therefore, this study aimed to explore the global, regional, and national burden of AF in older adults aged 60–89 between 1990 and 2019.

Methods: The morbidity, mortality, disability-adjusted life years (DALYs), and age-standardized rates of AF were refined from the Global Burden of Diseases study 2019. The epidemiological characteristics were assessed based on numerical values, age-standardized rates per 100,000 person-years, and estimated annual percentage changes (EAPC).

Results: Globally, a total of 33.31 million AF cases, 219.4 thousand deaths, and 65.80 million DALYs were documented in 2019. There were no appreciable changes in EAPC from 1990 to 2019. The disease burden of AF differed significantly across different territories and countries. At the national level, China exhibited the highest number of incident cases [818,493 (562,871–1,128,695)], deaths [39,970 (33,722–46,387)], and DALYs [1,383,674 (1,047,540–1,802,516)]. At the global level, high body mass index (BMI) and high systolic blood pressure (SBP) were two predominant risk factors contributing to the proportion of AF-related deaths.

Conclusion: AF in older adults remains a major public health concern worldwide. The burden of AF varies widely at both national and regional levels. From 1990 to 2019, the cases of incidences, deaths, and DALYs have shown a global increase. The ASIR, ASMR, and ASDR have declined in the high-moderate and high SDI regions; however, the burden of AF increased promptly in the lower SDI regions. Special attention should be paid to the main risk factors for high-risk individuals with AF, which can help control systolic blood pressure and body mass index within normal limits. Over all, it is necessary to illustrate the features of the global AF burden and develop more effective and targeted prevention and treatment strategies.

KEYWORDS

atrial fibrillation, aging, Global Burden of Disease, risk factors, older adults

Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmia (1), affecting more than 33 million people. Globally, it is a primary cause of coronary heart disease and mortality (2). Relevant research indicates that the incidence and prevalence of AF have been going up in Europe and North America from the 1970's to the early twenty-first century (3). The prevalence of AF is expected to rise in the next 30–50 years (4, 5). Hence, AF has become a worldwide public health problem and strained the healthcare system. Understanding the pattern of AF incidence and the temporal trends can facilitate the development of more well-directed preventive measures.

The Global Burden of Disease (GBD) study estimates the AF burden in 204 countries and territories worldwide, providing an excellent opportunity to comprehend the picture of AF (6). Recent studies have assessed the prevalence, disability-adjusted life years (DALYs), and AF-related mortality in all age groups using the data derived from the GBD (7, 8). However, of all cardiovascular diseases, AF commonly causes heart failure (9), imposing a substantial disease burden, especially on older adults. The overall health of older adults declines with age, and multimorbidity is prevalent, especially in cardiovascular disease. Therefore, it is necessary to pay particular attention to older adults. A cohort study found a significant increase in the prevalence of AF in older adults over 60 years of age (10). In addition, the proportion of the older population over 90 years old is only 2%. Therefore, we selected 60–89-year-olds as the research subjects. Based on the GBD Study 2019 data, the purpose of this study was to explore the burden of AF and its risk factors among older adults aged 60–89 years at global, regional, and national levels from 1990 to 2019. Our outcomes can act as a crucial supplement and expansion to previous research while also contributing to the formulation of AF prevention measures targeting various countries.

Methods

Data sources

We collected corresponding data from the Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool) (11), an online tool of the Global Burden of Diseases (GBD), Etiologies, Injuries, and Risk Factors Study. The quality of statistics has been recognized internationally, and the approaches employed in the GBD have been illustrated elsewhere. The GBD 2019 database consisted of epidemiological data (i.e., deaths, prevalence, incidence, and DALYs) for 204 countries and territories worldwide. Then, these countries and territories were divided into five regions in accordance with the sociodemographic index (SDI) (2). The regions ranged from high to low as follows: high SDI, high-middle SDI, middle SDI, low-middle SDI, and low SDI.

Furthermore, the world was geographically divided into 21 regions, such as Australasia and Eastern Europe. The Human Development Index (HDI) data were available for extraction from Human Development Reports (http://hdr.undp.org/en/data). It was a composite measure index of three elementary aspects of human development: life expectancy, education, and per capita income. In our research, HDI was assembled and utilized to match GBD data. The secondary analysis data in the present article did not require ethical agreement or approval from the ethics committee or the institutional review board.

Statistical analysis

The burden of AF was expressed in terms of number, age-standardized incidence rates (ASIRs), age-standardized mortality rates (ASMRs), age-standardized DALY rates (ASDRs), and estimated annual percentage change (EAPC) with a confidence interval of 95%. The ASRs were counted using a standardized global aging structure, which is necessary when comparing populations in different locations or sample groups over a period of time (12).

In the present study, we calculated the EAPC in the age-standardized rates of AF to further assess the burden of the disease. EAPC was a generalization and extensively used weighing measure for ASR's tendency within a specified interval. It was calculated using the referring regression line: $Y = \alpha + \beta X + \varepsilon$, where Y referred to ln (age-standardized rate), X presented the calendar year, β influenced the active or passive trends in ASR and ε meant error value. The EAPC can be given by the following formula: $100 \times [\exp(\beta) - 1]$, and its 95% confidence interval (CI) could be obtained from the linear regression model (12). There are three situations: (1) if the 95% CI and EAPC assessment were both <0, the ASRs were regarded as a descending trend, (2) if the 95% CI and EAPC were both >0, the ASRs were regarded as an increasing trend. (3) If not, the ASRs were regarded as a steady trend. The statistical analysis in the present study was accomplished using the R program (Version 4.1.2). If the p-value was < 0.05, it was deemed to be statistically significant.

Results

Global burden of AF

At the global level, a total of 3,331,144 (2,342,510–4,489,654) cases of AF were reported in 2019. The morbidity in both sexes increased by 1.1% from 1,583,024 (1,094,531–2,166,439) in 1990 to 3,331,144 (2,342,510–4,489,654) in 2019. Moreover, the ASIR fluctuated slightly by 0.05% from 58.54 (44.92–74.24) to 57.09 (44.07–71.9) during the past 30 years. Similarly, the mortality rate increased by 1.36% from 92,801 (82,995–111,456) in 1990 to 219,437 (190,526–249,642) in 2019. The ASMR demonstrates a mild increase of 0.04%, from 4.29 (3.73–5.09) in 1990 to 4.38 (3.7–5.05) in 2019 per 100,000 population. AF caused 6,579,978 (5,241,696–8,321,653) DALYs in 2019 worldwide, which was a 1.16% increase from 3,044,717 (2,363,647–3,900,467) in 1990. With regard to age-standardized rates, in 1990, the ASDR of AF was 110 (87.66–139.16) per 100,000 population, which slightly decreased to 107.13 (86.18–133.73) in 2019 (Table 1, Figure 1A).

Regional burden of AF

For SDI regions, the number of AF cases showed an upward trend in the five SDI countries from 2009 to 2019

TABLE 1 Incident cases, death, and DALYs of cardiomyopathy and myocarditis and ASRs per 10,000 population from 1990 and 2019 by Global Burden of Disease.

Characteristics	1990		2019		1990–2019	1990–2019
	Incidence cases No. (95% UI)	ASIR per 100,000 No. (95% UI)	Incidence cases No. (95% UI)	ASIR per 100,000 No. (95% UI)	Percentage change No. (95% CI)	EAPC No. (95% CI)
Overall	1,583,023.57 (1,094,531.35–2,166,438.85)	58.54 (44.92–74.24)	3,331,144.11 (2,342,509.66–4,489,654.42)	57.09 (44.07–71.9)	1.1% (1.06–1.16)	0.05 (−0.02–0.13)
Sociodemographic index						
Low SDI	59,083.69 (40,267.86–81,934.91)	40.67 (30.92–52.06)	135,864.94 (92,489.13–186,062.1)	41.97 (31.77–53.69)	1.19% (1.14–1.26)	0.12 (0.11–0.12)
Low-middle SDI	202,876.21 (138,996.1–280,233.52)	53.96 (41.04–68.62)	505,077.85 (346,414.8–690,949.01)	54.72 (41.51–69.76)	1.48% (1.4–1.57)	0.08 (0.06–0.09)
Middle SDI	342,872.23 (233,718.56–470,907.06)	52.39 (39.69–66.74)	922,124.53 (632,539.34–1,262,914.42)	54.27 (41.16–69.05)	1.57% (1.52–1.63)	0.14 (0.08–0.2)
High-middle SDI	435,935.66 (300,652.64–602,950.05)	60.34 (46.52–77.1)	827,741.17 (571,861.8–1,134,881.72)	57.97 (44.57–74.2)	0.9% (0.84–0.96)	−0.12 (−0.15 to −0.09)
High SDI	541,597 (376,964.16–733,826.69)	71.45 (55.34–90.2)	939,060.48 (696,820.22–1,228,719.31)	69.22 (55.37–85.18)	0.73% (0.63–0.87)	0.26 (0.09–0.44)
Regions						
Andean-Latin America	1,894.12 (1,297.77–2,554.18)	13.63 (10.08–17.53)	6,097.32 (4,265.51–8,160.3)	14.84 (11.11–19.17)	2.22% (2.07–2.38)	0.43 (0.35–0.52)
Australasia	17,400.97 (12,027.61–23,837.67)	98.68 (75.18–125.06)	32,335.39 (22,689.52–43,431.81)	90.39 (69.71–114.51)	0.86% (0.75–0.97)	−0.24 (−0.3 to −0.19)
Caribbean	5,691.5 (3,900.06–7,753.2)	29.33 (22.05–38.08)	11,441.62 (7,849.53–15,488.95)	29.72 (22.18–38.44)	1.01% (0.96–1.07)	0.07 (0.06–0.08)
Central Asia	18,123.03 (12,503.21–24,707.24)	63.51 (48.9–80.87)	27,908.61 (18,911.11–38,566.56)	64.77 (49.64–82.66)	0.54% (0.47–0.6)	0.1 (0.09–0.12)
Central Europe	69,623.44 (47,658.46–96,047.25)	72.77 (55.81–92.66)	98,521.6 (67,133.05–136,390.75)	70.59 (54.18–89.82)	0.42% (0.36–0.46)	0.02 (−0.06–0.11)
Central Latin America	17,879.46 (12,333.8–24,307.64)	31.81 (23.94–41.05)	53,721.27 (37,296.58–73,064.04)	31.77 (23.84–41.21)	2% (1.94–2.07)	0.01 (0–0.02)
Central Sub-Saharan Africa	4,453.46 (2,990–6,276.85)	33.03 (25.06–42.21)	9,596.86 (6,537.13–13,243.4)	32.22 (24.45–41.46)	1.15% (1.01–1.31)	−0.1 (−0.12 to −0.09)
East Asia	313,996.06 (212,426.67–436,983.35)	55.26 (41.95–70.12)	845,659.53 (583,221.77–1,164,608.61)	57.4 (43.67–72.99)	1.69% (1.61–1.8)	0.16 (0.04–0.28)
Eastern Europe	122,722.76 (84,488.3–167,427.12)	68.4 (52.4–87.04)	167,038.62 (114,134.66–231,211.1)	74.4 (57.18–95.28)	0.36% (0.32–0.4)	0.35 (0.32–0.38)
Eastern Sub-Saharan Africa	8,610.45 (5,833.87–11,972.16)	19.48 (14.83–25.05)	18,593.54 (12,619.36–25,545)	19.89 (15.18–25.61)	1.16% (1.11–1.22)	0.16 (0.1–0.23)
High-income Asia Pacific	31,243.1 (20,944.28–43,603.15)	26.92 (20.67–34.42)	49,432.85 (33,174.99–68,914.26)	21.12 (16.28–27.19)	0.58% (0.5–0.7)	−1.58 (−1.91 to −1.24)
High-income North America	265,521.57 (184,073.28–358,286.57)	95.3 (73.03–121)	548,955.86 (418,372.27–698,785.69)	108.53 (87.59–131.44)	1.07% (0.86–1.34)	1.33 (0.95–1.72)
North Africa and the Middle East	45,957.21 (31,425.75–63,186.57)	41.81 (31.63–53.41)	116,006.36 (80,041.9–158,616.64)	41.93 (31.66–53.56)	1.52% (1.46–1.61)	−0.08 (−0.11 to −0.05)
Oceania	1,027.48 (699.01–1,447.68)	57.91 (43.98–73.48)	2,374.01 (1,625.76–3,294.83)	59.26 (44.94–75.2)	1.31% (1.19–1.43)	0.07 (0.05–0.09)
South Asia	207,889.94 (142,458.26–289,158.44)	60.06 (45.66–76.21)	586,125.53 (400,228.16–804,858.9)	61.37 (46.53–78)	1.82% (1.74–1.94)	0.06 (0.06–0.07)

(Continued)

TABLE 1 (Continued)

Characteristics	1990		2019		1990–2019	1990–2019
	Incidence cases No. (95% UI)	ASIR per 100,000 No. (95% UI)	Incidence cases No. (95% UI)	ASIR per 100,000 No. (95% UI)	Percentage change No. (95% CI)	EAPC No. (95% CI)
Southeast Asia	97,679.58 (66,820.01–134,561.02)	61.29 (46.46–78.2)	247,606.5 (169,923.94–339,117.02)	62.77 (47.54–79.6)	1.53% (1.49–1.58)	0.09 (0.08–0.1)
Southern Latin America	13,914.25 (9,465.08–18,990.5)	40.73 (30.74–52.21)	25,772.38 (17,760.5–35,322.51)	41.8 (31.8–53.39)	0.85% (0.76–0.95)	0.07 (0–0.14)
Southern Sub-Saharan Africa	6,675.23 (4,564.91–9,166.84)	37.43 (28.33–48.01)	13,535.76 (9,269.77–18,486.87)	37.09 (28.17–47.62)	1.03% (0.98–1.08)	−0.02 (−0.03 to −0.01)
Tropical Latin America	26,492.79 (18,160.56–36,288.69)	43.44 (32.89–55.6)	77,585.15 (53,528.43–105,946.86)	44.8 (33.81–57.84)	1.93% (1.84–2.04)	0.55 (0.39–0.7)
Western Europe	286,609.98 (200,891.8–389,866.68)	72.79 (55.34–92.55)	352,998.6 (247,983.17–481,656.6)	63.01 (48.37–79.79)	0.23% (0.2–0.26)	−0.36 (−0.39 to −0.32)
Western Sub-Saharan Africa	19,617.2 (13,303.69–27,132.38)	35.51 (26.88–45.46)	39,836.76 (27,328.41–54,873.98)	36.01 (27.33–46.19)	1.03% (1–1.07)	0.05 (0.01–0.08)
Characteristics	1990		2019		1990–2019	1990–2019
	Deaths cases No. (95% UI)	ASMR per 100,000 No. (95% UI)	Deaths cases No. (95% UI)	ASMR per 100,000 No. (95% UI)	Percentage change No. (95% CI)	EAPC No. (95% CI)
Overall	92,801.05 (82,995.05–111,456.15)	4.29 (3.73–5.09)	219,437.14 (190,525.86–249,642.14)	4.38 (3.7–5.05)	1.36% (1.14–1.55)	0.04 (0.02–0.06)
Sociodemographic index						
Low SDI	3,728.16 (2,483.7–4,731.5)	3.73 (2.42–4.76)	10,484.14 (7,648.72–12,654.91)	4.3 (3.08–5.25)	1.81% (1.34–2.51)	0.5 (0.47–0.53)
Low-middle SDI	8,678.73 (6,914.63–10,558.98)	3.46 (2.66–4.14)	29,699.98 (25,034.79–34,583.16)	4.21 (3.5–4.87)	2.42% (1.76–3.14)	0.61 (0.55–0.67)
Middle SDI	16,620.38 (14,704.44–18,971.98)	3.82 (3.32–4.28)	52,178.17 (45,208.24–61,158.62)	4.11 (3.5–4.75)	2.14% (1.71–2.6)	0.21 (0.19–0.24)
High-middle SDI	27,689.09 (24,854.06–35,444.35)	4.64 (4.04–5.92)	58,332.62 (50,409.75–69,838.57)	4.47 (3.78–5.39)	1.11% (0.89–1.28)	−0.25 (−0.32 to −0.18)
High SDI	36,029.71 (31,280.88–45,846.61)	4.62 (3.93–5.82)	68,619.71 (56,411.87–81,382)	4.61 (3.67–5.52)	0.9% (0.65–1.04)	0.03 (0.01–0.06)
Regions						
Andean-Latin America	504.52 (424.82–588.91)	4.41 (3.67–5.06)	1,525.05 (1,231.71–1,852.46)	4.32 (3.48–5.24)	2.02% (1.46–2.77)	0.1 (0.03–0.18)
Australasia	1,158.23 (958.03–1,334.33)	7.38 (5.96–8.41)	2,511.5 (2,016.89–3,042.33)	6.86 (5.45–8.33)	1.17% (0.96–1.42)	−0.44 (−0.52 to −0.36)
Caribbean	697.31 (592.49–813.9)	4.46 (3.72–5.28)	1,549.42 (1,297.45–1,884.17)	4.73 (3.91–5.79)	1.22% (0.92–1.56)	0.26 (0.16–0.36)
Central Asia	933.47 (773.86–1,271.8)	3.62 (2.82–4.8)	1,951.57 (1,721.37–2,586.44)	5.75 (4.95–7.74)	1.09% (0.62–1.45)	1.49 (1.33–1.64)
Central Europe	4,332.08 (3,890.56–5,357.81)	4.51 (3.93–5.43)	8,073.21 (6,837.02–9,536.65)	4.83 (3.99–5.7)	0.86% (0.61–1.09)	0.15 (0.1–0.2)
Central Latin America	1,960.79 (1,699.83–2,517.32)	4.46 (3.76–5.68)	6,478.07 (5,267.49–8,265.53)	4.56 (3.72–5.83)	2.3% (1.87–2.71)	−0.09 (−0.17 to −0.01)
Central Sub-Saharan Africa	467.17 (268.6–797.97)	5 (2.85–8.21)	1,334.27 (857.82–1,933.42)	5.63 (3.55–8.24)	1.86% (1.15–2.84)	0.37 (0.29–0.45)
East Asia	14,205.46 (1,1974.33–16,636.49)	4 (3.31–4.63)	41,526.2 (35,287.76–47,920.9)	3.82 (3.19–4.42)	1.92% (1.36–2.59)	−0.26 (−0.31 to −0.21)

(Continued)

TABLE 1 (Continued)

Characteristics	1990		2019		1990–2019	1990–2019
	Deaths cases No. (95% UI)	ASMR per 100,000 No. (95% UI)	Deaths cases No. (95% UI)	ASMR per 100,000 No. (95% UI)	Percentage change No. (95% CI)	EAPC No. (95% CI)
Eastern Europe	7,005.17 (6,098.93–9,688.8)	4.03 (3.44–5.6)	11,419.28 (9,643.68–14,750.74)	4.62 (3.88–6.02)	0.63% (0.43–0.83)	0.22 (0.07–0.36)
Eastern Sub-Saharan Africa	1,440.88 (840.03–1,891.54)	4.23 (2.37–5.58)	3,586.81 (2,304.99–4,437.21)	4.69 (2.98–5.87)	1.49% (0.99–2.18)	0.34 (0.25–0.43)
High-income Asia Pacific	3,746.97 (3,218.5–4,775.05)	3 (2.54–4.03)	9,103.35 (7,090.93–11,637.45)	2.39 (1.87–3.19)	1.43% (1.13–1.72)	−0.85 (−0.94 to −0.75)
High-income North America	11,153.7 (9,461.43–13,912.54)	4.04 (3.36–4.99)	22,725.4 (18,505.88–27,506.97)	4.96 (4.01–6.05)	1.04% (0.84–1.12)	0.72 (0.64–0.8)
North Africa and the Middle East	2,650.72 (2,061.78–3,059.75)	3.48 (2.67–4.11)	7,696.85 (6,582.67–9,421.38)	3.66 (3.07–4.33)	1.9% (1.45–2.87)	0.19 (0.1–0.28)
Oceania	44.44 (32.32–62.72)	4.1 (2.76–6.01)	121.79 (92.59–161.5)	4.25 (3.24–5.5)	1.74% (1.25–2.31)	0.17 (0.12–0.22)
South Asia	7,479.16 (5,630.22–9,687.24)	3.33 (2.41–4.27)	29,215.99 (22,995.29–36,408.38)	4.1 (3.18–5.15)	2.91% (1.92–4.04)	0.59 (0.47–0.71)
Southeast Asia	3,464.3 (3,046.27–3,994.08)	3.19 (2.72–3.64)	11,360.88 (9,546.76–13,785.34)	3.99 (3.27–4.75)	2.28% (1.7–2.91)	0.76 (0.7–0.81)
Southern Latin America	1,383.83 (1,183.52–1,701.62)	4.92 (4.13–5.93)	3,074.48 (2,606.14–4,013.77)	5.32 (4.44–6.94)	1.22% (0.99–1.46)	0.29 (0.2–0.38)
Southern Sub-Saharan Africa	409.26 (344.19–464.65)	3.1 (2.59–3.5)	1,045.72 (916.49–1,151.35)	3.94 (3.38–4.37)	1.56% (1.23–1.91)	0.79 (0.59–0.99)
Tropical Latin America	2,187.75 (1,873.43–2,735.8)	4.78 (3.99–5.95)	7,598.03 (6,107.51–8,898.99)	5.03 (4.01–5.94)	2.47% (1.93–2.73)	0.5 (0.32–0.69)
Western Europe	25,871.16 (22,624.18–34,903.21)	5.77 (4.91–7.83)	43,760.97 (35,707.5–52,790.04)	5.76 (4.59–6.99)	0.69% (0.38–0.86)	0.06 (0.02–0.09)
Western Sub-Saharan Africa	1,704.67 (1,332.45–2,229.05)	4.5 (3.55–5.93)	3,778.27 (3,177.8–4,408.07)	4.75 (3.89–5.59)	1.22% (0.57–1.76)	0.08 (0.04–0.12)
Characteristics	1990		2019		1990–2019	1990–2019
	DALYs cases No. (95% UI)	ASDR per 100,000 No. (95% UI)	DALYs cases No. (95% UI)	ASDR per 100,000 No. (95% UI)	Percentage change No. (95% CI)	EAPC No. (95% CI)
Overall	3,044,717.13 (2,363,647.01–3,900,467.06)	110 (87.66–139.16)	6,579,977.8 (5,241,696.12–8,321,653.38)	107.13 (86.18–133.73)	1.16% (1.06–1.25)	−0.03 (−0.06–0)
Sociodemographic index						
Low SDI	114,659.53 (85,965.49–146,544.67)	84.28 (63.03–105.84)	287,302.79 (224,193.31–354,685.81)	91.91 (71.89–111.57)	1.51% (1.27–1.81)	0.3 (0.27–0.33)
Low-middle SDI	326,477.32 (249,420.63–425,285.99)	91.5 (71.71–114.77)	927,307.72 (727,621.88–1,164,150)	101.01 (81.22–123.92)	1.84% (1.58–2.13)	0.34 (0.32–0.37)
Middle SDI	577,551.29 (444,346.58–745,572.44)	93.38 (74.4–116.56)	1,648,790.75 (1,285,587.8–2,095,429.98)	97.9 (78.07–122.72)	1.85% (1.67–2.05)	0.17 (0.14–0.2)
High-middle SDI	903,441.18 (702,229.35–1,176,141.28)	116.99 (92.57–149.81)	1,752,067.46 (1,361,490.97–2,252,102.91)	110.21 (86.73–140.14)	0.94% (0.84–1.02)	−0.25 (−0.28 to −0.23)
High SDI	1,121,109.75 (882,347.51–1,445,544.14)	128.62 (101.73–165.21)	1,961,481.71 (1,561,092.24–2,473,050.53)	122.64 (97.3–153.57)	0.75% (0.64–0.83)	0.03 (−0.05–0.11)

(Continued)

TABLE 1 (Continued)

Characteristics	1990		2019		1990–2019	1990–2019
	DALYs cases No. (95% UI)	ASDR per 100,000 No. (95% UI)	DALYs cases No. (95% UI)	ASDR per 100,000 No. (95% UI)	Percentage change No. (95% CI)	EAPC No. (95% CI)
Regions						
Andean-Latin America	8,588.77 (7,326.22–10,022.07)	64.49 (55.4–74.42)	25,568.67 (21,197.9–30,491.13)	63.61 (52.67–75.22)	1.98% (1.5–2.57)	0.11 (0.04–0.18)
Australasia	35,222.44 (27,725.1–45,237.53)	183.72 (145.83–231.54)	70,166.25 (55,042.18–90,300.77)	168.28 (132.54–214.32)	0.99% (0.89–1.11)	−0.36 (−0.39 to −0.34)
Caribbean	14,971.71 (12,424.5–18,055.44)	79.4 (66.52–94.7)	31,795.63 (26,276.01–38,251.98)	83.27 (69.65–99.83)	1.12% (0.93–1.34)	0.19 (0.13–0.25)
Central Asia	35,540.25 (26,530.96–47,120.72)	109.82 (82.86–143.91)	61,772.11 (47,916.22–79,286.07)	138.35 (109.64–176.31)	0.74% (0.57–0.89)	0.82 (0.76–0.88)
Central Europe	155,815.55 (120,452.79–203,689.02)	134.74 (105.22–173.65)	251,596.5 (195,996.37–324,725.31)	136.04 (106.47–173.32)	0.61% (0.51–0.72)	0.07 (0.01–0.12)
Central Latin America	43,319.71 (36,219.34–53,516.31)	80.65 (68.44–98.18)	138,688.09 (113,679.15–171,245.23)	82.84 (68.32–101.95)	2.2% (1.93–2.47)	−0.01 (−0.05–0.04)
Central Sub-Saharan Africa	122,66.03 (8,247.28–18,438.06)	99.09 (65.94–148.49)	30,142.71 (21,400.77–39,321.26)	104.25 (72.95–138.1)	1.46% (0.98–1.99)	0.14 (0.07–0.2)
East Asia	519,048.51 (394,223.27–675,814.17)	98.28 (76.84–124.34)	1,432,517.88 (1,088,053.16–1,867,068.05)	96.78 (75.08–122.56)	1.76% (1.5–2.01)	−0.05 (−0.13–0.03)
Eastern Europe	258,196.1 (196,297.15–341,308.43)	120.85 (92.65–157.62)	384,777.08 (292,577.71–503,883.63)	136.59 (104.82–177.07)	0.49% (0.41–0.57)	0.36 (0.28–0.43)
Eastern Sub-Saharan Africa	31,126.86 (21,024.73–39,298.52)	73.06 (48.45–92.35)	71,336.96 (50,303.75–87,335.35)	77.09 (53.33–94.33)	1.29% (0.93–1.76)	0.18 (0.1–0.27)
High-income Asia Pacific	94,477.13 (77,636.52–118,368.25)	66.35 (54.42–82.7)	195,233.79 (157,805.14–243,046.5)	53.53 (43.1–66.58)	1.07% (0.92–1.23)	−1.06 (−1.22 to −0.91)
High-income North America	424,379.23 (327,241.59–558,162.82)	140.63 (108.35–183.61)	832,025.39 (649,706.07–1,063,351.64)	160.18 (125.7–202.67)	0.96% (0.83–1.09)	0.89 (0.71–1.07)
North Africa and the Middle East	81,921.61 (64,667.39–104,296.2)	79.91 (63.99–99.66)	217,791.49 (171,790.55–275,028.53)	81.61 (65.1–100.78)	1.66% (1.43–2.05)	0.01 (−0.01–0.04)
Oceania	1,714.91 (1,278.28–2,249.71)	109.88 (83.38–140.9)	4,265.72 (3,269.65–5,477.39)	116.58 (91.06–148.01)	1.49% (1.26–1.74)	0.23 (0.22–0.25)
South Asia	313,839.17 (233,856.25–415,086.12)	96.83 (73.96–124.55)	1,004,000.6 (767,638.51–1,284,863.5)	106.05 (82.89–132.86)	2.2% (1.83–2.62)	0.26 (0.22–0.31)
Southeast Asia	146,339.5 (109,111.94–193,284.06)	95.11 (73.3–122.94)	407,099.72 (309,292.37–534,122.36)	105.7 (82.22–133.52)	1.78% (1.59–2.01)	0.37 (0.34–0.4)
Southern Latin America	33,270.72 (27,276.91–41,107.45)	96.08 (79.7–117.41)	67,885.01 (55,648.18–84,703.48)	100.95 (83.35–125.77)	1.04% (0.92–1.17)	0.18 (0.13–0.22)
Southern Sub-Saharan Africa	12,289.22 (9,702.16–15,684.97)	71.59 (58.23–88.42)	27,739.42 (22,471.51–34,542.25)	79.24 (65.78–95.69)	1.26% (1.1–1.41)	0.36 (0.24–0.48)
Tropical Latin America	57,018.18 (46,603.14–71,324.15)	98.38 (81.69–120.63)	179,609.76 (147,086.35–221,530.81)	102.34 (84.28–124.34)	2.15% (1.86–2.3)	0.52 (0.4–0.64)
Western Europe	721,985.38 (571,968.84–930,654.64)	144.62 (114.54–185.07)	1,054,466.71 (845,195.76–1,323,431.16)	132.81 (105.93–168.11)	0.46% (0.32–0.56)	−0.19 (−0.22 to −0.16)
Western Sub-Saharan Africa	43,386.15 (33,451.62–54,984.95)	82.99 (65.49–103.45)	91,498.32 (73,641.02–111785.32)	86.19 (70–103.25)	1.11% (0.73–1.39)	0.08 (0.05–0.1)

ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; ASDR, age-standardized DALYs rate; EAPC, estimated annual percentage change; CI, confidence interval; UI, uncertainty interval.

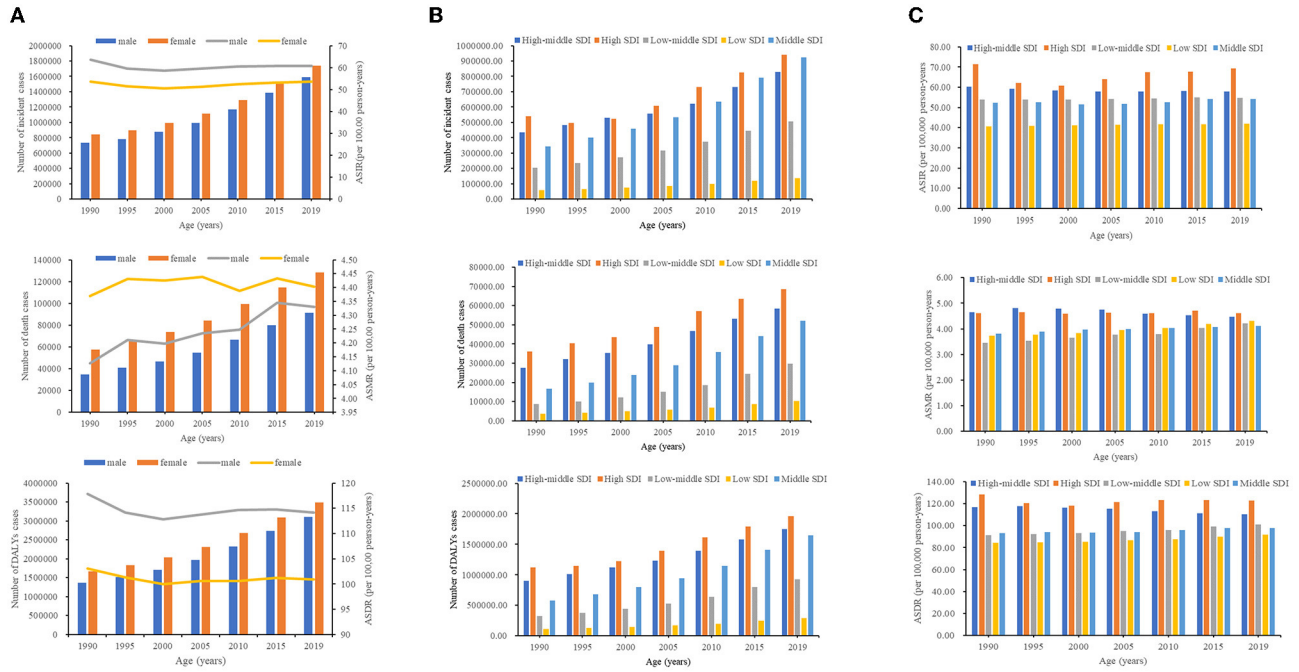

FIGURE 1
The number of cases and ASRs of AF from 1990 to 2019. **(A)** The number of cases of AF caused by global, from 1990 to 2019. **(B)** The number of cases of AF caused by SDI regions from 1990 to 2019. **(C)** The ASRs of AF caused by SDI regions from 1990 to 2019. SDI, sociodemographic index.

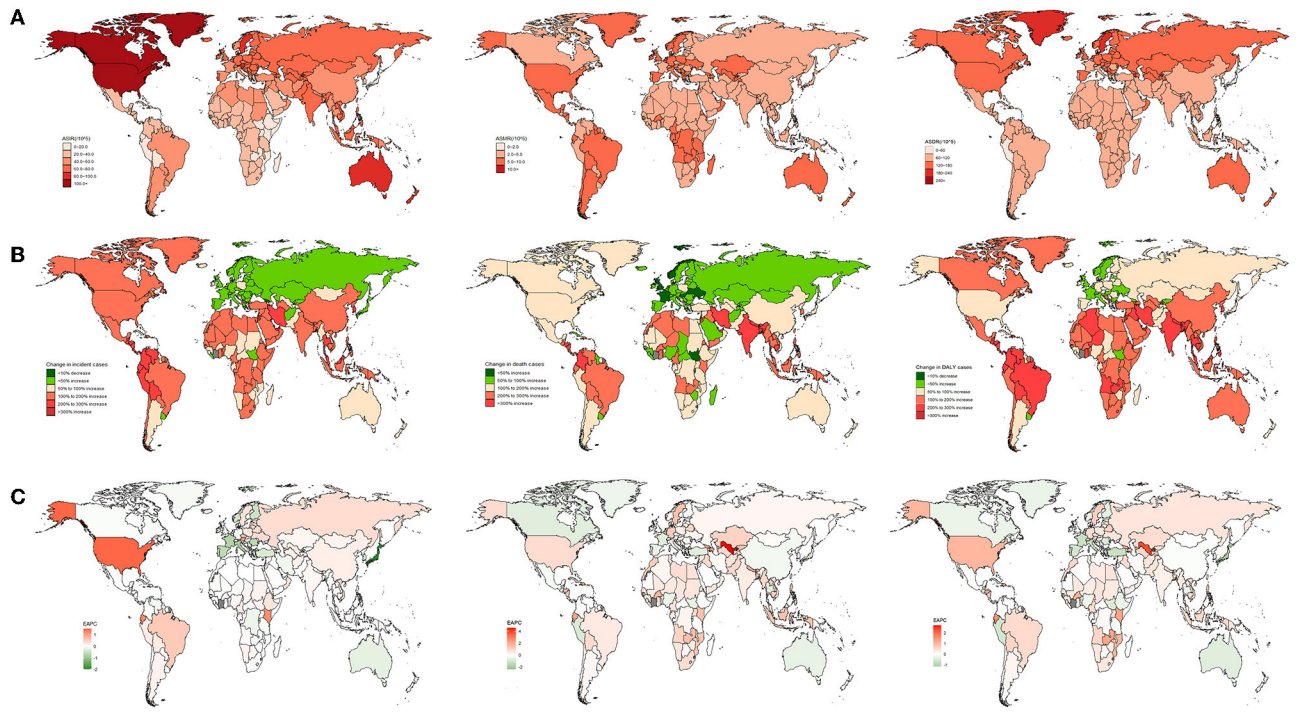

FIGURE 2
The national burden of AF for both sexes in 204 countries and territories. **(A)** The relative ASRs of AF between 1990 and 2019. **(B)** The relative changes of AF between 1990 and 2019. **(C)** The relative EAPCs of AF between 1990 and 2019.

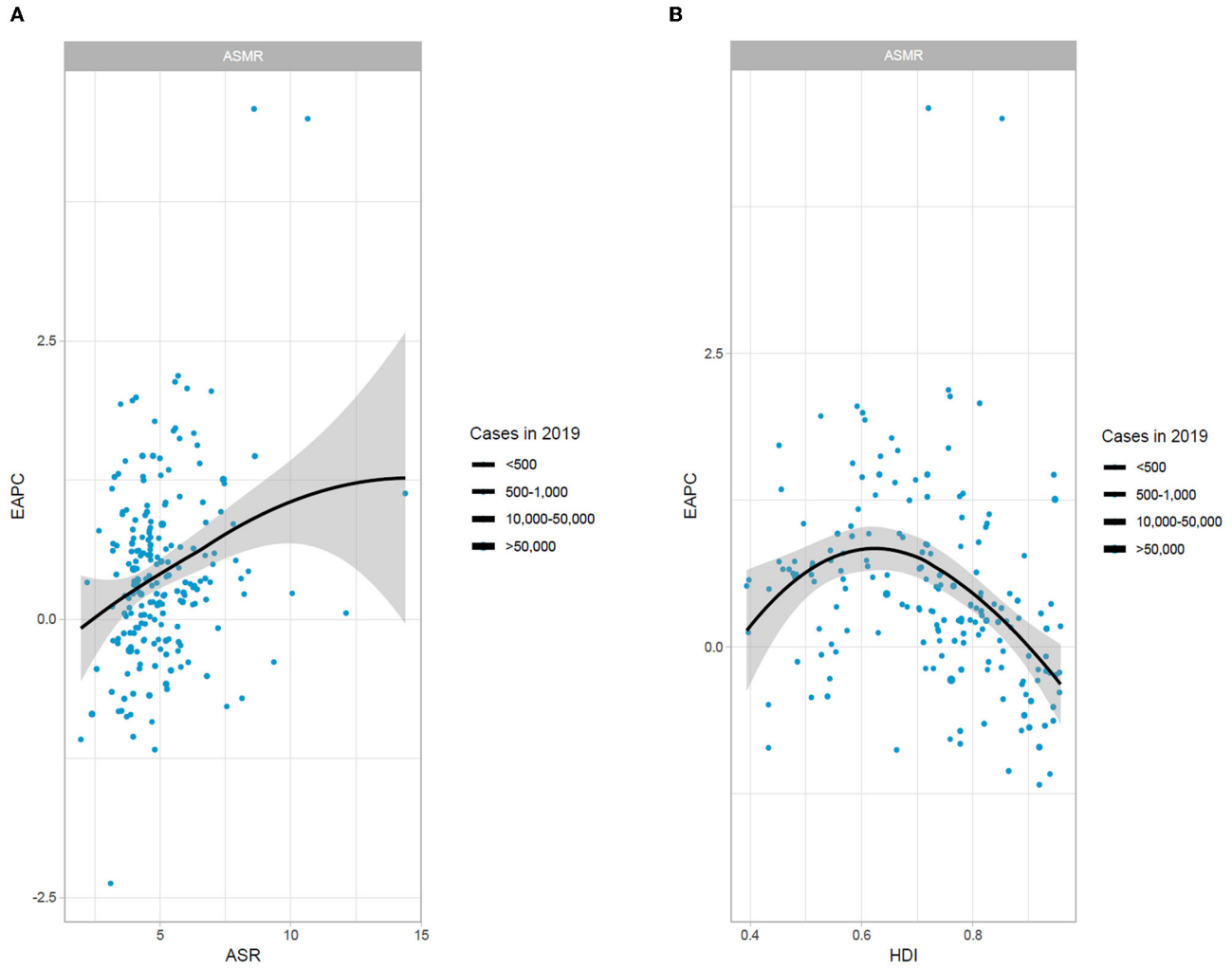

FIGURE 3
The association between EAPC and ASMR in 2019 and HDI in 2019. **(A)** The association between EAPC and ASMR in 2019. **(B)** The association between EAPC and HDI in 2019. EAPC, estimated annual percentage change; ASMR, age-standardized mortality rate; HDI, human development index.

(Table 1, Figure 1B). Interestingly, the higher the SDI region, the higher the morbidity and mortality. From 1990 to 2019, the number of incidences and DALY cases of AF rose most dramatically in the middle SDI. However, the number of deaths increased most substantially in low-middle SDI (Table 1, Figure 1B). Only high-middle SDI recorded a decreasing AF ASR, including ASIR (−0.12; 95% CI: −0.15 to −0.09), ASMR (−0.25; −0.32 to −0.18), and ASDR (−0.25; −0.28 to −0.23) of the EAPC (Table 1, Figure 1C, Supplementary Figure 1). Regarding the rest of the 21 GBD regions, the highest ASIR due to AF has occurred in high-income North America [108.53 (87.59–131.44)] since 2019 (Table 1, Supplementary Figure 2A). Similarly, the ASMR and ASDR of AF for men and women in Australasia were 6.86 (5.45–8.33) and 168.28 (132.54–214.32), respectively, which placed Australia in the top rank for AF related-mortality in 2019 (Table 1, Supplementary Figures 2B, C). It is also worth noting that the most prominent increases in the ASIR and ASDR were in high-income North America. Additionally, the most significant increases in the ASMR were exhibited in Central Asia, followed by southern sub-Saharan Africa, Southeast Asia, and high-income North America. During the research period, the most pronounced decrease in the ASIR, ASMR, and ASDR was reported, all in high-income Asia Pacific (Table 1, Supplementary Figure 3).

National burden of AF

In 2019, China presented the highest morbidity [818,493 (562,871–1,128,695)], mortality [39,970 (33,722–46,387)], and DALYs [1,383,674 (1,047,540–1,802,516)]. Coincidentally, all three accounted for approximately a quarter of the global caseload (Supplementary Tables 1–3). The United States of America exhibited the highest ASIR [109.52 (88.97–131.92)]; Montenegro showed the highest ASMR [14.38 (11.31–19.38)] and ASDR [250.62 (205.82–313.72)]. Conversely, Bolivia (Plurinational State of) had the lowest ASIR [14.41 (10.71–18.68)]; Singapore had the lowest ASMR [1.97 (1.44–2.37)] and ASDR [51.94 (40.06–67.04)] owing to AF (Supplementary Tables 1–3, Figure 2A). As for the percentage change, the most remarkable rise was in Qatar from 1990 to 2019, with a 7.91% increase in AF incidences; the most conspicuous

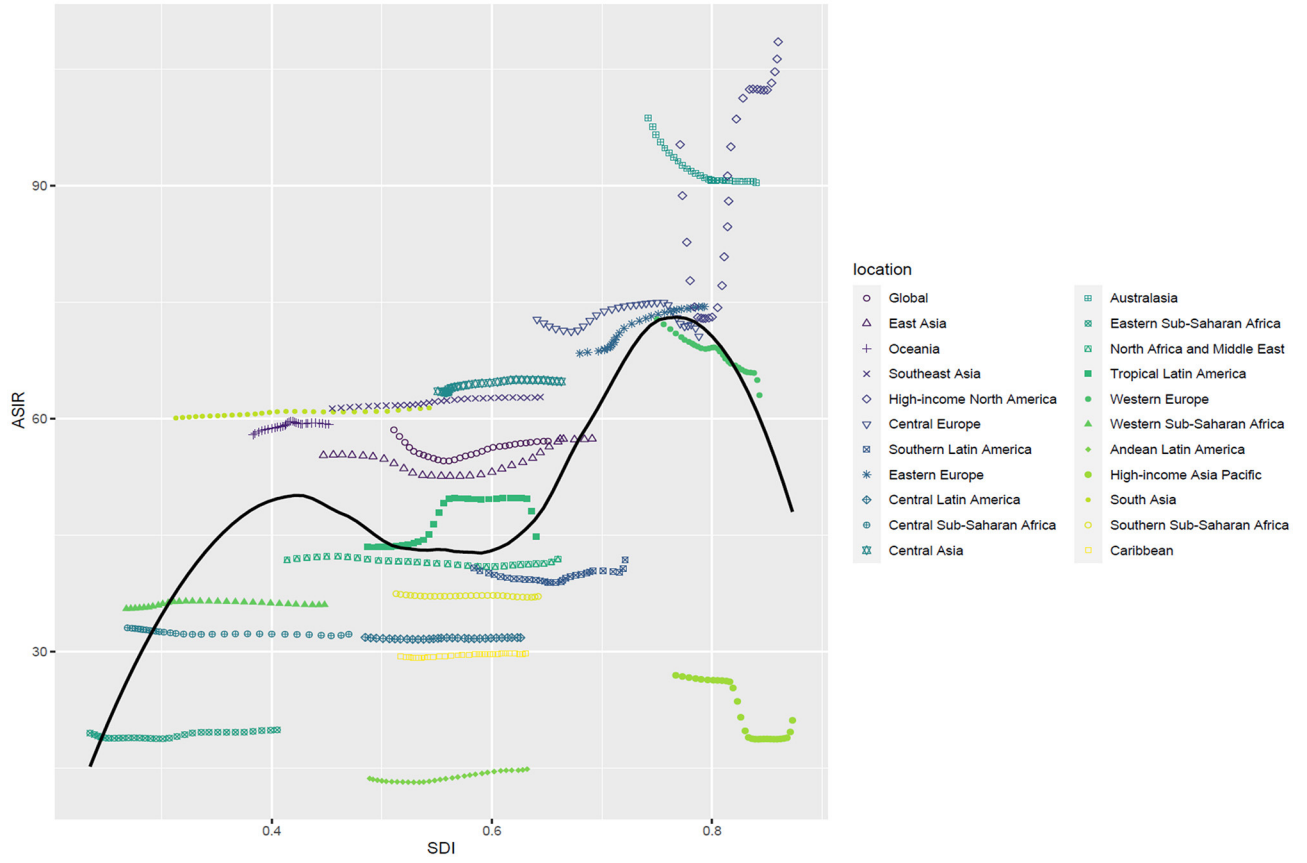

FIGURE 4
ASIR of AF in the global and 21 regions by SDI, 1990–2019. ASIR, age-standardized incidence rate; SDI, sociodemographic index.

rise was in Bahrain during the 30 years, with an 8.82% increase in deaths and a 6.51% increase in DALYs (Supplementary Tables 1–3, Figure 2B). Furthermore, the most apparent increase in ASIR was in the United States of America [1.51 (1.07–1.95)] from 1990 to 2019; the most significant rise in ASMR was in Uzbekistan [4.58 (4.23–4.94)]; the most demonstrable increases in the ASDR were in Bahrain [2.71(2.27–3.14)] and Uzbekistan [2.32 (2.17–2.47)] (Supplementary Tables 1–3, Figure 2C). By comparison, Japan displayed significant decreases in the ASIR and ASDR; Guam exhibited the most pronounced decline in the ASMR (Supplementary Tables 1–3, Figure 2C).

The influential factors for EAPC

Figure 3 shows that ASR (in 2019) and HDI (in 2019) seem to be particularly associated with EAPC. The ASMR of AF implies a healthy life expectancy from disease onset to eventual death. Meanwhile, HDI can be considered a metric to measure the accessibility and level of medical treatment. A significant positive relationship was observed between EAPCs and ASMR. Remarkably, a significant positive association was observed between EAPC and HDI when the HDI was restricted to <0.6. However, when the HDI was above 0.6, the countries with a higher HDI experienced a sharper decrease in EAPC of atrial fibrillation from 1990 to 2019 (Figure 3).

Relationship of ASRs with SDI

A non-linear association was investigated between SDI and ASIR in global and 21 regions. The highest ASIR was found in high-income North America, with an SDI of 0.86. The ASIR was lowest in the Andean-Latin America area when the SDI was 0.53. At the region level, the ASIR values of 10 areas based on SDI in 2019 were higher than the global level, consisting of high-income North America, Australasia, Central Europe, Eastern Europe, Western Europe, Central Asia, Southeast Asia, South Asia, Oceania, and East Asia (Figure 4). The biggest ASMR and ASDR both appeared in Australasia, with SDI values of 0.77 and 0.74, respectively.

At the national level, we explored the relationship between ASIR and SDI values, which were complex and non-linear in 2019. Further analysis revealed that the ASIR in 204 countries and territories was positively correlated with the SDI. The largest ASIR was in the United States of America, followed by Canada and Greenland, according to the SDI. The ASIR was larger than the anticipated level in a number of territories. Nevertheless, Bolivia (the Plurinational State of), Peru, Ecuador, Eritrea, Somalia, and numerous other countries held a smaller ASIR than the expected

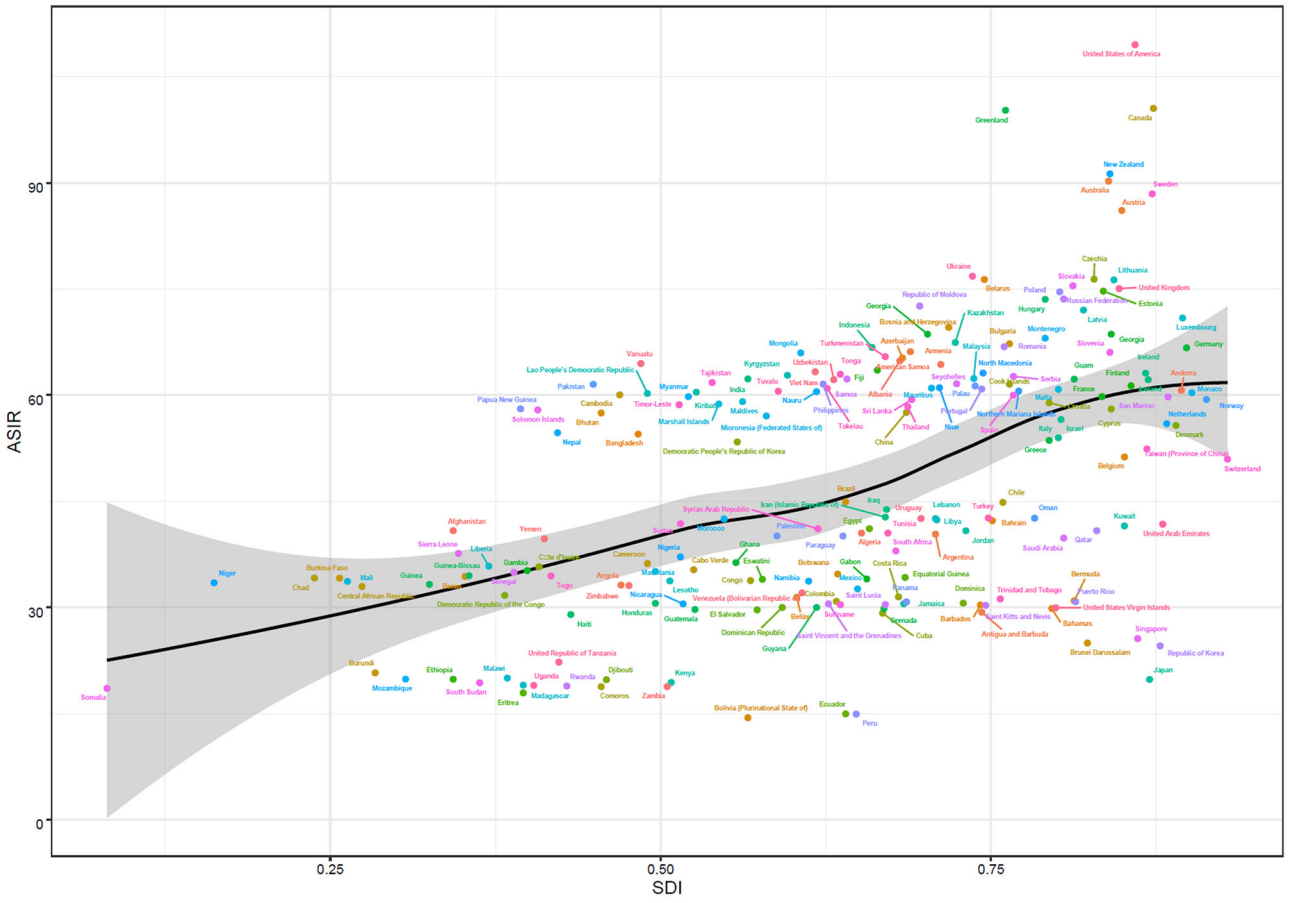

FIGURE 5
ASIR of AF in 204 countries by SDI, 1990–2019. ASIR, age-standardized incidence rate; SDI, sociodemographic index.

SDI (Figure 5). Non-linear relationships among the SDI, ASMR, and ASDR of atrial fibrillation were also surveyed. The highest ASMR and ASDR were both noted in Montenegro when the SDI value was 0.79. However, the lowest ASMR and ASDR occurred in Singapore, with an SDI value of 0.86. And the majority of countries had lower ASMR and ASDR levels than expected, such as Japan, Kuwait, and the Republic of Korea. Intriguingly, burden estimates experienced an upward trend with increasing SDI, yet ASDR had a higher rise than ASMR (Supplementary Figures 4A, B).

Risk factors for AF

Globally, 219,437 (190,526–249,642) individuals have died from AF. The mortality of AF in 2019 may be attributed to the referring risk factors evaluated by GBD: alcohol use, behavioral risks, a diet high in sodium, a high body mass index (BMI), high systolic blood pressure (SBP), lead exposure, metabolic risks, and smoking. Among them, the two main risk factors were a high BMI and a high SBP. The above risk factors displayed different percentages depending on the sexes at the regional level. For instance, the highest percentage of deaths due to smoking was detected in Central Europe, 52% for males. Simultaneously, the lowest percentage of deaths due to smoking was in High-income Asia Pacific, with 36% for females. In Central Europe, men (37%) and women (14%) had the highest mortality rates due to behavioral risks. Regarding high systolic blood pressure (SBP), the highest proportion of deaths occurred in southern sub-Saharan Africa (men, 41%; women, 43%) (Figure 6).

Discussion

This is the first study to estimate the global burden and trends of AF in older adults aged 60–89 years and to recognize the associated risk factors. The results indicated that the burden of AF is gradually increasing globally, with an ∼1.1-fold increase in incidences and an ∼1.4-fold increase in deaths from 1990 to 2019. It may be attributable to improved survival with chronic diseases and the global population rising and aging (4, 13, 14). Moreover, the ASIR was higher in high-income North America, Australasia, Eastern Europe, and Central Europe; it was lower in Andean-Latin America, Eastern Sub-Saharan Africa, and high-income Asia Pacific, which was in accordance with the prevalence of AF (13). However, it was worth noting that the rate of increase in the prevalence of AF was extraordinarily rapid in high-income North America and surrounding areas.

FIGURE 6
The age-standardized deaths are attributable to the risk factors.

This observation may be due to the rapidly evolving regional economy, the Westernization tendency of personal diet, and the higher morbidity of cardiovascular problems and metabolic disorders (15).

Our findings also revealed that the degree of disease burden in AF differed between men and women. In general, the number of incident cases was higher in women, but the result of the age-standardized incidence rate was completely opposite, which

was consistent with the perspectives of IHME (16). It may be related to our selection of older adults aged 60–89 years as our research subjects. An original research article demonstrated that the incidence rate of AF in women has increased significantly since the age of 60 (10). Longevity in women may be another reason for the increased morbidity of AF (10).

Furthermore, several studies have been conducted to show that estrogen plays a protective role against AF by prolonging the effective refractory period and reducing atrial pressure, which could profoundly interpret the increase in susceptibility to AF in post-menopausal women (17, 18). Andrade et al. also observed a higher prevalence of age-adjusted AF in men than in women (19), which may be partially explained by the lower lifetime risk of AF in women (20, 21). As for mortality, female patients with AF had a higher mortality rate, which may be due to the risk of thromboembolism (22). Previous studies have found female gender to be a major independent risk factor for thromboembolism in patients with AF (23, 24).

At the global level, the values of ASIR and ASDR were far higher than ASMR. Patients with AF were at higher risk for concurrent stroke, heart failure, hypertension, and other cardiovascular diseases than those without arrhythmias (25). In clinical practice, complications and co-morbidities have been documented as the leading cause of death in patients with AF (26). As a result, the actual number of deaths caused by AF may be hard to count, and the estimated disease burden of AF-related deaths is lower than the actual number of deaths. Our analysis also revealed characteristics in incidence, mortality rates, and DALYs in distinct SDI territories. In 2019, both morbidity and mortality were highest in high SDI regions, while the lowest morbidity and mortality occurred in low SDI and middle SDI regions, respectively. However, the most dramatic growth can be discerned in the low and low-middle SDI regions. From 1990 to 2019, ASIR, ASMR, and ASDR showed a decreasing trend in both high SDI and high-moderate SDI quintiles. In addition, the results reflected that the ASIR, ASMR, and ASDR were positively correlated with SDI, which signified that the higher the SDI region, the higher the burden of disease in older adults. These findings were roughly consistent with the research of other scholars (22, 27). Groups with higher access to health care, educational qualifications, and greater health awareness would focus more on their health (28–30). Therefore, AF was more likely to be discovered and reported in areas with a higher SDI. The effective and proven tactics used to manage the burden associated with AF in high SDI regions, such as the United States of America, may serve as a valuable source of policy inspiration for other regions with relatively low SDI quintiles.

Furthermore, we explored the association between ASMR, EAPC, and HDI. HDI is a meaningful indicator to evaluate the level of national social and economic development (31). There was an inverted U-shaped relationship diagram: mid-HDI regions had a higher EAPC of deaths than high-HDI regions. It implied that the ASMR of AF in high HDI areas experienced a decrease while low HDI areas experienced an increase. This may be attributed to the more powerful medical and health services, higher resource allocation, and residents' more aggressive attitude to prevent and treat AF and its complications (32). It was clear from the current study that the disease burden of AF is an urgent concern and an issue that needs to be addressed in less economically developed regions at present and in the future. Hence, it was imperative to establish health- and economic-based AF prevention initiatives for relevant national departments and regional health authorities.

Eventually, we explored the influencing risk factors of AF in older adults based on the GBD database, involving alcohol use, smoking, a diet high in sodium, a high BMI, a high SBP, lead exposure, and metabolic risks. The relationship between AF and the first six risk factors has already been identified (8, 33). Our analysis confirmed that high SBP and high BMI were principal considerations in the burden of AF. Credible evidence has demonstrated that high blood pressure (HBP) is an independent risk element for AF (34–36). A systematic review showed a 50% higher relative risk of AF in patients with HBP compared to those without HBP (37). Each 20 mm Hg increase in systolic blood pressure was associated with a 19% corresponding increase in the risk of atrial fibrillation (38). A few clinical mechanisms might account for the elevated risk of AF in people with HBP. Higher blood pressure leads to an increased risk of coronary artery disease and myocardial infarction (39), which can induce AF (4, 40, 41). Predictable epidemiological findings have demonstrated that increased blood pressure triggers inflammation in myocardial cells, contributing to fibrillation and an enlarged left ventricle (42, 43), which in turn raises the risk of suffering from AF (4, 44).

Furthermore, chronic hypertensive patients may experience impaired left ventricular hypertrophy and left ventricular contraction-diastolic function, which increase atrial pressure and eventually worsen atrial contraction (45). Experts believe controlling blood pressure within the normal range is conducive to reducing the occurrence of AF (46, 47). It is essential to adopt a low-salt diet and engage in home self-monitoring of blood pressure in daily life to prevent the occurrence of hypertension. High SBP and AF often co-exist, and the effect of obesity on AF should not be ignored. A former report highlighted that obesity elevated the risk of AF occurring by ∼50% (48). Moreover, every 1 kg/m^2 higher BMI was correlated with a 6% increase in risk (49), which was perceived as an independent predictor of incident AF (48, 50). Obesity exerted a proximate effect on cardiac muscle structure through enhanced exposure to oxidative strain (51). AF may be caused by electroanatomic remodeling in patients with a high BMI (52). Additionally, the role of BMI in generating the incidence of AF changed as age advanced. After the age of 60, alterations in physical components, such as increased fat mass and redistribution, may explain the increased influence of a high BMI on the risk of AF with age (53). As for the prognosis for patients with AF, a high BMI would increase the recurrence rate of AF (54) and the risk of paroxysmal atrial fibrillation developing into permanent atrial fibrillation (55). Therefore, weight control and physical exercise play a positive role in improving the prognosis and preventing the worsening of AF. In the future, both doctors and heart specialists are expected to incorporate recommendations on diet and lifestyle improvements, especially for obese older adults, into regular medical care. Moreover, metabolic syndrome may increase susceptibility to AF by activating significant oxidative stress signaling pathways and an inflammatory response (56). Metabolic syndrome is a kind of cardiovascular and metabolic disease that includes elevated blood pressure, overweight, hyperlipidemia, and

insulin resistance (57). In the section above, we described the effects of high SBP and high BMI on AF, which contributed most to the increased risk of AF among the components of the metabolic syndrome (58). Considering the important impact of the metabolic syndrome on AF, a low-fat, low-sugar diet and regular monitoring of blood glucose and lipids are essential for formulating targeted AF prevention strategies in older adults. Additionally, we can create prevention and monitoring precautions according to the risk factors in different regions and by gender. For example, South Asia has higher mortality rates due to lead exposure than other regions, so avoiding lead exposure and reducing environmental lead concentrations could be used for AF prevention in South Asia. It was worth mentioning that the attribution proportions for smoking and alcohol consumption were significantly higher for men than for women. For men, quitting smoking and limiting alcohol to prevent the occurrence of AF should be valued.

Based on the findings above, we can conclude that our research is valuable in developing a worldwide strategy for effectively for screening AF in certain groups. More precisely, screening programs targeting risk factors are more effective. First, we should pay special attention to the older female population. Regular electrocardiogram examinations are necessary for them. Second, high SBP and high BMI have the greatest impact on AF. Thus, blood pressure and weight measurements must be included in the screening programs. Finally, we can establish screening plans for other risk factors. Smoking, alcohol consumption, a high-salt diet, and chronic lead exposure are key populations for AF screening, especially in males. In other words, high-risk individuals with AF need to undergo regular medical check-ups in specialized medical institutions with the goal of early screening, timely treatment planning, and delaying the progression of AF.

The current study has several limitations. First, our analysis was impacted by deficiencies in the 2019 GBD study methodology, which have been documented in previous literature (59–61). Insufficient and untimely registration of AF in some underdeveloped regions resulted in the underestimation of patients as well as misdiagnosis or under diagnosis owing to the lack of adequate medical resources. Overall, the data from some countries were not integral, which affected the precision and reliability of the results. Second, the GBD research did not meticulously classify AF into first-diagnosed AF, paroxysmal AF, persistent AF, and so on, based on clinical characteristics. Third, other pathological factors, such as rheumatic heart disease, hyperthyroidism, and pre-excitation syndrome, were not considered. Finally, the outbreak and prevalence of COVID-19 have had a serious impact on the burden of AF (62), and more evidence is urgently needed to compare changes in AF during the epidemic.

Conclusion

In conclusion, AF in older adults is a major public health concern worldwide. The burden of AF varies widely at both national and regional levels. From 1990 to 2019, the cases of AF incidences, deaths, and DALYs have shown a global increase. The ASIR, ASMR, and ASDR have declined in the high-moderate and high SDI regions. However, the burden of AF increased promptly in the lower SDI regions. Moreover, it is necessary to consider the predominant risk factors for AF, such as high BMI and SBP, to encourage individuals with a high risk of AF to perform health management and early screening. By interpreting the burden of AF at different regional and national levels, our research illustrates the features of the global AF burden in pursuit of more effective and targeted prevention and treatment strategies.

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

MJ, CL, and QG conducted a statistical analysis of the data. MJ drafted the manuscript. AM and QG conceptualized and designed the research and revised the manuscript. YL and YW collected and sorted the data. 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.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1137230/full#supplementary-material

SUPPLEMENTARY FIGURE 1
The EAPCs of AF ASRs from 1990 to 2019, both sexes by SDI. SDI, sociodemographic index.

SUPPLEMENTARY FIGURE 2
The regional burden of AF for both sexes in 2019. **(A)** ASIR in regions, 1990–2019; **(B)** ASMR in regions, 1990–2019; **(C)** ASDR in regions, 1990–2019. ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate; ASDR, age-standardized DALYs rate.

SUPPLEMENTARY FIGURE 3
The EAPCs of AF at the regional level, from 1990 to 2019.

SUPPLEMENTARY FIGURE 4
ASRs of AF in 204 countries by SDI, 1990–2019. **(A)** ASMR in 204 countries and territories, 2019; **(B)** ASDR in 204 countries and territories, 2019. ASMR,

age-standardized mortality rate; ASDR, age-standardized DALYs rate; SDI, sociodemographic index.

SUPPLEMENTARY TABLE 1
The incidence of atrial fibrillation between 1990 and 2019 at national level.

SUPPLEMENTARY TABLE 2
The deaths of atrial fibrillation between 1990 and 2019 at national level.

SUPPLEMENTARY TABLE 3
The disability-adjusted life years (DALYs) of atrial fibrillation between 1990 and 2019 at national level.

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How heavy is the medical expense burden among the older adults and what are the contributing factors? A literature review and problem-based analysis

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In recent years, the aging population and increasing medical expenses among the older adults have emerged as significant public health concerns. National governments must conduct medical expense accounting and implement measures to reduce the burden of medical costs on the older population. However, limited studies have focused on total medical expenditure from a macro perspective, with many researches exploring individual medical expenses from different perspectives. This review introduces the trend of population aging and its impact on health cost change, reviews research on the medical expense burden of the older population and contributing factors, and points out underlying problems and limitations of current studies. Based on the present studies, the review emphasizes the necessity of medical expense accounting and analyzes the medical expense burden of the older population. Future studies should explore the impacts of medical insurance funds and health service system reforms on reducing medical expenses and developing a supporting medical insurance reform plan.

KEYWORDS

aging, medical expense, economic burden, health cost change, SHA 2011

Introduction

In recent years, the increasing aging population and the substantial medical expenses that burden the older adults have emerged as pressing issues in public health (1). To address these challenges, researchers worldwide have conducted numerous studies exploring the impact of population aging on changes in healthcare costs and accounting for medical expenses among the older adults. Although existing literature has focused on analyzing the contributing factors to medical costs, the disease composition, payment ability, and economic burden of the older adults, research on the complex nature and longitudinal studies of medical costs in the older adults remains limited. In this review, we present a comprehensive, multidimensional, and multifactorial analysis of population aging and its impact on healthcare costs, the medical

expense burden of the older adults, and the contributing factors to this burden. Our aim is to provide a theoretical basis for preventing age-related diseases and reducing the significant medical expense burden on the older population. This introduction conforms to the grammatical requirements and general scientific journal standards.

The trend of aging population and the impact on health cost change

The trend of aging population

Population aging is a global issue that has significant impacts on various aspects of human society (2). When the proportion of individuals older adults 60 years and above in a country or region reaches 10%, or the total population older adults 65 or above reaches 7%, it indicates that the country or region is entering an aging society.

Population aging initially surfaced in developed countries, such as the United States, Australia, and most Western European nations in the mid-20th century. Since then, the pace of aging worldwide has been increasing, with 71 countries entering aging societies by 2010. Developing countries have been slower in aging, but the number of older adults is rapidly increasing (3, 4). In China, for instance, the proportion of older adults over 65 years has grown from 7% in 2002 to above 11.4% in 2017 (5), with projections indicating it could reach 30% by 2050 (6). In Africa, the youth population is growing at an unprecedented pace, but early childhood survival and lower mortality rates in adulthood are expected to increase the older population significantly in the next 20 years, almost doubling to 58 million on the continent (7).

Impact of aging population on health cost change

The relationship between population aging and healthcare expenditure has been a topic of scholarly interest for decades. Scholars have explored two key issues in this field, including whether the aging population is the primary determinant of healthcare expenditure growth and the size of the effect of pure aging.

In the United States, scholars have found that healthcare cost changes are the result of multiple factors, with aging being a contributing factor but not the primary determinant of healthcare expenditure growth (8). While the age structure of the population is related to total healthcare expenditure, factors such as national income and *per capita* income play decisive roles in the demand for medical services (9–12). Some studies have found that population aging is associated with an increase in healthcare spending, with approximately 20% of healthcare spending growth predicted to be attributed to aging by 2025 (13, 14). However, increases in service price and intensity were found to have a much larger impact on healthcare spending (15).

In European countries, scholars have conducted in-depth studies to examine the association between aging and healthcare cost change (16). Primarily, they have found that the aging population is a significant determinant of healthcare expenditure growth. Studies in Spain and Italy have found that the older adults has a substantial weight on total healthcare expenditure, with factors such as real *per capita* income, acute care beds per 1,000 population, general practitioners, and policies listed among the determinants (17–19). Moreover, research in China has shown that a higher level of aging population results in more healthcare expenditure (20).

Despite the differing findings among studies, it is foreseeable that the growing proportion of older adults people will lead to mounting healthcare spending, even in low-income countries such as Pakistan. However, some studies have found that the long-run effect of aging on healthcare cost change is approximately zero in certain European countries (21). This result can be explained by competing models that balance out the offsetting influences described in "longevity and health scenarios." In a "healthy aging" scenario, if people live longer and are in good health, a longer life will postpone the high costs at the end of life.

The impact of the aging population on health expenditures differs across regions and health financing systems. A WHO investigation, utilizing panel data from 143 countries between 1995 and 2008, discovered that the percentage of the population over 60 years old was positively linked to government health expenditure in lower-middle income countries in the static model, but in the dynamic model, the population had no significant relationship in any income group (22). The percentage of the population over 60 was positively associated with OOP only for upper-middle-income countries (23). It was concluded that, aside from income, numerous factors contribute to this variation, ranging from demographic factors to the health system.

Studies examining the relationship between aging and health cost change generally use regression models or residual models, which can produce inconsistent results, as seen in the WHO study mentioned above. In regression models, health costs are the dependent variable, and aging is the independent variable. Thus, the coefficient of each variable can indicate its impact on health costs. However, the limitation of existing studies is the low strictness of data sources and low repeatability of results. The regression model and the residual method calculate the health cost increase caused by aging alone while controlling for irrelevant variables. Since demographic changes are in concert with socioeconomic conditions, the actual contribution of aging to health costs is calculated under the framework of *de facto* demographic changes. Therefore, studies that use this method may overestimate the impact of aging on health costs.

Although various studies produce different results, it cannot be denied that aging has affected health costs to some extent. Research on aging and medical costs can provide policy support for an aging society.

The medical expense of the older adults

Accounting methods for medical expenses in the older adults

The escalating healthcare costs and the aging population have emerged as a major concern for governments with regards to the medical expenses incurred by older individuals. To address this issue, the Organization for Economic Co-operation and Development, World Health Organization, and Statistical Office of the European Communities introduced the "SHA 2011" framework in 2011, which replaced the previous total health cost with a regular health cost. This system has been increasingly adopted by countries, and Chinese

researchers have been utilizing it since 2015 to calculate healthcare expenses for the older adults (24). The SHA 2011 framework has been acknowledged by some scholars for its usefulness in precisely tracking medical expenditures. It accounts for the final consumption of healthcare goods and services while excluding capital formation costs and expenses on preventive affairs. Moreover, it can distinguish between treatment costs and rehabilitation and nursing costs, although in China, these are often included in the former. Nonetheless, the SHA 2011 framework is considered to be an improvement over previous method. However, under China's current medical and health system, rehabilitation and nursing care constitute essential parts of medical services. Hence, rehabilitation and nursing costs are included in the treatment costs. It is regarded as an improved version of "SHA 2011."

The SHA 2011 framework can provide valuable insights into the benefits situation of the population, including the scale of medical expenses, how to raise funds for the older adults, and the proportion of personal burden. It can also analyze medical expenses by age, gender, disease, and region, making it possible to identify which diseases should be targeted for cost control in specific regions. The framework can also assist policymakers in determining whether to invest more in treatment or prevention and evaluating the impact of policy on the health sector. Overall, the SHA 2011 framework offers a more accurate and detailed approach to calculating medical expenses for the older adults, providing useful information for policymakers to make informed decisions (25).

The medical expense burden of the older adults

The escalating medical costs pose a significant financial burden on the government at a macro level (26, 27). This is compounded by the fact that a small percentage of the older adults consumes a significant share of healthcare resources (28). In China, for instance, healthcare expenditure rose by almost 10.47 times from 458.66 billion Yuan in 2000 to 5259.83 billion Yuan in 2017, exceeding the GDP growth rate (29). Moreover, medical expenses for senior citizens account for more than a quarter of total healthcare expenses, with the proportion being even higher in Beijing, where it is expected to surpass 66.7% by 2030 (30, 31).

At the micro level, the growing medical costs add to the burden on the older adults and their families. In the United States, *per capita* healthcare spending for the older adults was $2,026 in 1978, which was significantly higher than that of young people ($286) and middle-older adults ($764) (32). The mean expenditure per person for older adults 65 years and over was $12,411 in 2018, according to the Medical Expenditure Panel Survey commissioned by the U.S. Department of Health & Human Services (33). In Spain, the older population incurred higher medical expenses, especially drug expenses, during hospitalization compared to other groups (34). In Kenya, the family health expenses of the older adults were very high and involved intangible costs such as nursing and missed work (35). In China, hospitalization expenses for the older adults continuously rose from 2012 to 2015 (36). The presence of older adults over 65 years in a family is a key factor contributing to catastrophic health expenses in Chinese households (37). Even in India, where the proportion of the population in the younger age groups is one of the largest in the world, households with older adults had higher catastrophic OOP expenses compared to households without older adults (38).

The factors affecting medical expense burden in the older adults

Extensive research has been carried out to identify the factors that affect medical expenses among the older population, examining these factors from different angles. Various factors have been identified as having a significant impact on changes in health costs for older adults, including social, medical, family, and personal factors.

Social factors

Public policies and medical insurance systems can have a significant impact on the healthcare costs of the older population. In the United States, for example, the establishment of Medicare and Medicaid for the and the poor was followed by the implementation of the Prospective Payment System (also known as DRGs) and Managed care, which aimed to regulate healthcare costs by encouraging hospitals to limit resource use while maintaining high-quality inpatient care (39). This system also required patients to visit specific medical professionals for coverage of their visits. Japan adopted a similar approach by compensating care centers for the older adults after a law was enacted to reduce pensions (40). In Spain, policies aimed at ensuring equal access to healthcare services have been put in place, with the National Health Service emphasizing the equality of citizens' access and controlling the revenues allocated to regional public healthcare. In regions with high tax autonomy, a positive relationship between regional income and public expenditure on healthcare has been observed (16).

The provision of medical security systems for the older adults in China is primarily the responsibility of the government, and while the health insurance coverage is extensive, it has limitations that require improvement, leading to significant out-of-pocket expenses (41). The health insurance and welfare package fail to cater adequately to medically and financially vulnerable groups (42). In 2015, the overall reimbursement ratio for hospitalization expenses stood at 49.7% under the current medical insurance policy (43).Hence, it is crucial to raise the reimbursement ratio for the older population suffering from chronic diseases (44). The government must restructure the prevailing medical security systems by adjusting the proportion of reimbursement for inpatient and outpatient expenses to an appropriate range.

The older adults in developed countries tend to allocate more of their medical expenses towards disease prevention and community health services. Conversely, in China, a significant majority of medical expenses are directed towards large public hospitals (87.34%) (45). This reflects an uneven distribution of healthcare resources, as the older adults tend to spend a considerable amount on curative care in high-level hospitals, rather than basic medical and health institutions, ambulatory facilities, and public health institutions (25, 46). This underscores the prominent role of large public hospitals in the treatment of senile diseases. Furthermore, the hierarchical diagnosis and treatment system should be further enhanced.

Research conducted by Dutch scholars suggests a significant association between seasonal changes and medical expenses of the older population (47). Additionally, Chinese researchers have found that the older adults incur the highest medical expenses during the winter season (25). This observation can be attributed to the fact that cold weather during the winter season often leads to acute exacerbations of chronic diseases, thereby emphasizing the need for improved primary prevention measures for the older adults.

Medical factors

Polypharmacy accounts for a significant proportion of total healthcare expenses, particularly for the older adults. Hence, controlling drug expenses, modifying the composition of hospitalization expenses, and increasing the remuneration of medical personnel are essential (25, 47, 48). Interestingly, technological advancements in France (49), the Netherlands, and the United States have led to an increase in medication and hospitalization costs for the older adults (50, 51), as evidenced by the significant rise in treatment expenses for heart disease resulting from a surge in bypass surgery or catheterization procedures from 1984 to 1991 (51).

Family factors

Family size plays a significant role in determining how the older adults seek care, with about 70% of Chinese older adults living with their children in large families, compared to only 0.2% in Denmark, 0.5% in the United States, and 14.1% in Italy. This difference in family size leads to a variety of long-term care costs for the older adults. Household income, which includes individual income and income from a spouse or children, is positively associated with higher medical costs (52). In China, family attitudes towards the older adults strongly influence their treatment compliance (53). The older adults may choose different treatment schemes and medicines based on their family's attitudes, resulting in different health costs (54). However, similar outcomes have not been observed in other countries with satisfactory primary medical care systems, where the older adults can make independent decisions about receiving services provided by family doctors, without family interference.

Personal factors

Age, gender, education level, region of residence, registered residence, chronic diseases, medical examination, self-rated living standards, living model, individual income, and medical insurance are all significant factors affecting health expenditures in the older adults (55). Studies have shown that health costs increase with age, with proximity to death resulting in higher healthcare expenditure (55). In China, older adults at the end of their life incur the highest medical expenses, contributing significantly to the total medical costs (56, 57). Income and education level were found to be negatively correlated with outpatient and inpatient use, as those with higher levels of education, income, and living standards had better health awareness and were more likely to undergo regular health check-ups, resulting in reduced use of outpatient and inpatient services (58).

Globally, chronic diseases are the primary contributors to the medical expense burden of the older adults (59). According to Prince et al. (60) cardiovascular diseases (30.3%) and malignant neoplasms (15.1%) are the most prevalent chronic diseases. Similarly, in Singapore, cancer and stroke are the top health expenditure conditions among the older adults, while in Japan, obesity, diabetes, and heart diseases are major cost drivers (61). In Mexico, the lack of early diagnosis and treatment for chronic diseases among the indigenous older adults may require more medical resources (62). In China, nearly half (48.84%) of the country's health expenditure on chronic disease is consumed by 13.32% of the population over 60 years old, with circulatory, respiratory, digestive systems, cancer, and endocrine system-related chronic diseases being the highest cost (25, 36, 63). Li et al. found that cardio-cerebrovascular diseases inflict the highest cost among the 80–84 years old age group in Jilin province, reaching 3.489 billion Yuan (43). Chai et al. reported that the cost of nutritional diseases in the older adults was 63.930 billion Yuan, with malnutrition among cancer patients being the most expensive (64). Therefore, the incidence and cost of specific chronic diseases among the older adults vary across different countries, depending on factors such as drug expenses, medical service prices, and medical insurance policies.

Limitations of present studies and the existing problems

Limitations of present studies

The available literature on the medical expense burden has been constrained to a handful of diseases. To gauge the stroke burden in epidemiology, Pang et al. utilized disability-adjusted life years (DALYs) (65). With the advancement of science and technology, research techniques, theories, and evaluation metrics related to medical expense burden have also been devised (66).

The existing problems

Underestimating the morbidity

To accurately estimate the morbidity of a disease, it is important to consider the actual diagnosis and treatment patterns. In the case of chronic diseases, patients may choose to self-medicate rather than seek medical attention due to the long duration of illness and economic challenges. Underestimating the prevalence of a disease could lead to an overestimation of its economic burden. This highlights the need for accurate and comprehensive data collection methods when assessing the economic impact of chronic diseases (67–69).

The representability of data

Based on our experience in data collection from medical institutions, it is important to consider the hospitalization history of patients when analyzing their average hospitalization frequency and medical expenses. This is particularly relevant in cases where patients are hospitalized multiple times in different hospitals within a year. In such cases, the sample institutions may not have access to complete medical information for these patients, which can impact the accuracy of the data collected.

The compatibility of results

Ensuring high comparability of measurement results is crucial, especially when assessing the medical expense burden of patients with different diseases and age groups. Variations in calculation and estimation methods may lead to differences in the measurement results, which could affect the comparability of the findings.

The rationality of medical expense burden

The burden of medical expenses on patients can be influenced by irrational factors such as drug abuse and unreasonable pricing, while the introduction of new technologies and drugs may be a rational factor that drives up costs. However, regardless of the rationality of these factors, the burden on patients remains a tangible and undeniable reality that must be taken into account in research.

The proportion of medical insurance compensation

There is a growing demand for higher reimbursement rates for people over 65 in Medicare. Medical insurance has a significant impact on reducing medical expenses and the economic burden on the older adults. The medical expenses of older adults over 65 with medical security account for less than 65% of the total out-of-pocket expenses. On average, the total medical burden of older adults in urban and rural areas can be reduced by about a quarter, and the proportion of family out-of-pocket expenses in total expenses can be reduced by more than half. The variations in healthcare systems among different countries have resulted in different studies on the medical expenses of the older adults, as shown in Table 1. For accounting system of the medical expense in the older adults, China are different from other countries in accounting system. For studies about the influencing factors of medical expenses for the older adults, the Chinese study is relatively limited compared to other studies. For policy factors affecting on health cost of the older adults, different systems in each country lead to different results. The older adults in China is greatly influenced by family and family attitudes. Most health costs of the older adults in China flow to large public hospitals, rather than basic health services. Population aging has a significant impact on health costs in developed countries. Life expectancy carries more weight on *per capita* health costs.

Discussion

In recent years, the aging of the population and the economic burden of diseases on the older adults have become the hottest topics in the field of international health. China's population aging problem is particularly perturbing, which brings great pressure to health care system. At present, there are many literatures on economic burden, but most of them focus on the general population or only take chronic diseases as an influencing factor. There is a lack of comparison among the research objects, and there are few studies on special vulnerable groups, such as the older adults. So we reviewed and summarized relevant researches to highlight the medical expense burden in the older adults.

In this review, we not only made a detailed description of the medical burden of the older adults, but also summarized the aging population and its social problems, as well as the research on the medical costs of the older adults. This review has carried on the systematic summary to medical treatment expense in the older adults from two latitudes of time and country. Aging was not only the decisive factor in the increase of health costs, but also the result of multiple factors. This paper also centered on SHA2011. The latest internationally accepted method to-analyze the source and destination of health cost: the source of financing and the flow of health care cost to institutions. The continuous increase of medical expenses not only brings substantial financial pressure to the government, but also adds the burden to the older adults themselves and their families.

This review was the first of its kind to present a multi-dimension and multi-factor summary in the influencing factors of the medical expenses in the older adults. The variations in healthcare systems among different countries have resulted in different studies on the medical expenses of the older adults. Extensive research has been carried out to identify the factors that affect medical expenses among the older population, examining these factors from different angles. Various factors have been identified as having a significant impact on changes in health costs for older adults, including social, medical, family, and personal factors.

Policy implications

In this review, we not only made a detailed description of the medical burden of the older adults, but also summarized the aging population and its social problems, as well as the research on the medical costs of the older adults. This review has carried on the systematic summary to medical treatment expense in the older adults from two latitudes of time and country.

Future studies should explore the impacts of the medical insurance funds and health service system reforms on reducing the medical expense, and come up with a supporting medical insurance reform plan.

Limitations

To our knowledge, this study was the first of its kind to present a multi-dimension and multi-factor summary in the influencing factors of the medical expenses in the older adults. This study also had several limitations. First of all, since the study was limited to published literature, unpublished literature was not included, which may lead to bias. Second, we only selected relevant literature for summary, and did not list the literature screening process. Based on the problem orientation, we analyzed the medical costs and factors of the older adults, the existing problems and the direction of future research. Third, the literature is also timeliness, but it is also valuable to provide powerful research information for relevant researchers and policy makers.

Conclusion

It is crucial to investigate the medical expense burden of the older adults and the factors that affect it. As the older adults are prone to chronic diseases, their medical expenses need to be more comprehensively assessed. To analyze the medical expenses of the older adults, multidimensional comparisons, financing plans, and investigations into influencing factors should be utilized. Additionally, the effects of increasing medical costs on healthcare services and Medicare funding for the older adults, as well as supporting programs for medical insurance, should be explored. Policy makers should pay more attention to the medical cost of the

TABLE 1 Studies on medical expense of the in China and other countries.

Dimension	China	Other countries
Accounting system of the medical expense in the older adults	Improved "SHA2011": rehabilitation and nursing costs are included in the treatment costs	"SHA2011": expenditures on treatment, rehabilitation and nursing are calculated separately. Other system: capital formation costs and prevention cost included.
Studies about the influencing factors of medical expenses for the older adults	Few empirical studies Focus on a specific region	Systematic study using Andersen's medical service model and Grossman's health demand model. Multi-region study.
Policy factors affecting on health cost of the older adults	China's urban pay for the special services beyond the scope of basic medical care	Medical insurance system varies in different countries. The United States: Medicare and Medicaid for the, prepayment (DRGs) and Managed care. Japan: law to reduce pension, government compensation for care centers.
Family factors affecting on health cost of the older adults	About 70% of the live with their children. Family attitude matters	A small proportion of the live with their children. Family attitude is rarely reported as an influencing factor.
Cash flow of health expenditure to institutions	Most health costs of the flow to large public hospitals, rather than basic health services	Relatively reasonable health costs flow to institutions in developed countries.
The impact of population aging on health costs	No unified conclusion. Different characteristics in different regions	Population aging has a significant impact on health costs in developed countries. Life expectancy carries more weight on *per capita* health costs.
Variables included when analyzing aging and health cost change	Variables include aging, income, health insurance and advances in medical technology. Overestimation is common	Aging is the solo variable. Low strictness of data source and low repeatability of results.

older adults and its influencing factors, and formulate relevant policies in a multi-directional and comprehensive way to reduce the burden of the older adults.

Author contributions

JC conceived and designed the article and drafted the manuscript. JC, MZ, RZ, and WO conducted the literature review and analysis, under the leadership and instruction of PY. WO contributed the coordination and manuscript editing. PY designed ideas of research. 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.

Publisher's note

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Systems modelling as an approach for eliciting the mechanisms for hip fracture recovery among older adults in a participatory stakeholder engagement setting

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Introduction: Due to an aging population, the rising prevalence and incidence of hip fractures and the associated health and economic burden present a challenge to healthcare systems worldwide. Studies have shown that a complex interplay of physiological, psychological, and social factors often affects the recovery trajectories of older adults with hip fractures, often complicating the recovery process.
Methods: This research aims to actively engage stakeholders (including doctors, physiotherapists, hip fracture patients, and caregivers) using the systems modeling methodology of Group Model Building (GMB) to elicit the factors that promote or inhibit hip fracture recovery, incorporating a feedback perspective to inform system-wide interventions. Hip fracture stakeholder engagement was facilitated through the Group Model Building approach in a two-half-day workshop of 25 stakeholders. This approach combined different techniques to develop a comprehensive qualitative whole-system view model of the factors that promote or inhibit hip fracture recovery.
Results: A conceptual, qualitative model of the dynamics of hip fracture recovery was developed that draws on stakeholders' personal experiences through a moderated interaction. Stakeholders identified four domains (i.e., expectation formation, rehabilitation, affordability/availability, and resilience building) that play a significant role in the hip fracture recovery journey.

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Discussion: The insight that recovery of loss of function due to hip fracture is attributed to (a) the recognition of a gap between pre-fracture physical function and current physical function; and (b) the marshaling of psychological resilience to respond promptly to a physical functional loss via uptake of rehabilitation services is supported by findings and has several policy implications.

KEYWORDS

hip fracture recovery, rehabilitation, resilience building, system dynamics modelling, group model building

1. Introduction

With its high and increasing life expectancy (1), Singapore is likely to see a rise in osteoporosis, accidental falls, and consequent hip fractures (2, 3). Osteoporosis, a condition of progressive bone loss, resulted in an estimated 1.26 million hip fractures globally in 1990; this number is projected to increase to 4.5 million by 2050 (4), with the majority of this increase coming from Asia (4, 5). With a rising prevalence of osteoporosis, there are increasing concerns about hip fractures among older adults, as osteoporosis is associated with a six to seven-fold increase in the likelihood of hip fractures (6). In 2015, approximately 2,000 older adults were hospitalized locally due to hip fractures (7). Between 2007 and 2009, the age-standardized incidence of hip fractures in Singapore was estimated to be (per 100,000) 156 in men and 331 in women (8). Hip fractures are costly and demand considerable resources from the healthcare system, accounting for a large proportion of fracture-related healthcare expenditure and mortality in men and women over 50 (9–11). Considering this demographic reality, the economic burden of hip fractures on health systems is expected to increase. In Singapore, the mean cost of hospitalization due to hip fractures was approximately S$13,314 per patient in 2011, and an additional cost of S$2,690 may result from complications (12). Furthermore, considering post-acute rehabilitation, nursing, and caregiving costs (both formal and informal), total lifetime costs are likely to be considerably higher. In the United States, for instance, overall lifetime costs (taking into account lost productivity and other indirect costs) due to hip fractures were estimated to amount to more than US$81,000 (in 1997 US dollars) (13).

Furthermore, though hip fracture patients often undergo early surgical fixation, many cannot return to their pre-fracture levels of physical function and independence (14). Prioritizing only functional and performance targets alone may lead to poor outcomes for patients as it potentially excludes the preferences and psychosocial needs of patients recovering from hip fractures (15). Additionally, care transitions are a particularly vulnerable time for patients as they transition from the hospital post-surgery back into their home environment. As many older adult hip fracture patients often have other complicated comorbidities, these patients may have to transition between settings such as tertiary hospitals and community hospitals before discharging back into the community (16). During this transition process, patients typically receive fragmented information from various healthcare providers and even fragmented care, leading to unmet patient needs (16, 17). Should care transitions be poorly managed, this can result in hospital readmissions, poor functional outcomes, quality of life, and patient satisfaction (18, 19). During this time, caregivers, often family members, take on the overwhelming responsibility of caring for hip fracture patients. With the importance of caregivers in the recovery process, it is crucial to involve caregivers from the onset of care. Hence, it is essential to consider integrating patient - and family-centered care for hip fracture patients. Encouraging patients and their families to be involved in recovery can promote active collaboration and shared decision-making between patients, families, and clinicians (20). The benefits of this approach to care promote autonomy and independent living among hip fracture patients and decrease dependency on healthcare providers.

As alluded to above, the greater demand for care for hip fracture patients can strain informal caregivers, who are the primary source of help for dependent older adults in Singapore (21). As hip fracture patients have limitations in independent ambulation and functional ability, they are highly reliant on their caregivers in the performance of their daily activities, especially in the early stages of recovery and care transitions. Due to its acute nature, many informal caregivers assume the caregiver role with little or no preparation. Caregiving often involves difficult tasks and a complex relationship with the care recipient; this can affect informal family caregivers' psychological and physical well-being. Evidence suggests that excess caregiver burden is associated with depression (22, 23), a decline in physical health, and increased healthcare utilization (24). Caregivers of older adult hip fracture patients in Singapore have been found to experience significant stress that begins as early as hospital admission and continues to remain high even six months post-admission (25). Role strain may also arise if caregiving responsibilities compete with labor market participation and compromise the caregiver's performance in either role (26). Caregivers who are employed may also find it challenging to maintain work roles while assisting a family member, as evidenced by their reported missed days, interruptions at work, leave of absence, and reduced productivity because of their caregiving obligations (27). Moreover, the competing demands of caregiving can affect the quality of caregiving, thus hindering a functional recovery in the patient.

These issues highlight the importance of enhancing functional recovery in hip fracture patients to reduce dependency and facilitate independent living within the community. Moreover, to ensure that a patient and family-centered care approach is adopted, this research aims to actively engage stakeholders (including doctors, physiotherapists, hip fracture patients, and caregivers) using the systems modeling methodology of Group Model Building (GMB) to elicit the factors that influence hip fracture recovery, incorporating a feedback perspective to inform system-wide interventions.

Most research on hip fracture recovery trajectories tends to concentrate on identifying factors associated with hip fracture recovery using models such as the growth mixture modeling approach (28) and logistic regression (29). Even with the evident contribution of these approaches, however, a new approach is needed to tackle the critical question relevant to clinical and policy action, i.e., what are the mechanisms by which these determinants of hip fracture recovery operate to promote or hinder recovery? Our study suggests how functional decline and recovery manifest through an interplay of stressors (hip fracture) and how individuals respond to those stressors (30–32). Complicating the dynamics of hip fracture trajectory of functional ability is the presence of feedback loops, in which variables are both the cause and effect (e.g., stressors reduce functional ability, and reduced functional ability promotes the occurrence of stressors). Using a qualitative system dynamics method through the engagement of stakeholders in a GMB can provide a valuable complement to empirical studies for understanding dynamically complex phenomena. Based on explicit, testable hypotheses about causal relationships, a model promotes developing and testing improved hypotheses about hip fracture recovery and identifying potential interventions to optimize recovery based on underlying drivers of functional loss or recovery.

2. Methods

Group Model Building is a participatory system dynamics method that engages stakeholders in developing conceptual maps and simulations for complex problems to gain a whole system perspective, leveraging the diagramming conventions of systems modeling (33, 34). The stakeholder's engagement in GMB refers to the process in which stakeholders are deeply and actively involved in model construction through the exchange, assimilation, and integration of mental models into a holistic system description (35). The GMB activities use ScriptMap (36) to describe the sequences of activities in a GMB session. Depending on the negotiated time with stakeholders, specific scripts are selected to ensure that the aim of the GMB is achieved during the session. The GMB method was used for this research to engage diverse stakeholders to develop a structured, explanatory, and coherent set of interconnected statements/theories of the factors that promote or inhibit hip fracture recovery.

2.1. Study context

The research team from Duke-NUS Medical School conducted two half-day workshops in Singapore on 29th August 2022 and 31st August 2022. 25 stakeholders participated in the workshop, representing Singapore General Hospital, Changi General Hospital, St. Andrew's Community Hospital, patients, caregivers, and researchers. The stakeholders include three medical doctors, six physiotherapists, two nurses, eight hip fracture patients, one caregiver, and five researchers. Informed consent was obtained from all participants before the start of the workshop sessions. The stakeholders were selected from doctors, nurses, physiotherapists, nurses, patients, and caregivers in a resilience and hip fracture recovery study funded by the National Medical Research Council of Singapore.

2.2. Study design

Group exercises based on two main scripts from GMB literature (37) were conducted with the stakeholders over the two half-day workshops. The outcome was to develop a preliminary qualitative model of the factors that promote or inhibit hip fracture recovery among older adults in Singapore and to identify leverage points for interventions to improve recovery. The activities were designed to build on each other to enhance understanding and participation among the stakeholders. **Table 1** shows the list and sequence of activities. The first session focused on providing a comprehensive update on the demographic characteristics of the patients recruited for the ongoing hip fracture study to understand the impact of psychological resilience on hip fracture recovery and introduce the stakeholders to basic principles of systems thinking and system dynamics. The

TABLE 1 List and sequence of group activities of the GMB.

Agenda	Team Activity
Day #1	
Introduction and Background	• Introduction of the research team and stakeholders. • Background and aims of the GMB workshop.
System Dynamics Introduction	• Introduce stakeholders to causal loop diagramming. • Draw a bathtub with a faucet and drain. Use it to explain stock and flow.
Concept Model Presentation	• Presentation of concept model. • Distribution colored sheets for writing questions/comments/clarification of the concept model. • Facilitator collects the sheets and clusters on the wall and goes through them with stakeholders.
Variable elicitation	• Elicit factors: distribute colored sheets for writing factors that promote or inhibit hip fracture recovery. • In a round-robin fashion, stakeholders present factors that promote or inhibit hip fracture recovery. • Cluster the variables on the wall. • Group the variables into sub-groups.
Day #2	
Structure Elicitation	• Sketching the concept model on white paper and fixing it on the wall. • The facilitator selects a sub-group of the clustered factors, then chooses a variable at a time and asks stakeholders to identify the connection between the factor and the concept model. • Facilitators ask questions to establish the nature of the causal relationship. • After establishing the causal relationship, the facilitator asks a stakeholder to summarize by telling a story embedded in the causal relationship.
Exploration of Policy Options	• The facilitator leads the discussion with the stakeholders to identify leverage points for intervention to improve hip fracture recovery.

second session of activities focused on presenting a preliminary conceptual model of hip fracture recovery, eliciting stakeholder comments regarding the model structure, and clarifying the model concept, variables, and polarities. For the third session, stakeholders were asked to list all the factors that promote or inhibit hip fracture recovery not represented in the preliminary concept model. Lastly, the stakeholders were led by the facilitator (a research team member) to explore the interactions and interdependences among these factors and identify leverage points for interventions. The workshop scripts and procedures planned for the sessions have been approved by IRB.

2.3. GMB exercise

A detailed description of the activities conducted during the workshop is provided herein. After introducing the agenda for the workshop, the stakeholders were divided into three groups. Each group consists of individuals from different backgrounds and organizations. The facilitators for the workshop clarified the purpose of the meeting, provided a detailed update on the patients recruited for the study, introduced stakeholders to basic principles of systems thinking and system dynamics, and described in detail the expected output from the two half-day workshops.

2.3.1. Presentation of preliminary concept model

This exercise aimed to introduce the stakeholders to the initial conceptual model of functional loss and recovery from a hip fracture developed by the research team and elicit suggestions to improve the model structure. Following a stepwise and detailed explanation of the initial conceptual model, the stakeholders were allowed to review and critique the conceptual model of functional loss and recovery individually and as a group. The guiding question presented to stakeholders to facilitate discussion was: *What is wrong with this conceptual model?* Each group was given 30 min to review the conceptual model, discuss it among the group members, and list each of their questions and comments on separate post-it notes. In a round-robin fashion, each group presented one critique or clarification at a time. The process was repeated across all groups until all reviews, comments, suggestions, and clarifications were presented. Each critique, comment, suggestion, and clarification listed on post-it notes was affixed to a wall. The facilitators sought clarifications to ensure a common understanding among the stakeholders. The workshop facilitator reviewed all the post-it notes with the stakeholders to ensure that all the critiques, comments, suggestions, and clarifications were addressed to the satisfaction of all the stakeholders.

2.3.2. Variable elicitation exercise

The exercise aimed to elicit causal factors that promote or inhibit hip fracture recovery. The stakeholders were urged to list all direct and indirect factors influencing hip fracture recovery based on personal and institutional experience. The guiding question provided to the stakeholders to stimulate discussion was: *What are the factors that promote or hinder hip fracture recovery, based on your experience as a patient, doctor, physiotherapist, caregiver, or nurse, that is not included in the initial conceptual model?* Like the earlier exercise, each group was given 30 min to discuss and list all the variables they believe have a role in hip fracture recovery on separate post-it notes. In a round-robin fashion, each group presented one factor at a time. The process was repeated across all groups until all factors that promote or hinder hip fracture recovery identified by each group were discussed. Each factor is listed on a post-it note and affixed to a wall after clarification from the facilitator to ensure common understanding. After that, the research team from Duke-NUS Medical School clustered all the factors listed into 14 sub-groups (see Appendix A). They are nutrition, caregivers, resilience building, comorbidities, expectation of recovery, family, care at home, communication, pain perception, income, education, individual factors, accessibility of resources, and healthcare professionals' perspective.

2.3.3. Structure elicitation exercises

This group exercise involves connecting the factors elicited by the stakeholders to the conceptual model. It began with a brief overview of the conceptual model by the facilitator. After that, the facilitator led the stakeholders to connect the factors by starting from the sub-group with the least factors. First, elements in a sub-group are randomly selected. Stakeholders are asked to suggest how that factor is connected to the conceptual model and provide a personal or institutional experiential-based story related to that factor. When another stakeholder challenges a proposed connection or relationship, the facilitator helps to clarify the concerns until a consensus is reached. The process was continued until all the elements in the 14 sub-groups were used. The facilitator discarded factors that became redundant based on the advice of the stakeholders. In connecting all the factors, initially suggested connections were revisited and changed when necessary to represent the complex interconnections between the elements better. Additional variables subsequently identified were also added to represent the causal relationships between variables better. Details of exercise are reported in the results. The field model developed with stakeholders can be found in Appendix B.

3. Results

Results: This section describes the preliminary concept model (**Figure 1**) and the qualitative model developed with stakeholders (**Figure 2**). The suggested interventions to improve hip fracture recovery is presented in the discussion. The qualitative model developed with stakeholders was divided into four segments, as shown in **Figure 2**.

3.1. Preliminary concept model

Within the context of the conceptual model (see **Figure 1**) adapted from the reference as cited (38) as part of the study by the authors, we define the key variables in the model as follows.

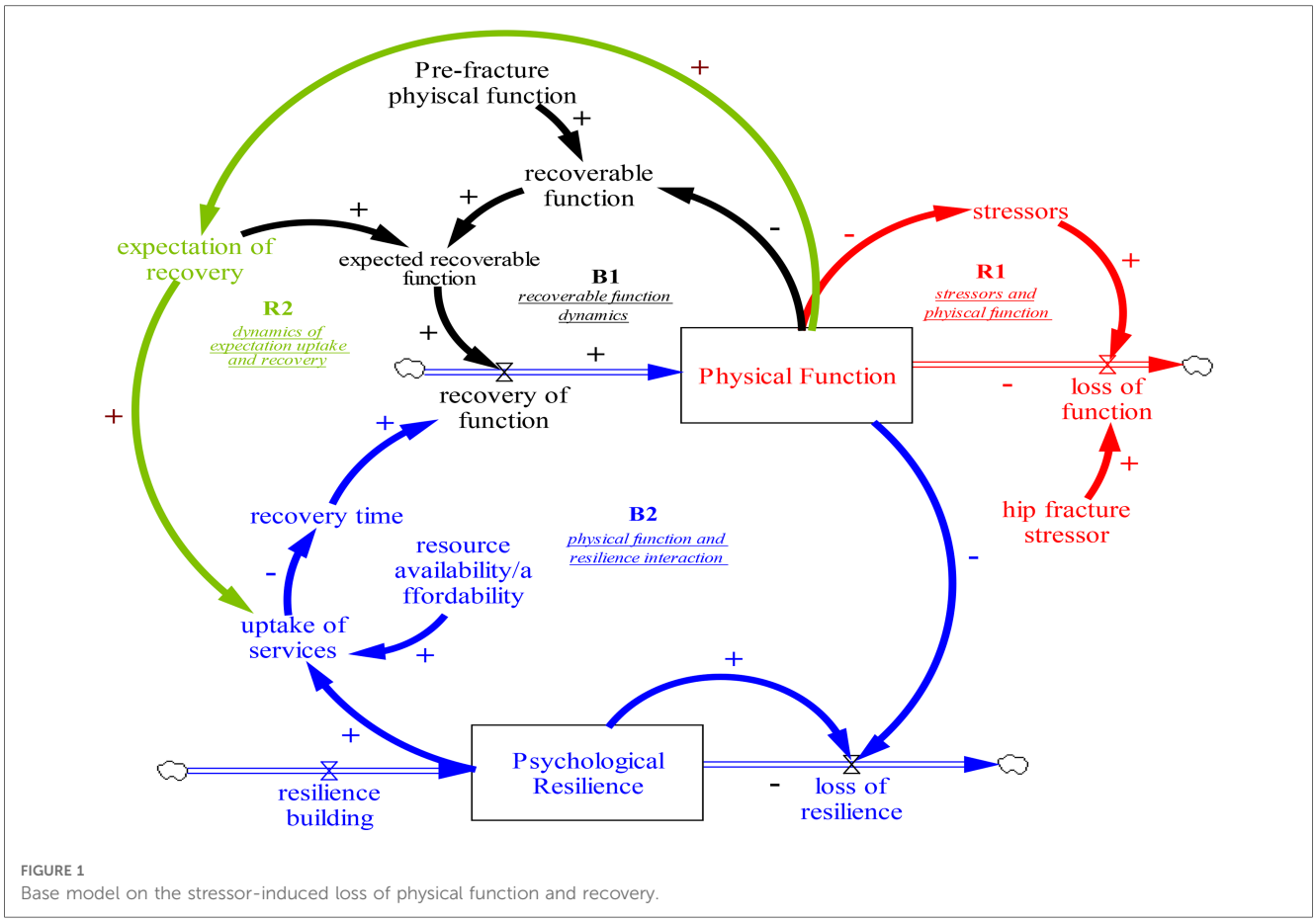

FIGURE 1
Base model on the stressor-induced loss of physical function and recovery.

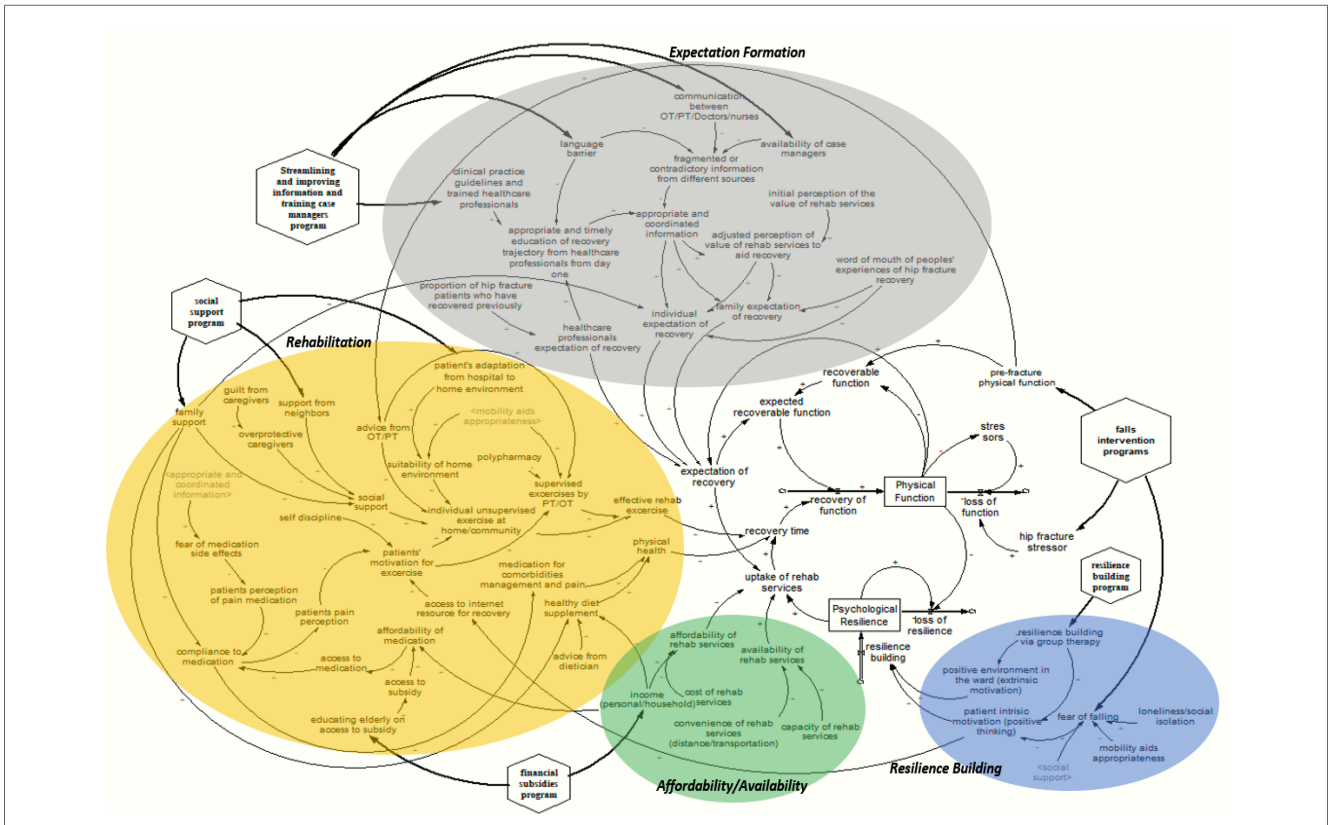

FIGURE 2
Qualitative model developed with stakeholders.

Physical function refers to the level of activity an individual achieves in his day-to-day function. This function comprises cognitive and physical capacity that influence an individual's ability to perform activities of daily living (39–41). Pre-Fracture physical function is the pre-fracture function in the absence of stressors. It is the reference function, which is assumed to remain unchanged over 12 months in the context of this study. It provides a benchmark for comparing physical function. A stressor is any event (e.g., hip fracture) that reduces functional ability. Larger stressors correspond to larger reductions in physical function. Psychological resilience reflects the psychological features of an individual that promote or inhibit recovery. A person with high psychological resilience will respond to stressors in a manner that promotes rapid recovery from physical function loss. In contrast, a person with low psychological resilience will respond in a way that leads to a slow recovery or deterioration of physical function (42–44). The expectation of recovery is what an individual expects may recover from the difference between pre-fracture physical function and physical function. This expectation could be a reflection of an individual's optimism (45). Individuals with a higher expectation of recovery should have a complete recovery, while individuals with lower expectations will likely have less complete recoveries. Despite other definitions of resilience that encompass some expectations, we define the expectation of recovery as a distinct characteristic from our definition of resilience. The feedback loop R1 describes the feedback relationship between stressors and physical function. R1 stipulates that individuals with low physical function are more likely to experience stressors than those with higher physical function. This increased rate of stressors exacerbates the reduction in physical function, ultimately leading to a greater vulnerability to future stressors. These causal relationships form a reinforcing feedback loop where exposure to stressors decreases physical function, leading to a higher likelihood of experiencing more stressors over time. Feedback loop B1 describes the balancing feedback relationship between recoverable loss of function and recovery rate. Individuals with a higher expectation of recovery will expect a larger recoverable function lost due to stressors. The loss of actual function due to stressors creates a gap between pre-fracture physical function and physical function. The gap is referred to as "recoverable function," a weighted average difference between the pre-fracture physical function and physical function. The weight is the value assigned to the "expectation of recovery" and can vary between individuals and within individuals over time. A weight of one indicates an expectation that the potential for the physical function is equivalent to the expected function. In contrast, a weight of less than one means a lower recovery expectation. When an individual has a higher expectation of recovery (close to one), this individual will engage more in activities that promote the recovery of that lost function. Hence, the individual will recover more quickly and close the gap between the individual's pre-fracture physical function and current physical function. As that gap closes, the rate at which the individual recovers decreases until the gap closes. Feedback loop B2 describes the negative reinforcing relationship between physical function and psychological resilience. When an individual experiences a decline in physical function due to stressors, the individual will not be able to engage in activities that maintain the psychological, social, and physiological drivers of recovery. Hence, an individual with poor physical function also experiences a more rapid depletion of psychological resilience. This individual will be less likely to take up services and engage in other activities that promote recovery of the lost function. Therefore, the individual will have a longer recovery time and is less able to improve his physical function. Feedback loop R2 relates the dynamic relationship between the expectation of recovery, uptake of services, and physical function. We postulate here that high expectations of recovery will stimulate the appropriate use of services to promote recovery of physical function. Consequently, as physical function recovers expectation of recovery is likely to increase further.

4. Qualitative model developed with stakeholders

This section describes the expanded qualitative conceptual model developed with key stakeholders. The expanded qualitative model is divided into four sectors: (a) expectation formation, (b) rehabilitation, (c) affordability/availability, and (d) resilience building.

4.1. Expectation formation

Figure 2 shows the qualitative model developed with stakeholders, clearly indicating the expectation formation sector. Stakeholders identified three main factors that contributed directly to the "expectation of recovery" of hip fracture patients. They are (a) individual expectation of recovery, (b) family expectation of recovery, and (c) healthcare professionals' expectation of recovery.

Stakeholders suggested that individual expectation of recovery was driven by four main factors: (a) the appropriate and coordinated information provided to the patients while at the hospital, (b) perception of the value of rehabilitation services, (c) word of mouth of other patients' experiences of hip fracture recovery, and (d) family support. Appropriate and coordinated information provided to the patients is determined by the factually correct and timely education on hip fracture recovery. This education should be delivered by healthcare professionals immediately upon a patient's admission to the hospital. *A healthcare professional argued that the information provided to patients must also be tailored to the specific needs of the patient.* When information is provided to patients in a coordinated manner, patients' perception of the value of rehabilitation services for their hip fracture recovery is substantially improved. In contrast, incoherent and uncoordinated provision of information is likely to worsen a patient's negative perception of the value of rehabilitation services. Patient stakeholders felt that

fragmented and contradictory information was often communicated to them during their stay in the hospital. Furthermore, *A healthcare professional stakeholder mentioned that the negative tone of some healthcare professionals might negatively affect a patient's perception of the recovery process, for instance, by only highlighting the high risk of surgery without talking about the expected recovery trajectory. Hence*, stakeholders suggest that having clear clinical practice guidelines to guide healthcare professionals in engaging patients and family members will likely enhance the recovery trajectory of patients. Likewise, the stakeholders postulated that fragmented and contradictory information from different sources could also be caused by language barriers, lack of availability of care managers, and poor communication between healthcare professionals and patients. Patients in our stakeholder group agreed with such a sentiment. One stakeholder *mentioned that during her time at the hospital, she had to assist the healthcare team to translate their care instructions for a fellow patient in the ward because the healthcare team did not speak the Chinese dialect with which the patient was most comfortable communicating in.* Another factor influencing an individual's expectation of recovery is the perception of the value of rehabilitation services. This perception is postulated to be shaped by an initial perception of the value of rehabilitation services held by patients and the information provided to patients regarding the role of rehabilitation services and patients' recovery. Stakeholders also felt that word of mouth from other patients' experiences of hip fracture recovery would influence their expectations of recovery. This word of mouth consists of stories about other patients' experiences of hip fracture recovery. *A doctor stakeholder shared that he uses a positive story about a previous patient's experience as a way to foster a positive expectation of recovery.* These positive recovery stories can potentially increase an individual's expectation of recovery, whereas negative recovery stories are likely to lower individuals' expectations of recovery.

Stakeholders suggested that better family support, especially from caregivers involved in a patient's recovery, is associated with the positive individual expectation of recovery. The family's expectation of recovery was found to have similar influences as the individual's expectation of recovery, and they are (a) appropriate and coordinated information, (b) perception of the value of rehabilitation services to aid recovery, and (c) word of mouth of other patients' experiences of hip fracture recovery. As suggested by the stakeholders, appropriate and coordinated information delivered to the family regarding the patient's recovery trajectory will directly influence the family's expectation of recovery and the family's perception of the value of rehabilitation services to aid recovery. *Stakeholders believed that when family members positively perceive the value of rehabilitation services, they will support the patient through their recovery journey with their time, financial resources, and rehabilitation equipment and provide encouragement, amongst other means and resources, to aid their functional recovery in the long run.* Thus, the appropriate and coordinated information received by the family, the positive perception of the value of rehabilitation services to aid in recovery, adjusted by known stories of hip fracture recovery of other individuals, determine the family's expectation of recovery.

Lastly, stakeholders shared that healthcare professionals have their own expectations of patient recovery. This is influenced by their institutional and personal knowledge and experiences working with hip fracture patients. It is hypothesized that healthcare professionals adjust their advice to patients and family members on a patient's recovery trajectory based on their expectation of recovery informed by past experiences in treating similar patients.

4.2. Rehabilitation

The stakeholders identified two main factors related to rehabilitation that directly contributes to recovery time. The factors are effective rehabilitation exercises and physical health. Based on stakeholder knowledge, effective rehabilitation exercises were hypothesized to be driven by patients' participation in supervised exercises provided by physiotherapists or occupational therapists (PT/OT) and unsupervised exercises conducted at home or in the community by the patient. Supervised exercise with the PT/OT is determined by the uptake rate of supervised exercise referral by PT/OT (advice from PT/OT) and adjusted by patients' motivation to exercise to improve recovery from hip fracture, availability of appropriate mobility aids to support patients, and polypharmacy. According to the Stakeholders, mobility aids help the gradual progression of exercises tailored to the patient's recovery. Physiotherapists in the stakeholder group assert that PT/OT advice involves making recommendations of individualized exercises tailored to the patient based on the knowledge of the patient's pre-fracture physical function. *A physiotherapist gave an example of when a patient's recovery journey begins; they first do exercises with a walking frame, then do more advanced exercises. They suggested that it was important for the physiotherapist to start by teaching the simple patient tasks first before gradually moving on to more complex tasks.* Thus, advice from PT/OT is influenced mainly by patients' pre-fracture physical function. These recommendations are prescribed to patients during supervised physiotherapy appointments. The stakeholders postulate that the following factors influence the uptake of individual unsupervised exercise at home. They are the suitability of the home environment, social support, advice from PT/OT, and patients' motivation to exercise. The suitability of the home environment is hypothesized to be influenced by patients' adaptation from the hospital to the home environment and the availability of appropriate mobility aid. It was argued that patients who engaged in individual unsupervised exercise at home are primarily individuals who have managed to adapt to the home environment following their discharge from the hospital. A suitable home environment enables patients to practice exercises in a comfortable and familiar space. *A doctor stakeholder suggested that not everyone is interested in going for rehabilitation sessions but may prefer to do their exercises at home where they feel safe and more comfortable.* In addition, social support was argued to be a crucial factor for hip fracture patients

to engage in individual unsupervised exercise at home. Social support comes from the support shown by family members and neighbors. However, overprotective caregivers can negatively affect the level of social support a hip fracture patient experiences. The stakeholders emphasized that the higher the caregiver overprotectiveness (especially in Singapore, where most hip fracture patients are likely to have lived-in foreign domestic workers as caregivers), the greater likelihood that the hip fracture patients will not engage in individual unsupervised exercise to aid recovery. *Patients in the stakeholder group shared that overprotective caregivers (including family members) may prematurely terminate rehabilitation sessions or reduce them significantly because of pain and discomfort experienced by the patient. Furthermore,* overprotective caregivers may be excessively supportive and remove patients' independence due to guilt and fears of a coming fall.

Patients' motivations for exercise are influenced by self-discipline, patients' pain perception, and access to internet resources for recovery. *Patients in the stakeholder group agreed that self-discipline is essential for motivating oneself to exercise, despite the presence of fear of falling after a hip fracture.* Self-discipline is an individual characteristic, and stakeholders believe it is crucial for continuous exercise. Another factor that affects patients' motivations for exercise is a patient's pain perception. A patient's pain perception was argued to be influenced by compliance with medication which is determined by access to medication, patients' perception of pain medication, and family support. Increased perceived pain and discomfort would lead to less willingness to exercise. A *nurse in the stakeholder group shared that patients' negative views of medication affect compliance to take the appropriate prescribed dose of medication.* Access to medication required by hip fracture patients is a function of affordability determined by personal/household income and access to medication subsidies provided by the government. *According to the stakeholders, subsidies are available to help patients afford the required medication. However, many patients are often unaware that these subsidies are available or lack the knowledge to navigate the bureaucracy to apply for them.* Therefore, by educating patients on public subsidies the affordability and accessibility to medication. Another factor influencing patients' pain perception is the fear of medication side effects. *Stakeholders argued that patients have a negative perception of pain medication due to misconceptions about the potential side effects of medication and fears of becoming over-reliant on pain medication.* Healthcare professionals can address these fears by providing appropriate and coordinated information to patients at the hospital. Hence, the clinician team's appropriate and coordinated information would be vital to clarifying the misconceptions, providing assurance, and alleviating concerns. Lastly, accessing internet resources regarding recovery may help educate patients on the value of exercise, increasing patients' motivation for exercise. Patients who actively access resources independently are influenced by their intrinsic motivation for recovery.

On physical health, factors such as (a) medication for comorbidities and pain management and (b) healthy diet and supplementation were identified as the main drivers. Patients' compliance with medication for managing comorbidities and pain affects patients' physical health. As explained earlier, compliance with medication can be affected by the access and affordability of medication, as well as patients' perceptions of pain medication. Furthermore, a healthy diet and optimal nutrition would also directly impact physical health. Dieticians advise healthy dietary habits and optimal nutrition in the hospital post-hip fracture surgery. *Patients in the stakeholder group also argue that healthy diets may be more expensive. Thus, they feel that patients need sufficient financial resources to support these changes to their eating habits.* In addition, family support, through consistent reminders or preparation of nutritious food, is vital in ensuring patients adhere to their new healthy diets.

4.3. Affordability/availability of rehabilitation services

Stakeholders concurred that the uptake of rehabilitation services is directly affected by two main factors: (a) affordability and (b) the availability of rehabilitation services. The affordability of rehabilitation services is determined by personal/household income and the cost of rehabilitation services. One's income includes personal income and/or the income of other household members. *Many stakeholders agreed that immediate family members might be able to financially support hip fracture patients on their recovery journey, contributing to greater uptake of rehabilitation services. Stakeholders highlight that most hip fracture patients are usually unable to work and sustain a regular income after an operation.* Therefore, having household members who can assist in paying for services could mitigate income loss and encourage patients to take up rehabilitation services. On the contrary, if the cost of rehabilitation services is too high or unaffordable, patients would be less likely to take up any rehabilitation services.

The availability of rehabilitation services also plays a significant role in the uptake of services. The availability of rehabilitation services is directly affected by (a) the convenience of rehabilitation services and (b) the capacity of rehabilitation services in the healthcare system. *Patients in the stakeholder group emphasized that easily accessible rehabilitation services in the community where hip fracture patients live are needed.* As recovering hip fracture patients have poor mobility, they are unwilling to travel to a rehabilitation center, deterring them from utilizing these services. However, should a rehabilitation center be located nearby and easily accessible by transport, this would increase the likelihood of a patient using the rehabilitation services. The overall capacity of rehabilitation services is essential in the uptake of services. *Stakeholders mentioned that even if they were willing to take up services, they would only be able to access them if high-quality services were available.* This means that the provision of good quality services, in addition to convenience and availability, can also be a reinforcing mechanism in encouraging patients to attend rehabilitation on a sustained basis.

4.4. Resilience building

Stakeholders emphasized how resilience building is shaped by two factors (a) a person's intrinsic motivation, described by many stakeholders as having "positive thinking, and (b) a positive environment or extrinsic motivation. Intrinsic motivation, combined with an encouraging extrinsic environment, develops and strengthens psychological resilience. Meanwhile, a positive environment starts from the ward and continues into the community. *One patient in the stakeholder group shared about a church outreach group that reaches out to older adults living alone to do regular exercises together.* Stakeholders discussed how a patient"s intrinsic motivation, or the presence of positive thinking, is shaped by patients" fear of falling. Fear of falling, in turn, is affected by three factors, (a) loneliness/social isolation, (b) social support, and (c) appropriate mobility aid. Stakeholders mentioned how loneliness and/or social isolation, coupled with relatively poor social support, can lead to an increased fear of falling. As discussed earlier, social support consists of support from neighbors and family members. Their regular presence around the patient helps the patient to recover psychologically. In addition, using appropriate mobility aids can reduce the patient's fear of falling by empowering them to move independently and confidently.

A hip fracture patient's intrinsic motivation and a positive environment can be facilitated by participating in group therapy. Stakeholders indicated how group therapy could build resilience by providing a platform for mutual guidance and encouragement. *A physiotherapist in the stakeholder group mentioned that patients share information and learn from one another when they exercise together during group therapy.* Through group therapy, patients can share exercise-related information and learn exercise techniques from one another, including how others conduct their exercises, adjusting their techniques, and motivating each other. Group therapy also provides a platform for patients to connect with others who share similar experiences, serving as an avenue for social interaction and companionship. Patients tend to be more motivated to continue their therapy if they participate in a group rather than on their own. *As shared by stakeholders, group therapy enables one to be aware of the ordinary, everyday shared experiences and challenges other hip fracture patients face.*

5. Discussion

First, the insight that recovery of loss of function due to hip fracture is attributed to (a) the recognition of a gap between pre-fracture physical function and current physical function; and (b) the marshaling of psychological resilience to respond promptly to a physical functional loss via uptake of rehabilitation services is supported by findings from studies as cited (46–49) and has several policy implications. The recognition of the gap between current and pre-fracture physical function and marshaling psychological resilience to close this gap was found to be determined by the expectation of recovery, which is in turn influenced by the quality of the information provided to patients and their families by healthcare professionals and the appropriate and coordinated delivery of this information. From a policy perspective, this suggests that hip fracture care must prioritize patient education and coordinated communication to raise the expectation of recovery. A rise in the expectation of recovery will lead to increased uptake of rehabilitation services and, consequently, better recovery outcomes. Thus, it is essential to emphasize that well-coordinated information provided by healthcare professionals to patients is a critical component for patients' hip fracture recovery journey. This insight informed the identification of a program intervention by the stakeholders that focuses on streamlining and improving the information provided by the healthcare professional to patients and family members and ensuring that the information and the delivery process are carefully detailed in clinical practice guidelines. This information includes early goal setting (setting realistic expectations and aligning family and patients' expectations), laying out the appropriate rehabilitation services needed, providing dietary recommendations, having open communication between patients, families, and healthcare professionals, and adjudicating differences in expectations. This involves clinicians managing expectations and incorporating preferences, needs, and decisions from patients and their families instead of dictating the course of recovery via a top-down approach. A shared understanding of what is expected during recovery is essential for all stakeholders so as to facilitate better recovery outcomes.

In addition, healthcare professionals can provide caregivers of patients with systematic training and specific guidelines, such as concise, appropriate, and targeted information to support patient recovery at home. Stakeholders suggested the need to leverage IT platforms to coordinate information sharing to help the healthcare team stay on the same page when communicating with patients. More importantly, healthcare professionals required to deliver the information to patients should be well-trained and familiar with what they must provide. To prevent potential miscommunication or dissemination of fragmented information, stakeholders suggested the need to develop a program that aims to train case managers that specialize in coordinating information provided by healthcare professionals. The role of these case managers ensures that there is one reliable contact point between healthcare providers and hip fracture patients and their families. This approach ensures that patients and their families have a clear and comprehensive understanding of the aligned expected recovery trajectory and the expected actions of the patients and families to support the recovery process. Stakeholders observed that case managers who were readily available to answer questions from patients and family members helped to build a more apparent, more explicit expectation of recovery after a hip fracture.

Second, the findings from this study suggest that support from family caregivers, friends, and neighbors is essential for the uptake of effective rehabilitation services. This has several policy intervention implications. Social support refers to providing emotional support, allowing hip fracture patients to engage in prescribed exercises recommended by physiotherapists, helping

patients use mobility aids to walk, creating a positive environment that encourages patients to adhere to treatment and recovery regimes, and decreasing fear of falling. This insight led the stakeholders to identify social support programs that educate family members, caregivers, and the public about the importance of social support to older individuals in dealing with life stressors, including hip fractures. Nevertheless, it is vital to emphasize that overprotective support from caregivers (family or neighbors) can inhibit patients' recovery within the social support mechanism, as overprotective caregivers may actively limit patients' engagement with rehabilitation activities. Hence, healthcare professionals need to guide patients' recovery process by continuously engaging caregivers to ensure that they understand and are engaged with the expected trajectory of recovery and the expected actions they should be undertaking to promote recovery.

Third, the insight that hip fracture patients need financial support to subsidize the cost of medication, rehabilitation services, and mobility aids was reinforced by stakeholders' experience of the significant cost burden of hip fracture. Stakeholders indicated that the process of recovery from hip fractures is costly and requires substantial resources. For most older adults, the financial burden, especially if they have no external support from children, family members, and the government, is significant and can affect their ability to take up essential services and negatively impact their recovery trajectory. This finding informed the stakeholder's identification of a financial subsidy program that provides subsidies to support hip fracture patients, especially low and middle-income patients, who require financial assistance to enhance rehabilitation services uptake and promote recovery. Furthermore, it is also essential to educate patients and their caregivers on the subsidies available and how to apply for them to increase their access to subsidies.

Lastly, the insight that in the wake of a stressor-induced physical function loss (such as a hip fracture), a person with high psychological resilience will respond in a way that promotes rapid recovery, while an individual with low psychological resilience will react in a way that leads to a slow recovery or deterioration has policy/intervention implications. Based on this insight, stakeholders suggested that healthcare systems should consider implementing resilience-building programs that help older adults to build psychological resilience to prepare them for responding to life stressors over their life course. Psychological resilience assists individuals in developing individual characteristics and the ability to cope with life stressors. The findings indicate that building psychological resilience among patients includes engaging them through a mix of formal and informal support. Formal support structures include group therapy in hospital settings, hip fracture patient group creation, and community support. Informal support includes social support from the patient's family, friends, and community. Creating a positive-eco system for patient recovery is pivotal to building psychological resilience for better recovery outcomes. Moreover, empowering patients through elements of patient-centered care (i.e., alignment and management of patient expectations, providing coordinated information and care through case managers) can also increase patients' self-efficacy and strengthen their resilience toward recovery. The stakeholders also suggested that the psychological resilience programs should be paired with fall prevention programs. According to the stakeholders, targeted fall intervention programs could help improve the overall pre-fracture physical function of the general population. A falls prevention program aims to reduce the frequency of falls by building strength and addressing associated risks and fears related to falls. A fall is a significant stressor for older adults and a large contributor to the initial hip fracture; hence it could significantly impact their life course trajectory. Therefore, a comprehensive fall prevention program that includes components of resilience building can reduce the likelihood of falls and contribute to faster recovery from hip fractures.

5.1. Strengths and limitations

The strength of the present study is that it is one of the first to delve into the recovery processes of hip fracture patients, incorporating a multidisciplinary set of stakeholders who are directly affected or are involved in the care of hip fracture patients. It is also one of the first to synthesize the responses of occupationally diverse and multi-ethnic stakeholders into a comprehensive and extensive dynamic model.

A limitation of this study is that this study is conducted in Singapore, and therefore, the model may be applicable to a different context. The responses from participants in this study are based on local experience with a specific healthcare configuration that may operate differently in another country. Likewise, as the older age groups change in terms of health literacy and other factors, changes may be needed to be made to the model. The study did not actively discuss the hip fracture journey of individuals with dementia. Future studies should consider including the needs of hip fracture patients with dementia.

6. Conclusion

This paper explains the factors that promote or inhibit hip fracture recovery, incorporating a feedback perspective to inform system-wide interventions. The insight from the study suggests that recovery of loss of function due to hip fracture is attributed to (a) the recognition of a gap between pre-fracture physical function and current physical function; and (b) the marshaling of psychological resilience to respond promptly to a physical functional loss via uptake of rehabilitation services. However, recognizing the gap and marshaling psychological resilience to close it is determined by the expectation of recovery, which is influenced by the quality of the information provided to patients and their families by healthcare professionals and the appropriate and coordinated delivery of this information.

In light of these insights, hip fracture care in Singapore should consider streamlining and improving the information to patients and family members and ensuring that the information and the

delivery process are carefully detailed in clinical practice guidelines. The streamlining of the information has the potential for the healthcare team and caregivers to reinforce the positive benefits of rehabilitation to patients to improve recovery expectations. In addition, policies that focus on providing social support to hip fracture patients, financial subsidies, and resilience-building programs have the potential to facilitate hip fracture recovery among older adults in Singapore.

Data availability statement

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

Ethics statement

The studies involving human participants were reviewed and approved by National University of Singapore IRB. The patients/participants provided their written informed consent to participate in this study.

Author contributions

JA: Conceptualization, Methodology, Investigation, Writing - Original Draft, Visualization, Supervision, Funding acquisition AW-YC: Investigation, Data Curation, Writing - Review & Editing, Visualization, Project administration WL: Investigation, Data Curation, Writing - Review & Editing, Visualization VK: Investigation, Data Curation, Writing - Review & Editing, Visualization JK: Resources KG: Resources WY: Resources TH: Resources DS: Resources KM: Resources DB: Resources SV: Resources AY: Resources AE: Resources AW-MC: Resources DM: Supervision 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.

Publisher's note

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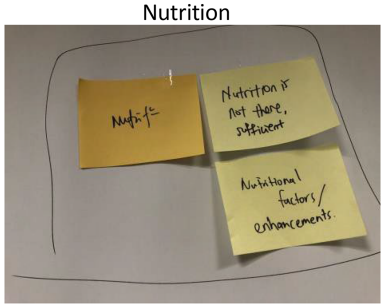
Appendix

Appendix A: Factor elicitation variables

Nutrition



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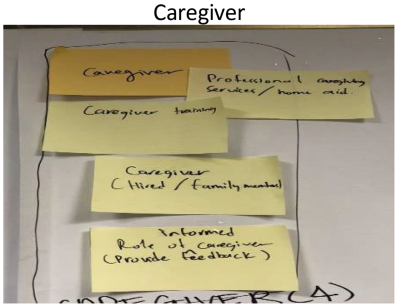

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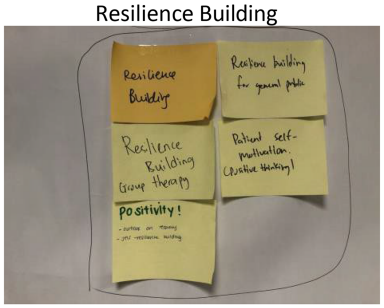
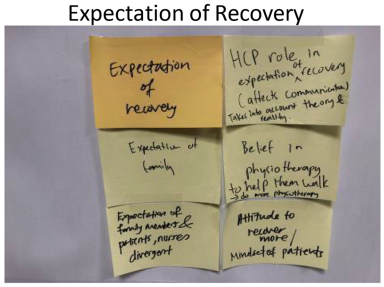


Expectation of Recovery



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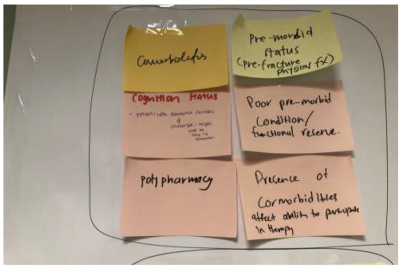
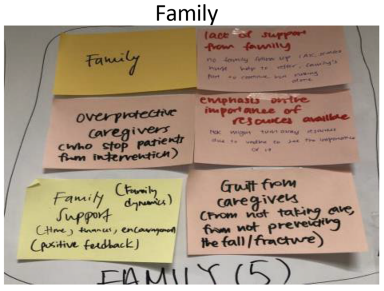
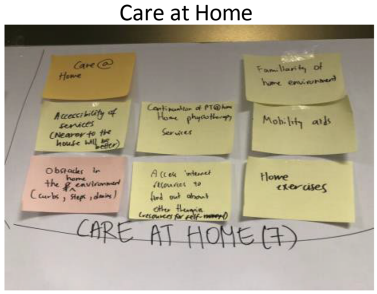


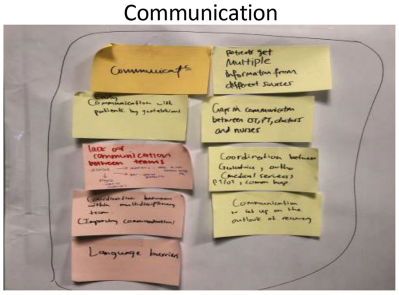
Family



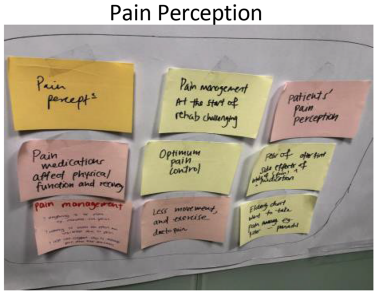
Care at Home



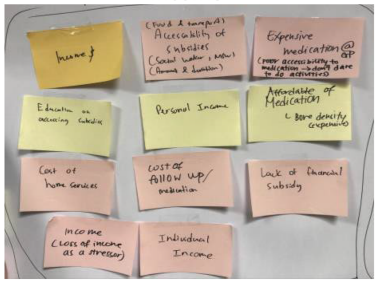
Communication



Pain Perception



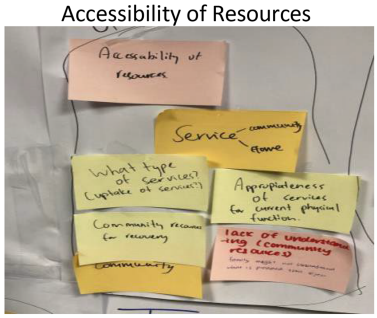
Income



Education

Individual Factors

Accessibility of Resources



Healthcare Professionals Perspective

Appendix B: Qualitative model developed with stakeholders.

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The effects of pharmaceutical interventions on potentially inappropriate medications in older patients: a systematic review and meta-analysis

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Introduction: Potentially inappropriate medications (PIMs) is a particular concern in older patients and is associated with negative health outcomes. As various interventions have been developed to manage it, we performed a systematic review and meta-analysis to evaluate the effect of pharmaceutical interventions on outcomes of PIMs in older patients.

Methods: Meta-analysis of eligible randomized controlled trials (RCTs) was conducted to report the outcomes of pharmaceutical interventions in older patients searching from the databases of Cochrane Library, PubMed, Embase, Web of Science, Clinicaltrials.gov, SinoMed and Chinese Clinical Trial Registry (ChiCTR). The PRISMA guidelines were followed and the protocol was registered in PROSPERO (CRD42019134754). Cochrane bias risk assessment tool and the modified Jadad scale were used to assess the risk bias. RevMan software was used for data processing, analysis and graphical plotting.

Results: Sixty-five thousand, nine hundred seventy-one patients in 14 RCTs were included. Of the primary outcomes, pharmaceutical interventions could significantly reduce the incidence of PIMs in older patients (OR=0.51, 95% CI: 0.42, 0.62; $p<0.001$), and the number of PIMs per person (MD=-0.41, 95%CI: −0.51, −0.31; $p<0.001$), accompanying by a low heterogeneity. Subgroup analysis showed that the application of computer-based clinical decision support for pharmacological interventions could remarkably decrease the incidence of PIMs and two assessment tools were more effective. Of the secondary outcomes, the meta-analysis showed that pharmacological interventions could reduce the number of drugs used per person (MD=-0.94, 95%CI: −1.51, −0.36; $p=0.001$) and 30-day readmission rate (OR=0.58, 95%CI: 0.36, 0.92; $p=0.02$), accompanying by a low heterogeneity. However, the pharmaceutical interventions demonstrated no significant improvement on all-cause mortality and the number of falls.

Conclusion: Our findings supported the efficacy of pharmaceutical interventions to optimize the use and management of drugs in older patients.

Systematic review registration: https://clinicaltrials.gov/, CRD42019134754.

KEYWORDS

rational use of drugs, pharmaceutical interventions, older patients, potentially inappropriate medications, meta-analysis

Introduction

The social and economic implications of older population are becoming increasingly apparent worldwide. The World Health Organization (WHO) has estimated that more than one in five individuals will be aged over 60 years by 2050, accounting for a total of 2 billion people in the world (1). Due to the prevalence of diverse diseases among older people, medications are commonly used to control the progression of diseases (2). In addition, the majority of older patients are treated by different therapeutic strategies. Therefore, concurrent treatment with polypharmacy is common among older people (3).

With the degradation of organs and physiological functions in older people, the pharmacokinetics and pharmacodynamics in the system could also change, thus, the risks of adverse drug reaction (ADR) and adverse drug event (ADE) could be elevated (4, 5), as well as increasing the rate of mortality (6) and the incidence of potentially inappropriate medications (PIMs). PIMs comprise a number of suboptimal prescribing practices, including inappropriate dose or duration of medication, drug–drug interaction, and drug-disease interaction (4). PIMs in older people are highly prevalent across a variety of healthcare settings, and are associated with the increased risk of ADEs, morbidity, mortality, health expenditure, healthcare utilization and frequent falling (7–10). It was estimated that 20–30% of all hospital admissions were related to prescription of drugs (11, 12), and up to 10% of all ADEs could be life-threatening or fatal (13).

Pharmaceutical intervention is the combination of modern pharmacology and clinical medicine, aiming to optimize the individualized drug therapy, improve the therapeutic effects of drugs, reduce the risk of the drug therapy, and ensure the safety and cost-effectiveness of the drug therapy (14). Pharmaceutical interventions could be performed specifically according to the epidemiology of PIMs and strategies, including specific health education and targeted interventions, which could substantially reduce the incidence of PIMs in older people (15).

However, current evidences vary substantially, and there are still debates on the influences of pharmaceutical interventions on outcomes of PIMs in older patients. Previous Cochrane systematic reviews (15, 16) could not draw robust conclusions from the evidences due to variability in design, interventions, outcomes and results. The most recent systematic review (17), which included all types of studies, suggests that PIM-setting-directed interventions should be developed to promote the wellbeing of the older patients through PIM reduction. However, it only reviewed and compared different interventions and outcomes, and did not conduct a meta-analysis. Therefore, we performed a systematic review and meta-analysis base on high-quality RCTs to evaluate and provide more reliable evidence of pharmaceutical interventions on PIMs in older patients.

Methods

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (18). It has been registered in the International Prospective Register of Systematic Reviews (CRD42019134754).

Search strategy

The systematic search was undertaken in February 17, 2021, using the defined PICOS statement (population, intervention, comparison, outcomes, study type) to identify all relevant articles: Cochrane Library, PubMed, Embase, Web of Science, Clinicaltrials.gov, SinoMed and Chinese Clinical Trial Registry (ChiCTR) databases. Population was defined as older patients, which included the patients older than 65 years old or the studies clearly defined older patients. For the intervention, we focused on the pharmaceutical interventions on potentially inappropriate medications, including all kinds of strategies and tools/criterions. For outcome, we included studies reporting the rationally of medication use (incidence of PIMs, the number of drugs used and so on) and the prognosis of patients (mortality， falls and so on). RCT followed our PICOs framework was included. The terms used in the searching process included "aged" and "inappropriate medications" for English databases, and the corresponding Chinese terms were used in the Chinese databases. The references of the included studies were also reviewed to reduce the rate of missing data. The Appendix Table 1 listed as example of full search strings applicable to PubMed.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) RCTs; (2) subjects who aged ≥65 years old; (3) involvement of pharmaceutical intervention in the study group, and routine diagnosis and treatment in the control group; (4) outcome included the occurrence of PIMs.

The exclusion criteria were as follows: (1) unclear study design; (2) unclear interventions; (3) unclear outcomes; (4) duplicate publication; (5) unpublished studies; and (6) full-text could not be retrieved.

Compared with the protocol registered (CRD42019134754) in PROSPERO, since few studies reported the number of drugs used, it is difficult to determine polypharmacy, and the non-hospitalized patients such as outpatient and emergency department could not be ignored, the included population was expanded to all older patients over 65 years old. At the same time, intervention was usually not performed and completed by pharmacists independently, and it is impossible to evaluate the effect of pharmacist interventions alone, so it is expanded to all pharmaceutical interventions.

Data extraction and quality assessment

Data were extracted using the predefined data extraction form by two investigators independently and cross-check was also performed. The disagreements were resolved by making discussion between the two investigators or involved the third investigator. The extracted data

included: (1) general characteristics and data of the included studies, involving the first authors' full-name, year of publication, country, study type, subjects' age, and sample size; (2) indicators of study quality, such as the methods of randomization, allocation concealment, blinding, drop out, and loss to follow-up; (3) detailed measurement of intervention; and (4) indicators of clinical outcomes (PIMs-related clinical and economic outcomes, as well as humanistic outcomes, for example, health-related quality of life, patient satisfaction, medication adherence and so on).

Cochrane bias risk assessment tool (19) and the modified Jadad scale (20) were utilized for the assessment of the included studies. The Cochrane bias risk assessment tool covered the following 7 aspects: (1) randomization; (2) allocation concealment; (3) blinding to subjects and investigators; (4) blinding to evaluators; (5) completeness of outcome data; (6) selective report of data; and (7) other sources of bias. The modified Jadad scale evaluated the quality of the included studies from 4 aspects, such as randomization, allocation concealment, blinding, and drop out, and the assessment results were classified as "appropriate," "unclear," and "inappropriate," with the corresponding scores of 2, 1, and 0, respectively. Studies with the total score of 4–7 points were considered as high-quality, and studies with the total score of 1–3 points were considered as low-quality.

Statistical analysis

Review Manager 5.4 software was used for data processing. Heterogeneity was assessed by the I^2 index and Q test (21). $I^2 \leq 50\%$ indicate low heterogeneity, and the fixed-effects model was used to pool the results. Otherwise, $I^2>50\%$ represent substantial or considerable heterogeneity, and the random-effects model was utilized (22). For the pooled analysis of binary variables, odds ratio (OR) and corresponding 95% confidence interval (CI) were estimated. For the pooled analysis of continuous variables, mean difference (MD) and 95% CI were estimated. For outcome indicators that could not be analyzed by the meta-analysis, the descriptive analysis was applied.

Results

Search strategy

Totally, 48,345 studies were retrieved by the initial screening. After further screening according to the inclusion and exclusion criteria, 14 RCTs were finally included in review 8 RCTs included in meta-analysis. The study flowchart is shown in Figure 1.

General characteristics of the included studies

The detailed general characteristics of 14 RCTs are presented in Table 1.

The included studies were, respectively, performed in 7 countries, including 1 in Ireland (23), 1 in Spain (24), 1 in Israel (25), 2 in Belgium (26, 27), 3 in Canada (28–30), 3 in the United States (31–33), and 3 in Sweden (34–36).

6 of the 14 RCTs included the old patients from nursing home (24, 25, 29, 34) or community-dwelling (28, 30, 34), which is the main facility for long-term medication treatment of older patients. The subjects were veterans in 1 study (31), cancer patients in 1 study (32), and patients with dementia or cognitive dysfunctions in 1 study (36). Finally, 65,971 subjects, including 32,941 in the study group and 33,030 in the control group, were involved in the present meta-analysis.

Pharmaceutical intervention strategies are diverse and distinctive, with assessment and management of medication being the most common intervention.12 (23, 25–27, 29–40) of the 14 studies implemented similar interventions, for example, a team to provide strict surveillance and feedback for all medications. Interventions in 8 studies (23, 25, 30, 32–36) was to optimize medication use through clinical pharmacist-physician discussion in meetings, face-to-face, telephone call, e-mail communication. Regarding interventions for patients, medication education is provided through paper materials or online videos (28, 35) and face-to-face communication (32).

The tools for assessing PIM, included Beers' criteria, screening tool of older person's potentially inappropriate prescription (STOPP)/screening tool to alert doctors to the right treatment (START) criteria, and PIM list designed by the pharmaceutical council. In addition, 12 studies (23–25, 27, 28, 30–36) used one assessment tool, 2 studies (26, 29) utilized 2 assessment tools, 5 studies (26, 28, 29, 31, 32) employed the Beers' criteria, 5 studies (24–26, 29, 35) used the STOPP/START criteria, and 6 studies (23, 27, 30, 33, 34, 36) utilized the PIM list designed by the pharmaceutical council.

From the 14 RCTs included in the study, a total of 13 outcomes were reported (the outcome column of Table 1), of which PIMs was the most widely evaluated and considered as the primary outcomes. All the 14 studies (23–36) evaluated PIMs, 4 studies (23, 28, 29, 34) reported all-cause mortality, 3 studies (24, 29, 36) reported all-cause emergent admission rate, 3 studies (24, 25, 30) reported the number of drugs used, 2 studies (24, 29) reported length of stay in hospital, 2 studies (29, 36) reported readmissions rate within 30 days of hospital discharge, 2 studies (24, 25) reported the number of falling events, 1 study (31) reported incidence of ADR, 1 study (25) reported cost of drugs, 1 study (24) reported the number of delirium episodes events and the number of visits to physician or nurse. Besides, 4 studies (26, 28, 29, 33) utilized the computer-based clinical decision support (CCDS) for intervention.

Quality assessment

Quality assessment was performed for the methodology of included studies Appendix Figure 1 shows the results of quality assessment by Cochrane bias risk assessment tool, in which "+" indicates meeting the requirements, "-" represents no satisfaction of the requirements, and "?" denotes an unclear status. There were 2 studies (31, 34), in which all the items met the requirements. Appendix Figure 2 illustrates the percentage of each item for quality assessment of the included studies. All the 14 included studies (23–36) used randomization, without selective reporting of data. Allocation concealment was applied in 10 studies (23, 24, 28–32, 34–36), double-blinding in 6 studies (24, 31, 33–36), blinding to evaluators in 9 studies (23, 24, 28, 30, 31, 33–36), complete data in 2 studies (31, 34), and other sources of bias in 3 studies (23, 25, 36).

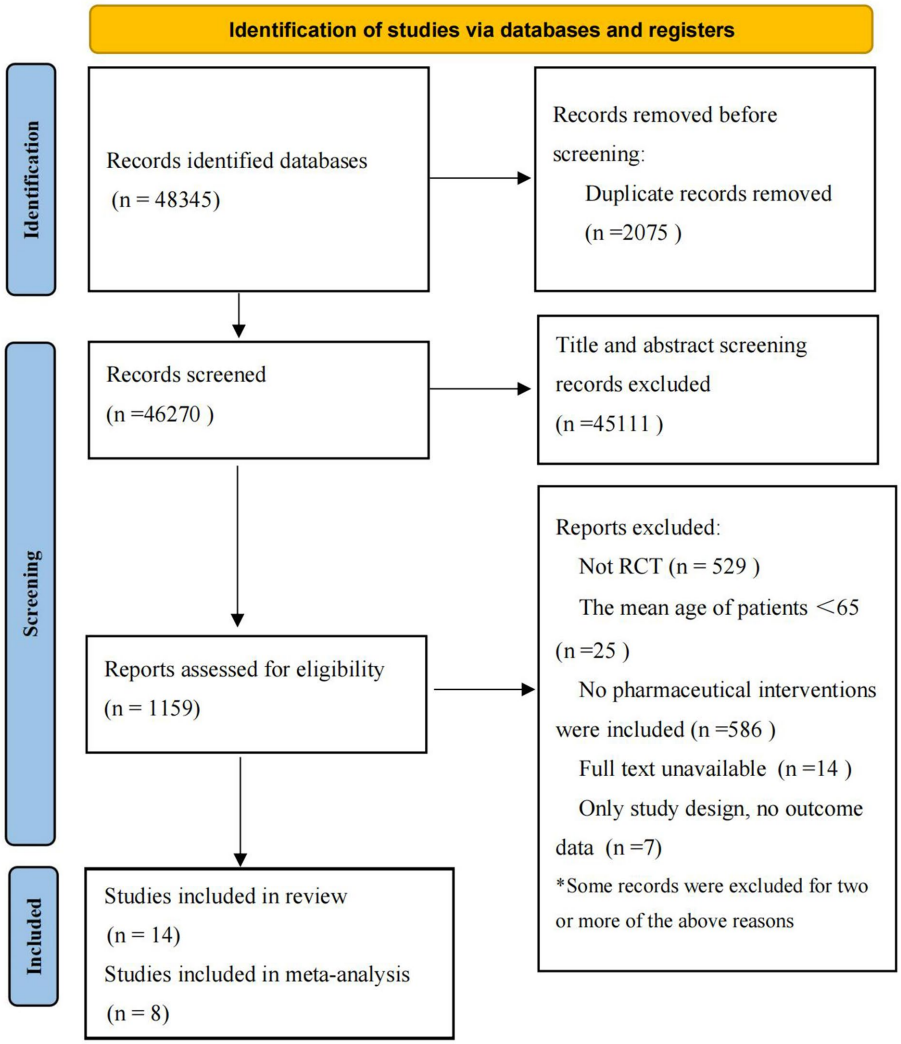

FIGURE 1
Process of study selection for RCTs.

Base on the modified Jadad scale, 10 studies (23, 24, 28, 29, 31–36) had the quality score of 4–7 points, indicating that the risk of bias was low and the quality of studies was high. Moreover, 4 studies (25–27, 30) were found with the quality score of 1–3 points, demonstrating that the quality of studies was relatively low (Appendix Table 2).

Primary outcomes

Incidence of PIMs

PIMs were reported in 14 studies, in which 6 studies (24–26, 29, 30, 36) that enrolled 1933 subjects (989 in the study group and 944 in the control group) reported the incidence of PIMs. The heterogeneity test showed a low heterogeneity among studies ($I^2 = 0\%$, $p = 0.50$), and thus, the fixed-effects model was used for the pooled analysis. The findings revealed that pharmaceutical intervention could significantly reduce the incidence of PIMs (OR = 0.51, 95%CI: 0.42, 0.62; $p < 0.001$; Figure 2A). Subgroup analysis was performed based on the application of CCDS, selection of assessment tools, and interventional strategies.

Of the 6 studies that reported the incidence of PIMs, 2 studies (26, 29) used the CCDS. The CCDS could automatically acquire the basic characteristics of patients, such as age, gender, body weight, comorbidities, medications, and examination results. In addition, the CCDS could send alerts when the medication changes, assisting the mediation assessment and pharmaceutical interventions. The comparison of the incidence of PIMs between the study group and control group that employed the CCDS showed that the difference was statistically significant (OR = 0.41, 95%CI: 0.29, 0.57; $p < 0.001$). The comparison of the incidence of PIMs between these two groups that did not employ the CCDS indicated that the difference was also statistically significant (OR = 0.57, 95%CI: 0.45, 0.73; $p < 0.001$). Although both subgroup comparisons achieved statistical significance, the pooled intervention effects of trials employing CCDS were superior to those without employing CCDS in terms of the magnitude of effect size (Appendix Figure 2A).

Of the 6 studies that reported the incidence of PIMs, 2 studies (26, 29) used the Beers' criteria, 4 studies (24–26, 29) utilized the STOPP/START criteria, and the other studies employed the PIM list designed

TABLE 1 Characteristics of included trials.

First author, published year	Country	Patients	Age (year)	Sample size		Organization of intervention	Strategies of intervention	Tools for assessing PIM	CDSS	Outcomes	Follow-up (months)
				Intervention	control						
Schmader et al. (31)	America	Veterans	≥65	430	404	Multidisciplinary team	A, B	a,b	No	1,2,5	12
Ryan 2019 (32)	America	Patients with cancer	≥65	29	31	Pharmacists led	A, C, D, E	b	No	1,4	2
Martin et al. (28)	Canada	Community patients	≥65	248	241	Pharmacists led	F, G	b	Yes	1,6	6
Goedele 2019 (26)	Belgium	Nursing home patient	≥65	847	957	Multidisciplinary team	A, B	b,c	Yes	1	15
Cossette et al. (29)	Canada	Hospitalized patients	≥65	126	128	Multidisciplinary team	A, B	b,c	Yes	1,6,7,10,11,13	2.5
Veronica 2013 (34)	Sweden	Nursing home or community patients	≥75	182	187	Multidisciplinary team	A, D, E	d	No	1,6	2
Ulrika 2013 (35)	Sweden	Older patients	≥80	182	186	Multidisciplinary team	A, E, G	a,c	No	1,2	12
Van der Linden et al. (27)	Belgium	Hospitalized patients	≥65	32	29	Pharmacists led	A, B	d	No	1	2
Maria 2018 (36)	Sweden	Dementia or cognitive impairment patients	≥65	212	217	Multidisciplinary team	A, E	d	No	1,7,11,13	6
Dvora 2017 (25)	Israel	Nursing home patient	≥65	160	146	Pharmacists led	A, E	c	No	1,3,8,12	12
García et al. (24)	Spain	Nursing home patient	≥65	344	372	Pharmacists led	F, H	c	No	1,3,7,8,9,10	6
Patterson et al. (23)	Ireland	Nursing home patient	≥65	173	162	Pharmacists led	A, D, E	d	No	1,6	12
Allard et al. (30)	Canada	Community patients	>75	136	130	Multidisciplinary team	A, E	d	No	1,3	12
Marsha 2007 (33)	America	Older patients	≥65	29,840	29,840	Multidisciplinary team	A, E	d	Yes	1	12

Strategies of intervention: A, medication assessment; B, medication management; C, face-to-face communication with patients; D, recording of medications; E, communication of pharmacologists with doctors on medication strategy through discussion in meetings, face-to-face communication, telephone call, e-mail, and fax; F, dispatching materials of education to medical staff; G, providing health education for patients through paper materials or online videos; and H, providing training for medical staff. Tools for assessing PIM: a. MAI index, b. Beers criterion, c. STOPP/START criterion, d. the list of potentially inappropriate medications prepared by the Drug Commission. Outcomes:1. potentially inappropriate medications (PIMs), 2. MAI index, 3. the number of drugs used, 4. Vaccination coverage rates, 5. Incidence of adverse reactions, 6. Mortality rate, 7. Emergency attendance rate, 8. Average number of falls, 9. Average number of deliriums, 10. Length of stay, 11. Readmission rate, 12. Cost of medicines, 13. Readmission time.

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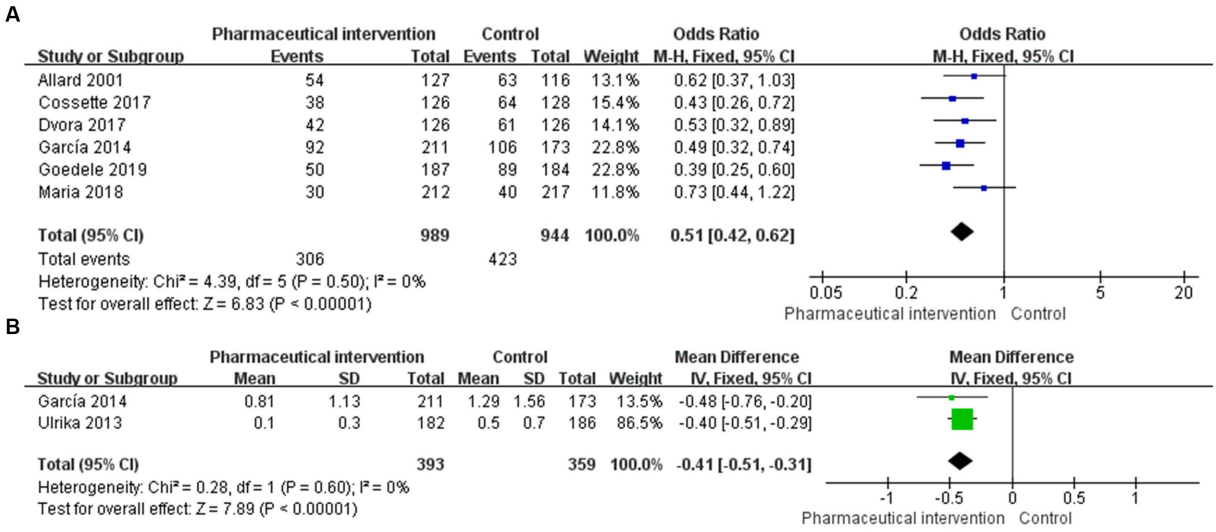

FIGURE 2
Forest plot for PIMs of eligible RCTs comparing pharmaceutical intervention with usual care **(A)** PIMs, **(B)** PIMs per person.

by the pharmaceutical council. Besides, 2 studies (26, 29) of the 6 studies used two assessment tools.

The comparison of the incidence of PIMs between the two groups that used one assessment tool revealed that the difference was statistically significant (OR = 0.57, 95%CI: 0.45, 0.73; $p < 0.001$). The comparison of the incidence of PIMs between the two groups that used two assessment tools showed that the difference was also statistically significant (OR = 0.41, 95%CI: 0.29, 0.57; $p < 0.001$). Although both subgroup comparisons achieved statistical significance, the pooled intervention effects of trials using two assessment tools were superior to those using single assessment tool in terms of the magnitude of effect size (Appendix Figure 2B).

Potentially inappropriate medications per person

Of the 14 studies that reported the incidence of PIMs, 2 studies (24, 35) reported PIMs per person, which totally included 752 subjects (393 in the study group and 359 in the control group). The heterogeneity test showed a low heterogeneity among the included studies ($I^2 = 0\%$, $p = 0.60$), and thus, the fixed-effects model was used for the pooled analysis. The findings demonstrated that pharmaceutical intervention could significantly reduce the incidence of PIMs per person in older people (MD = -0.41, 95%CI: −0.51, −0.31; $p < 0.001$; Figure 2B).

Secondary outcomes

The number of drugs used per person

Among 3 studies that reported the number of drugs used, 2 studies (24, 25) that enrolled 637 patients (311 in the study group and 326 in the control group) reported the number of drugs used per person. The heterogeneity test showed a low heterogeneity among the included studies ($I^2 = 0\%$, $p = 0.79$), and the fixed-effects model was used for the pooled analysis. The results showed that pharmaceutical intervention could significantly reduce the number of drugs used per person in older people (MD = -0.94, 95%CI: −1.51, −0.36, $p = 0.001$; Figure 3A).

30-day readmission rate

In 2 studies (29, 36) that reported the 30-day readmission rate, 683 subjects were enrolled, including 338 in the study group and 345 in the control group. Heterogeneity test showed a low heterogeneity among the eligible studies ($I^2 = 0\%$, $p = 0.48$), and the fixed-effects model was used for the pooled analysis. The findings revealed that the pharmaceutical intervention could significantly reduce the 30-day readmission rate (OR = 0.58, 95%CI: 0.36, 0.92; $p = 0.02$; Figure 3B).

All-cause mortality

There were 4 studies (23, 28, 29, 34) that reported the all-cause mortality and enrolled 1,446 subjects, of whom 729 and 717 subjects were in the study group and control group, respectively. Heterogeneity test showed a low heterogeneity among the included studies ($I^2 = 0\%$, $p = 0.58$), and the fixed-effects model was used for the pooled analysis. The results revealed that the effects of pharmaceutical intervention on the all-cause mortality were not significantly different between the two groups (OR = 0.93, 95%CI: 0.64, 1.37; $p = 0.73$; Figure 3C).

Falls

In 2 studies (24, 25) that reported the average number of falls, 968 subjects were enrolled, including 470 and 498 subjects in the study group and control group, respectively. Heterogeneity test showed a moderate heterogeneity among the eligible studies ($I^2 = 55\%$, $p = 0.14$), and the random-effects model was used for the pooled analysis. The findings showed that the effects of pharmaceutical intervention on the average number of falls were not significantly different between the two groups (MD = -0.23, 95%CI: −0.57, 0.12; $p = 0.21$; Figure 3D).

Discussion

The present study systematically reviewed 14 RCTs to compare the effects of pharmaceutical interventions on older people. The results indicated that the incidence of PIMs, the number of PIMs per person,

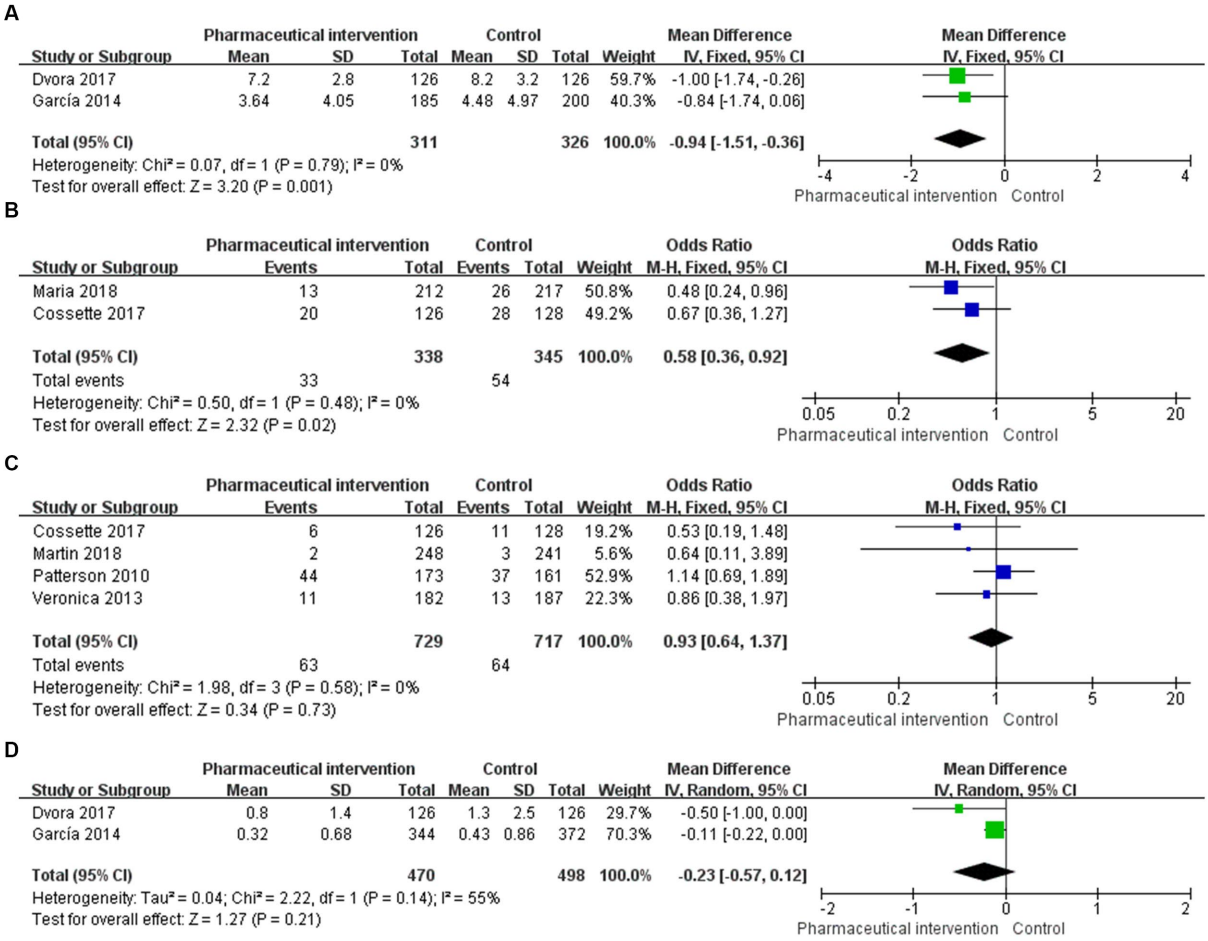

FIGURE 3
Forest plot for outcomes of eligible RCTs comparing pharmaceutical intervention with usual care **(A)** number of drugs used, **(B)** 30-days readmission, **(C)** all-cause mortality, **(D)** falling.

the number of drugs used, and 30-day readmission rate were significantly lower in the pharmaceutical intervention group, and the subgroup analysis showed that the application of the CCDS and assessment tools, such as Beers' and STOPP criteria, could markedly reduce the incidence of PIMs. It is noteworthy that the current study further comprehensively evaluated the effect of pharmaceutical intervention on potentially inappropriate medications in older patients by including high-quality RCTs and integrating intervention effects through meta-analysis.

PIMs are associated with risks that are greater than their potential benefits, and older patients are at a greater risk of ADEs from PIMs. Reducing the incidence of PIMs will be significant to reduce the incidence of ADEs and improve the prognosis of older patients. There are a variety of intervention strategies and methods that can effectively reduce the incidence of the PIMs. Subgroup analysis showed that the application of CCDS could reduce the incidence of the PIMs, which is consistent with the result of a previous study (37). The advantage of CDSS is not only associated with the efficient and accurate identification and reduction of PIMs, but also with the ability to change the prescribing behavior of physicians (38). In the present study, further subgroup analysis suggested that using single assessment tool may not be comprehensive in assessing PIMs, and the multiple assessment tools achieved a more desirable intervention result. This finding is consistent with the conclusion of Kurczewska-Michalak et al. (41) that no "gold standard" is identifiable and advisable, and the complexity, applicability and usability of tools needs to be considered. The complementarity of the different tools was also confirmed by Lisowska et al. (42), the PILA tool that included STOPP/START v.2 and Amsterdam tool identified the highest number of PIMs and achieved the most comprehensive assessment of pharmacotherapy appropriateness in geriatric patients. Overall, CDSS combining different prescription indicators should be considered as an important tool to optimize drug prescription for older patients.

Pharmaceutical interventions could significantly reduce the number of drugs used per person and 30-day readmission rate. Deprescribing is the process of systematically reviewing a patient's medications and discontinuing drugs in instances, in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient's care goals, current level of functioning, life expectancy, values, and preferences (39, 40). A growing body of evidence related to the adverse effects of polypharmacy on older patients supported the need for deprescribing (43), and the number of drugs that a patient is taking is the most important predictor of ADEs (44). Therefore, the number of drugs used per person and 30-day readmission rate reflect the efficacy and safety

of drug therapy, as well as being important indicators for testing the effects of pharmaceutical interventions. Additionally, regarding the economic endpoint, although only one study (25) reported the cost of drugs, pharmaceutical interventions could effectively reduce the cost of drugs in the study group compared with that in the control group. Economic systematic reviews (45) focusing on polypharmacy have expressed the same view, with interventions generally associated with a reduction in medication expenditure. Available evidence suggests that the potential benefits of interventions to optimize medication use outweigh the costs of their implementation, and the results of the included cost–benefit analysis studies (46–48) showed a net benefit that was null or positive.

The all-cause mortality and average number of falls were both lower in the study group than those in the control group, however, the differences were not statistically significant. The mortality rates were consistent with those reported previously (15). This can be related to contribution of other factors affecting mortality, of which disease progression is noteworthy. However, there are still some drug-related factors that require clinicians' attention (49–51). Several studies (52, 53) have shown that targeted pharmacological interventions for fall risk, including withdrawal of potential fall-risk-increasing drugs (FRIDs), pharmacist-conducted clinical medication review, and computerized drug alerts, were effective in reducing fall risk. However, tools for assessing PIM, such as Beers' and STOPP criteria, do not concentrate on FRIDs. Therefore, in the comprehensive pharmacological intervention, the management of FRIDs still needs to be improved, and it is suggested to reduce the fall risk in older patients with polypharmacy.

Because no "gold standard" has been identified, multiple interventions toward PIMs are advised, so the diversity of interventions included and analyzes in our meta-analysis is critical. Compared with the a scoping review of available interventions published in 2012 (41), relevant interventions, including prescription deprescribing, CDSS, medication therapy management (MTM) and so on, were all included in this meta-analysis. Regarding the setting and supporter of pharmaceutical interventions, the most common setting is primary healthcare team. Additionally, some interventions were provided at community or hospital pharmacies, in the form of pharmacists alone or in cooperation with a physician or nurse. In summary, the following steps involved pharmacists are the key to appropriate medications in older patients: patients' evaluation and data collection, medication review, being agree with patients on treatment objectives, prescription decision, communication and obtaining patient agreement, medication dispensing, medication usage, monitoring and assessment (41, 54).

Totally, 14 eligible RCTs were involved in the present study, which were mainly accompanied by a relatively high-quality. However, the limitations of this study were summarized as follows: (1) outcomes in the included studies varied, and only relatively few studies reported the same outcomes; (2) the data of the included studies were reported inconsistently, and thus, some outcomes could not be pooled; (3) only one study reported the cost of drugs; (4) difference in ethnicity, language, educational level, places for interventions and follow-up time among the subjects and studies all might influence the outcomes. (5) the possibility of missing studies not included in the databases we used and the articles published in other langue not being included in our analysis, (6) the risk of bias cannot be excluded, although most heterogeneity is acceptable. Therefore, more rigorously designed multi-center RCTs with larger sample size and longer follow-up with high-quality are needed to further validate the findings of the present study.

Conclusion

In summary, pharmaceutical interventions may improve the prognosis of older patients via reducing the incidence of PIMs, the number of PIMs per person, the number of drugs used, and 30-day readmission rate. Our findings supported the efficacy of pharmaceutical interventions to optimize the use and management of drugs for older patients.

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

CY and ZhY: literature search. LR, ZoY, and LL: screening of the search results. ZS, LR, and ZhY: risk of bias assessment. LR and LL: interpretation of the results. ZS, ZX, TZ, and ZoY: drafting and revising the article. ZS, LR, ZX, and LH: final approval of the version to be published. 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

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Effects of Tai Chi combined with tDCS on cognitive function in patients with MCI: a randomized controlled trial

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Background: Mild cognitive impairment (MCI) is a critical stage of dementia. Previous reviews have suggested that physical exercise combined with non-invasive brain stimulation is more beneficial for improving cognitive function. However, no targeted studies have confirmed the effect of Tai Chi combined with transcranial direct current stimulation (tDCS) on the improvement of cognitive function in patients with MCI. Thus, this randomized trial was conducted to assess the effect of Tai Chi combined with tDCS on the cognitive performance of patients with MCI.

Methods: From April 2018 to February 2020, a randomized, single-blind clinical trial was conducted, involving 180 participants with MCI who were divided into four intervention groups: Tai Chi combined with tDCS (TCT), Tai Chi combined with sham tDCS (TCS), walking combined with tDCS (WAT), and walking combined with sham tDCS (WAS). All participants were assessed at baseline and 12 weeks for global cognitive function, memory, attention, and executive function.

Results: At baseline, there were no significant differences in age, gender, education duration, body mass index, or the Baker Depression Inventory among the four groups ($P \geq 0.05$). After 12 weeks of intervention, the TCT group showed greater improvements in MOCA scores, memory quotient scores, and digit-symbol coding task reaction time compared to the TCS, WAS, and WAT groups ($P < 0.05$). The TCT group also had a shorter Stroop test color reaction time compared to the WAS and WAT groups ($P < 0.05$), a higher increase in Auditory Verbal Learning Test-immediate recall than the TCS and WAT groups ($P < 0.05$), a shorter visual reaction time than the TCS group ($P < 0.05$), and a shorter sustained attention time compared to the WAT group ($P < 0.05$).

Conclusion: Tai Chi combined with tDCS effectively improves global cognitive performance, memory, execution function, and attention in patients with MCI. These findings suggest the potential clinical use of Tai Chi combined with tDCS as a physical exercise combined with a non-invasive brain stimulation intervention to improve cognitive function in older adults with MCI.

Clinical trial registration: ChiCTR1800015629.

KEYWORDS

Tai Chi, transcranial direct current stimulation, mild cognitive impairment, randomized clinical trial, cognitive function

Introduction

Alzheimer's disease (AD) is an irreversible degenerative disease of the central nervous system. Mild cognitive impairment (MCI) is considered the prodromal stage of AD, mainly manifested as memory or cognitive impairment (1). Epidemiological studies have shown that the prevalence of MCI in people over 65 years is 10–20% worldwide (2). It is estimated that if the onset of AD is delayed by 5 years, the overall prevalence of AD would be reduced by ∼50%, thereby significantly reducing the burden on caregivers and institutional care and improving their quality of life (3). The conversion rate of MCI to AD is as high as 32% over 5 years and increases significantly with time (4). Currently, MCI is considered a critical window for the early intervention and rehabilitation of dementia, which can effectively delay the progression to AD (5). Therefore, finding appropriate interventions to improve the cognitive function of MCI and thus reduce the conversion rate of dementia is a major scientific problem that needs to be solved in the field of geriatric health (6).

However, there is a lack of high-quality evidence to support the efficacy of drug interventions in patients with MCI (7). Some drugs have been clinically validated for dementia; however, they have not been shown to improve cognitive function in patients with MCI (8). Thus, the use of non-pharmacological therapies to improve cognitive function in patients with MCI is receiving increasing attention (9).

As MCI causes several intricate neurophysiological abnormalities, comprehensive rehabilitation may be more effective in treating patients with MCI. Recent systematic evaluations support the efficacy of non-invasive brain stimulation (10) and physical exercise (11) on cognitive function in patients with MCI. In 2018, the American Academy of Neurology updated its MCI guidelines to include physical activity as an official recommendation for MCI intervention for the first time (7). A growing number of reviews have highlighted the possibility of combining physical exercise with non-invasive brain stimulation, suggesting that this combination is beneficial for improving cognitive function (12).

A meta-analysis of Tai Chi, a traditional Chinese aerobic exercise, showed a positive effect on improving global cognitive, executive, and memory functions in patients with MCI (13, 14). According to clinical research, 6 months of Tai Chi practice may dramatically enhance test results for memory in older individuals with MCI (15). Moreover, Tai Chi training is helpful for enhancing global cognition, memory, and executive function in older individuals with MCI (16).

Transcranial direct current stimulation (tDCS) is increasingly used as a non-invasive brain stimulation technique to promote functional brain rehabilitation (17). Studies have found that tDCS stimulation of the dorsolateral prefrontal cortex (DLPFC) is effective in improving memory function performance in MCI (18, 19), controlling neurotransmitter release, enhancing synaptic connections, affecting local hemodynamics, and selectively exciting and inhibiting cortical neural activity (20). A randomized controlled trial in which participants received a 4-month tDCS combined with an aerobic exercise intervention showed significant improvements in several cognitive domains compared with both techniques alone (21).

Therefore, we hypothesized that Tai Chi combined with tDCS is beneficial for improving the cognitive function of patients with MCI; however, no targeted studies have confirmed the effect of Tai Chi combined with tDCS on improving the cognitive function of patients with MCI. Therefore, we designed a randomized controlled trial to evaluate the effect of Tai Chi combined with tDCS on cognitive function in patients with MCI.

Methods

Design and ethical approval

In this randomized clinical trial, all patients signed an informed consent form before the intervention. The study protocol was reviewed and approved by the Ethics Committee of the Affiliated Rehabilitation Hospital of the Fujian University of Traditional Chinese Medicine (FJTCM) (No. 2017KY-010-02). FJTCM was responsible for the integrity and conduct of this study. The trial was prospectively registered in the Chinese Clinical Trial Registry (ref. ChiCTR1800015629).

Recruitment and screening

Between April 2018 and February 2020, we recruited participants with MCI from the community in Fuzhou City by posting posters, sending leaflets and brochures, and setting up a recruiting station at the community center. Potential participants first completed a screening questionnaire aimed at assessing their cognitive function to determine their eligibility for the study.

Sample size

The Montreal Cognitive Assessment (MoCA) score was used as the main indicator of this effect. Referring to the results of previous studies on the effects of Tai Chi and tDCS on cognitive function in patients with MCI, the predicted sample loss rate was ∼20%. Using G-Power software with the effect size set at 0.3, power set at 0.8, and α set at 0.05, the calculated required sample size was at least 180 participants.

Participants

Inclusion and exclusion criteria

The inclusion criteria were as follows: participants (1) who met the diagnostic criteria of MCI; (2) with $18 < \text{MoCA score} < 26$; (3) who aged between 50 and 75 years; and (4) did not engage in regular exercise in the last 6 months. The exclusion criteria were as follows: participants (1) with the presence of medical conditions that made exercise unsafe or an inability to exercise (such as patients with uncontrollable blood pressure and hypertension); (2) with a history of severe alcohol and drug abuse; (3) with Baker Depression Inventory (BDI) ≥ 10; (4) with cognitive impairment caused by other reasons; (5) having a history of mental illness (such as personality disorder and schizophrenia), or suffering from

severe aphasia, audiovisual impairment, or severe organ failure (such as severe heart failure, respiratory failure, liver failure, and renal failure), history of musculoskeletal system diseases (such as myasthenia gravis, congenital myotonia, fractures, suppurative arthritis, etc.), other motor contraindications (such as unstable angina pectoris, aortic stenosis, etc.), systemic infection, etc.; and (6) who participated in other experiments that influence this study.

Randomization and masking

The random grouping sequence of the participants in this study was generated by dedicated statistical staff using Statistical Package for the Social Sciences (SPSS) Statistics 20.0 (IBM, Chicago, IL, USA). Random grouping sequences were stored in a light-impermeable sealed envelope. A total of 180 eligible participants with MCI were randomly assigned into the Tai Chi combined with tDCS group (TCT), Tai Chi combined with sham tDCS group (TCS), walking combined with tDCS (WAT), and walking combined with sham tDCS group (WAS) in order of inclusion. Although blinding is not possible for participants in exercise intervention research, the staff collecting the outcomes and data analysts will have no knowledge of the group assignment. Blinding was performed after the statistical analysis of the study was completed.

Intervention

All participants with MCI received health education on the etiology and prevention of cognitive impairment prior to the intervention. Health education includes topics, such as MCI and Alzheimer's disease prevention and treatment, as well as the promotion of healthy lifestyles.

Tai Chi combined with the tDCS group

Participants in the TCT group underwent a 12-week, 24-form Tai Chi training program combined with tDCS. tDCS was performed during the first 20 min of Tai Chi training.

(1) Tai Chi exercise: The interventions included three 1-h Tai Chi training sessions per week. Certified instructors delivered Tai Chi training with at least 5 years of experience in directing their respective interventions.

(2) tDCS stimulation: The anode of tDCS (The Brain Stimulator v3.0 Deluxe tDCS Kit) was placed over F4 (in EEG 10–20 standard system) with the long axis of the pad pointing toward the vertex of the head. The cathode electrode was positioned over the contralateral eyebrow (Fp1 EEG electrode site, also referred to as the supraorbital position) with the long axis of the pad parallel to the horizontal plane. The electrode assembly consists of two square-shaped electrodes (3 mm × 3 mm). Electrode preparation will involve saturating a sponge electrode with exactly 10 cc of 0.9% saline solution using a marked syringe (5 cc/side) to provide adequate electrode saturation without oversaturation. The same batch of adjustable cross straps is used to secure the sponge pieces and is regularly replaced. Impedances were kept equal to or below 6 kΩ during the whole stimulation session. For the active condition, the current was ramped up to 2.0 mA over 30 s, remained at 2.0 mA for 19 min, and ramped down to 0 mA over 30 s.

Tai Chi combined with the sham tDCS group

The participants in the TCT group participated in a 12-week 24-form Tai Chi program combined with sham tDCS. Tai Chi training was consistent with those in the TCT group. In the sham tDCS condition, the current was initially ramped up to 2 mA over 30 s and immediately ramped down to 0 mA to prevent the actual stimulation of the target region.

Walking combined with the tDCS group

The WAT group underwent fitness walking training combined with tDCS for 12 weeks. The exercise intensity was 50–70% of the maximum heart rate for three 1-hour weekly sessions. The tDCS stimulation site, intensity, and duration were consistent with the TCT groups. tDCS was performed during the first 20 min of fitness walking training.

Walking combined with the sham tDCS group

Participants in the WAS group underwent a 12-week fitness walking training program combined with sham tDCS. Fitness walking training was consistent with the WAT group. In the sham tDCS condition, the current was initially ramped up to 2 mA over 30 s and immediately ramped down to 0 mA to prevent the actual stimulation of the target region.

During the treatment of true and sham tDCS, we have researchers who monitor the entire process, record the subjects' sensations, such as numbness, itching, tingling, and pain felt during treatment at the stimulation site, and report adverse events on time.

Outcome measures

The outcomes will be assessed at baseline and after 12 weeks of intervention. Examinations were conducted in accordance with a uniform implementation plan and standard operating procedures.

Primary outcomes

The MoCA and Chinese Wechsler Memory Scale-Revised Memory Quotient (MQ) were used to assess global cognition and memory functions, respectively. The MoCA scores range from 0 to 30, with higher scores indicating better cognitive function. The MQ has a score range of 51 to 150, with higher scores indicating better memory.

Secondary outcomes

The secondary outcomes included other cognitive subdomain tests performed from baseline to 12 weeks. The episodic memory was assessed using the auditory–verbal learning test (AVLT), while the visual memory function was evaluated using the Rey–Osterrieth complex figure (ROCF). The executive function was assessed using the color-word matching Stroop test, while the attention function was assessed using the Test of Attentional Performance (TAP) (V.2.3, Vera Fimm, Psychologische Testsysteme), which included divided attention (auditory reaction time and visual reaction time), sustained attention, and digit-symbol coding (DSC) tasks.

Statistical analysis

Data were analyzed using SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA). The categorical data were tested using the chi-square test or Fisher's exact test as appropriate. We performed a Shapiro–Wilk test to check the normality of the continuous variables. For data with a normal distribution, one-way analysis of variance (ANOVA) was used to compare baseline characteristics, and the analysis of covariance (ANCOVA) was used to compare post-intervention changes across the four groups, with age (years) and education (years) as covariates. If there is a statistically significant difference between groups for a certain indicator prior to intervention, this indicator will be included as a covariate in the analysis after intervention. *Post hoc* analysis with Šídák correction was used to explore between-group differences. For non-normally distributed continuous data, we used the Kruskal–Wallis test to compare group differences. Differences were considered statistically significant at a p-value of < 0.05.

Results

Descriptive data

Overall, 1,889 subjects were recruited for this study from April 2018 to February 2020. Ultimately, a total of 180 eligible subjects were randomly divided into four groups: (i) TCT group; (ii) TCS group; (iii) WAT group; and (iv) WAS group. The flow diagram for this trial is presented in Figure 1.

In total, 30 participants withdrew from the study, of which 7, 6, 9, and 8 withdrew from the TCT, TCS, WAT, and WAS groups, respectively. There was no significant difference in the dropout rate among the four groups ($P \geq 0.05$). Randomly grouped participants were included in an intention-to-treat (ITT) analysis. The baseline characteristics of the study participants are presented in Table 1.

Primary outcomes

After 12 weeks of intervention, there were statistically significant differences in MoCA scores between groups ($P < 0.001$, F (3,174) = 7.415) (Table 2); furthermore, *post-hoc* analysis showed that TCT was more effective compared with TCS, WAT, and WAS ($P = 0.012$, $P = 0.032$ and $P < 0.001$, respectively) and compared to WAS, the TCS and WAT groups showed higher scores (Figure 2A).

We added the pre-intervention MQ scores to the covariates for the analysis. The results showed a statistically significant difference among the four groups ($P = 0.015$, F (3,173) = 3.584) (Table 2), and *post-hoc* analysis showed that TCT was more effective than TCS, WAT, and WAS ($P = 0.022$, $P = 0.024$, and $P = 0.002$, respectively) (Figure 2B).

Secondary outcomes

In the AVLT test, the scores of AVLT-immediate recall showed statistically significant differences among the four groups ($P = 0.025$, F (3,174) = 3.207) (Table 2), and a *post-hoc* analysis showed that the score of TCT was higher than that of TCS and WAT ($P = 0.013$ and $P = 0.032$, respectively), and the score of WAS higher than TCS ($P = 0.032$) (Figure 2C).

In the Stroop test, the reaction time of the Stroop test color showed statistically significant differences among the four groups ($P = 0.035$, F (3,174) = 2.938) (Table 2), and a *post-hoc* analysis showed that the reaction time of TCT was shorter than that of WAT and WAS ($P = 0.008$ and $P = 0.022$, respectively) (Figure 2D).

In the TAP test, the auditory reaction time showed no statistically significant differences among the four groups ($P = 0.050$, F (3,174) = 2.660) (Table 2), while the visual reaction time showed statistically significant differences among the four groups ($P = 0.004$, F (3,174) = 4.536) (Table 2), and a *post-hoc* analysis showed that the reaction time of TCT was shorter than that of TCS ($P = 0.007$), and the reaction time of TCS was higher than that of WAT and WAS ($P < 0.001$, and $P = 0.006$, respectively) (Figure 2E). The sustained attention time showed statistically significant differences among the four groups ($P = 0.015$, F (3,174) = 3.609) (Table 2), and a *post-hoc* analysis showed that the reaction time of WAT was higher than that of TCT and TCS ($P = 0.007$, $P = 0.003$, respectively) (Figure 2F). The DSC reaction time showed statistically significant differences among the four groups ($P < 0.001$, F (3,174) = 7.846) (Table 2), and a *post-hoc* analysis showed that the reaction time of TCT was shorter than that of TCS, WAT, and WAS ($P < 0.001$, $P < 0.001$, and $P = 0.004$, respectively) (Figure 2G).

In the ROCF-copy trial test, no statistically significant differences were seen between the four groups ($P = 0.062$, F (3,174) = 2.489). In the ROCF-recall trial test, no significant differences were seen between the four groups ($P = 0.635$, F(3,174) = 0.571).

Discussion

To the best of our knowledge, this is the first study to focus on the effects of Tai Chi exercise combined with tDCS on cognitive function in patients with MCI. Among patients with MCI, Tai Chi combined with tDCS was more effective than the other three groups in terms of MoCA, MQ scores, and DSC after 12 weeks of intervention. The results of this study suggest that Tai Chi combined with tDCS improves global cognitive function, memory, and attention in patients with MCI.

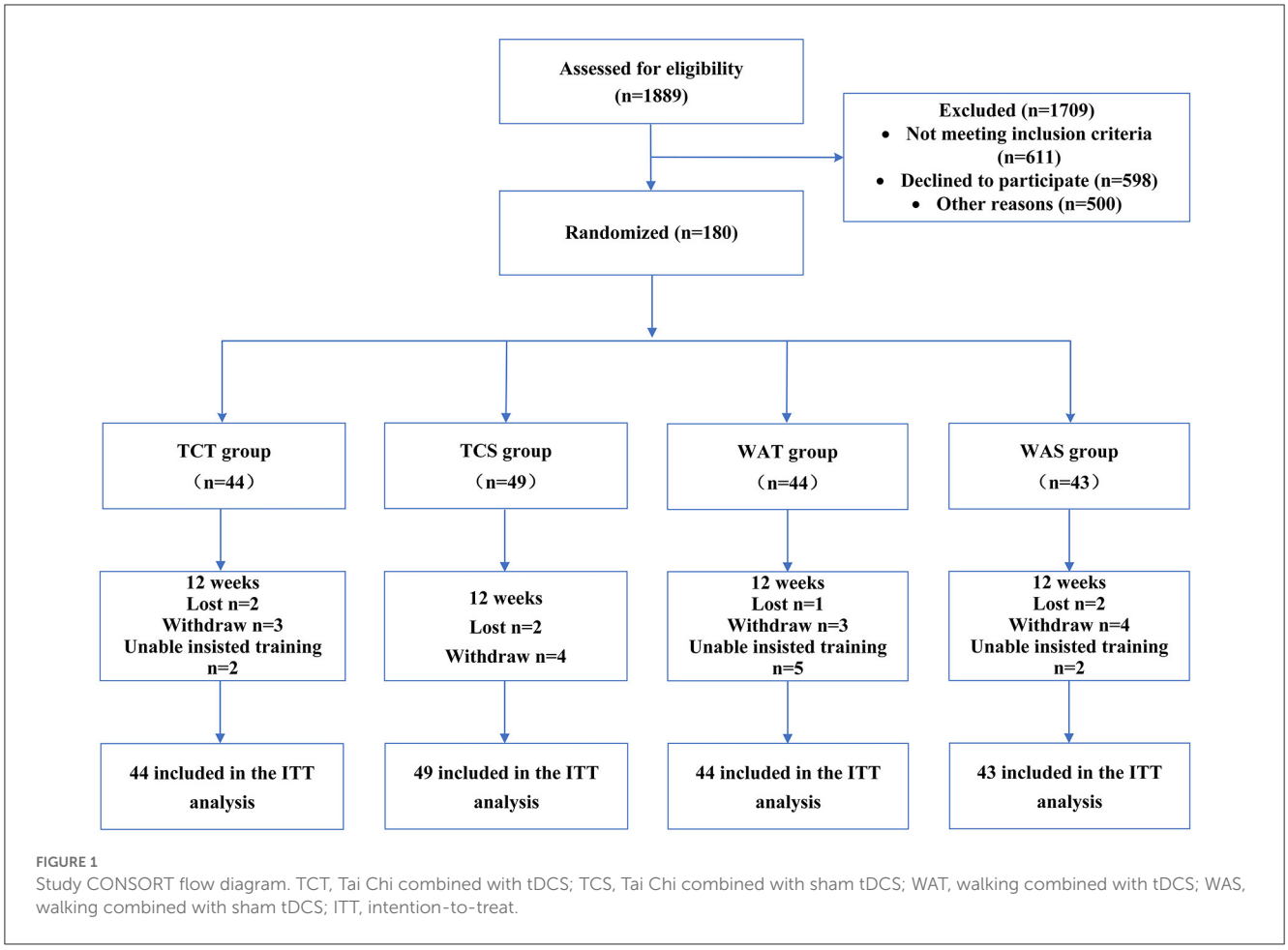

FIGURE 1
Study CONSORT flow diagram. TCT, Tai Chi combined with tDCS; TCS, Tai Chi combined with sham tDCS; WAT, walking combined with tDCS; WAS, walking combined with sham tDCS; ITT, intention-to-treat.

TABLE 1 Baseline characteristics of participants.

Characteristics	TCT group ($n = 44$)	TCS group ($n = 49$)	WAT group ($n = 44$)	WAS group ($n = 43$)	F/Z/χ^2	*P*-value
Age, years	59 [8.75]	61 [8.5]	63 [12.75]	58 [8]	−1.921	0.278[b]
Gender (male/female)	12/32	19/30	21/23	17/26	3.950	0.267[a]
Education duration, years	9.5 [3.75]	9 [5]	9 [4]	9 [4]	−0.598	0.228[b]
BMI, (Kg/m^2)	22.69 [3.44]	23.78 [3.59]	23.94 [3.47]	24.34 [3.75]	−0.646	0.059[b]
BDI	5.5 [5.75]	5 [5.5]	4 [3.75]	5 [4]	−0.098	0.427[b]

SD, standard deviation; IQR, interquartile range; TCT, Tai Chi combined with tDCS; TCS: Tai Chi combined with sham tDCS; WAT, walking combined with tDCS; WAS, walking combined with sham tDCS; BMI, body mass index; BDI, Baker Depression Inventory.
Data are presented as mean±SD or median [IQR].
[a]Using chi-square test.
[b]Using Kruskal–Wallis test.

Currently, most published tDCS studies on patients have focused on the combination of tDCS technology and cognitive training (22). Only one small-sample study has investigated a combination of tDCS and Tai Chi exercises (23). This study observed the comprehensive effects of Tai Chi combined with tDCS on the dual-task gait performance and cognitive function in patients with MCI and found that 12 weeks of Tai Chi combined with tDCS were superior to Tai Chi combined with sham tDCS in improving the dual-task gait. However, the cognitive function results were not significant after correction. In contrast, our study showed a significant improvement in the cognitive function of patients with MCI after 12 weeks of Tai Chi combined with tDCS. The reason for this difference may be the relatively small sample size (20 cases) of the previous study, which may not have demonstrated the effectiveness of Tai Chi combined with tDCS technology in improving cognitive function.

The results of our study showed that, in terms of global cognitive function, the TCT was more effective than the TCS, WAT, and WAS. There was no significant difference between TCS and WAT, although TCS and WAT showed a more significant

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TABLE 2 Comparison of outcomes among groups.

Characteristics	TCT group ($n = 44$)	TCS group ($n = 49$)	WAT group ($n = 44$)	WAS group ($n = 43$)	F/Z	*P*-value
Primary outcomes						
MoCA						
Baseline	23.5 [3]	22 [3]	22.5 [3]	22 [3]	−0.095	0.924[b]
12 weeks	25 [2.83]	25 [2]	24.24 [1.61]	23.66 [2.1]	7.415	**<0.001**[c]
MQ						
Baseline	97.02 ± 11.84	91.80 ± 15.57	87.41 ± 16.14	91.02 ± 13.07	3.376	**0.020**[a]
12 weeks	108 [17]	100 [16.66]	95.91 [19.01]	99 [18]	3.584	**0.015**[c]
Secondary outcomes						
AVLT-learning score						
Baseline	19.07 ± 4.88	18.16 ± 5.67	19.48 ± 4.87	19.37 ± 5.03	0.637	0.592[a]
12 weeks	21.90[6.75]	21 [7]	21.80 [3.75]	22.26 [7]	2.557	0.057[b]
AVLT-IR						
Baseline	6.5 [4]	6 [4]	5 [5]	6 [3]	−1.005	0.315[b]
12 weeks	7.24[4.75]	6[5]	5.65[4.25]	7.99[3.16]	3.207	**0.025**[c]
AVLT-DR						
Baseline	12 [4]	12 [3]	12 [3]	12 [2]	−0.878	0.380[b]
12 weeks	13[3]	12[3.86]	12.58 [2.73]	12[2.66]	1.130	0.338[c]
ROCF-copy trial						
Baseline	32 [4.75]	33 [4]	32 [5.5]	34 [4]	−1.659	0.097[b]
12 weeks	33.5 [4.43]	34 [3.5]	32 [4.93]	34 [3.87]	2.489	0.062[c]
ROCF-recall trial						
Baseline	15.48 ± 6.62	14.66 ± 7.78	14.41 ± 5.82	16.19 ± 6.86	0.620	0.603[a]
12 weeks	18[8]	17 [8.09]	15 [10.81]	16.78 [11]	0.571	0.635[c]
Stroop test color, ms						
Baseline	17.02 [7.61]	18.94 [8.17]	20.43 [8.54]	19 [7.11]	−0.262	0.793[b]
12 weeks	16.81 [5.51]	18.43 [8.04]	19.17 [5.36]	18.84 [6.9]	2.938	**0.035**[c]
Stroop test word, ms						
Baseline	22.64 [8.02]	23.46 [7.92]	26.16 [10.78]	22.79 [6.8]	−0.305	0.760[b]
12 weeks	22.18 [6.36]	21.92 [6.90]	23.87 [10.09]	23.77 [7.74]	2.505	0.061[c]
Stroop test color-word, ms						
Baseline	38.59 [10.78]	34.7 [13.68]	36.43 [8.71]	34.16 [11.59]	−0.372	0.710[b]
12 weeks	32.78 [15.35]	33.14 [10.74]	34.13 [12.90]	34.12 [8.73]	0.058	0.982[c]
Auditory reaction time, ms						
Baseline	696 [137]	740 [222]	730.22 [216.45]	766 [137]	−0.966	0.334[b]
12 weeks	704 [179.5]	738 [283.69]	808.58 [373.62]	795 [203.51]	2.660	0.050[c]
Visual reaction time, ms						
Baseline	940.34 [215.5]	1010 [239.31]	1048.5 [287.25]	1010 [247]	−0.579	0.563[b]
12 weeks	938.29 [180.58]	1076 [327.97]	941.75 [260.57]	965.82 [156]	4.536	**0.004**[c]
Sustained attention time, ms						
Baseline	420.96 [74.5]	430 [123.5]	471.22 [101.08]	454 [95]	−0.978	0.328[b]

(Continued)

TABLE 2 (Continued)

Characteristics	TCT group ($n = 44$)	TCS group ($n = 49$)	WAT group ($n = 44$)	WAS group ($n = 43$)	F/Z	*P*-value
12 weeks	442.59 [105.34]	447.27 [140.54]	498.5 [102.70]	458.75 [81]	3.609	**0.015**[c]
DSC reaction time, ms						
Baseline	330.25 [104.25]	335.5 [161.75]	393.66 [126.37]	360.84 [104]	−1.029	0.303[b]
12 weeks	308.65 [83.04]	415.88 [213.94]	421.64 [153.56]	380 [144.52]	7.846	**<0.001**[c]

SD,standard deviation; IQR, interquartile range; ANOVA, analysis of variance; TCT, Tai Chi combined with tDCS; TCS, Tai Chi combined with sham tDCS; WAT, walking combined with tDCS; WAS: walking combined with sham tDCS; MoCA, Montreal Cognitive Assessment; MQ, memory quotient; AVLT-IR, auditory verbal learning test-immediate recall; AVLT-DR, auditory verbal learning test-delayed recall; ROCF, Rey–Osterrieth complex figure; DSC, digit-symbol coding task.
Data are mean ± SD or median [IQR]. Bold text indicates a *P*-value of < 0.05.
[a]Using one-way ANOVA.
[b]Using Kruskal–Wallis.
[c]Using ANCOVA.

improvement than WAS. As an aerobic exercise, Tai Chi induces functional neuroplastic changes in the brain, which prepares tDCS to target and regulate local brain areas (20). Improvement in cognitive function with Tai Chi is a gradual process. Therefore, it is believed that combining the two may have stronger effects on cognitive improvement by stimulating local neural networks in the brain in a more targeted and focused manner and by promoting brain neuroplasticity.

Furthermore, when compared to walking, Tai Chi calls for subjects to pay more attention to the exercise process, the purpose of following their bodies, and the ability to notice tiny changes in their bodies and minds as they perform complicated moves. This may be one of the reasons why Tai Chi combined with tDCS is more beneficial for improving cognitive function in patients with MCI. Therefore, we believe that Tai Chi combined with tDCS may be more effective in improving global cognitive function.

Regarding the memory function assessment, the MQ scores of the Tai Chi combined with the tDCS group were significantly higher than those of the other three groups. This suggests that Tai Chi combined with tDCS has a positive effect on memory function in patients with MCI, which is consistent with the findings of previous studies. Ward et al. (21) found that cognitive training combined with non-invasive brain stimulation significantly improved participants' learning and working memory scores compared to cognitive training alone in a study of 318 healthy adults over 48 sessions over 16 weeks, suggesting that the combined intervention could improve learning and memory function in adults.

Although the present study and Ward's (21) study differed in the population of the intervention and modality of the exercise, both found that the multimodal intervention significantly improved the memory function of the participants compared with the single intervention modality. This finding suggests that there may be a synergistic effect of the combined intervention program that facilitates the improvement of memory function in patients with MCI and may provide a reference for future studies to improve memory function in patients with MCI.

Attention is the basis of memory production and is closely related to other cognitive domains (24). However, the process of attentional impairment in patients with MCI is subtle and is typically accompanied by decreases in other cognitive domains, including memory function (25). Several studies have shown that aerobic exercise improves attention in patients with mild cognitive impairment. According to a meta-analysis of 632 participants, Tai Chi can help normal older persons improve cognitive function in several areas, including attention (26). In another randomized controlled study on the effects of tDCS on attention, 26 subjects received tDCS/sham tDCS stimuli in the right posterior parietal cortex and underwent attentional network tests before and after the intervention, showing that tDCS significantly improved the subjects' orienting performance of attentional functions compared with pseudo-stimuli, whereas executive control effects were not affected (27). In this study, the subjects' attention was assessed using TAP 2.3, an attention test system. The results of this study showed that the Tai Chi combined with the tDCS group had significantly higher sustained attention scores than the other three groups, indicating that Tai Chi combined with tDCS is more beneficial for improving the attention of patients with MCI.

An increasing body of research indicates that tDCS and aerobic exercise have synergistic effects, whereby aerobic exercise causes neuroplastic changes across the brain, intensifies local targeting of tDCS to the brain, and improves cognition (20, 28). Aerobic exercise encourages the production of neurotrophic factors, boosts neurogenesis and synaptogenesis, and delays cognitive impairment. Non-invasive brain stimulation integrates regenerated neural regions into functional brain circuits. Consequently, multimodal therapies emphasizing functional compensatory mechanisms can help enhance cognitive performance in individuals with cognitive decline and promote neurological compensation. Studies have shown that the combination of tDCS and aerobic exercise has beneficial effects (29, 30). Anodal tDCS stimulation of the prefrontal cortex combined with aerobic exercise improves cognitive function (24). In this study, Tai Chi as a moderate-intensity aerobic exercise combined with tDCS had a more positive effect in improving the global cognitive function, memory function, and attention compared to TCS, WAT, and WAS, and the results support the above view.

This study used a strict randomized controlled approach and strengthened quality control during the intervention to minimize possible bias with the aim of providing reliable clinical evidence. However, this study has some limitations. First, the implementation site of this study was mainly outdoors, making it impossible to avoid the effect of rain on Tai Chi and walking training. Although subjects were asked to practice at home on their own,

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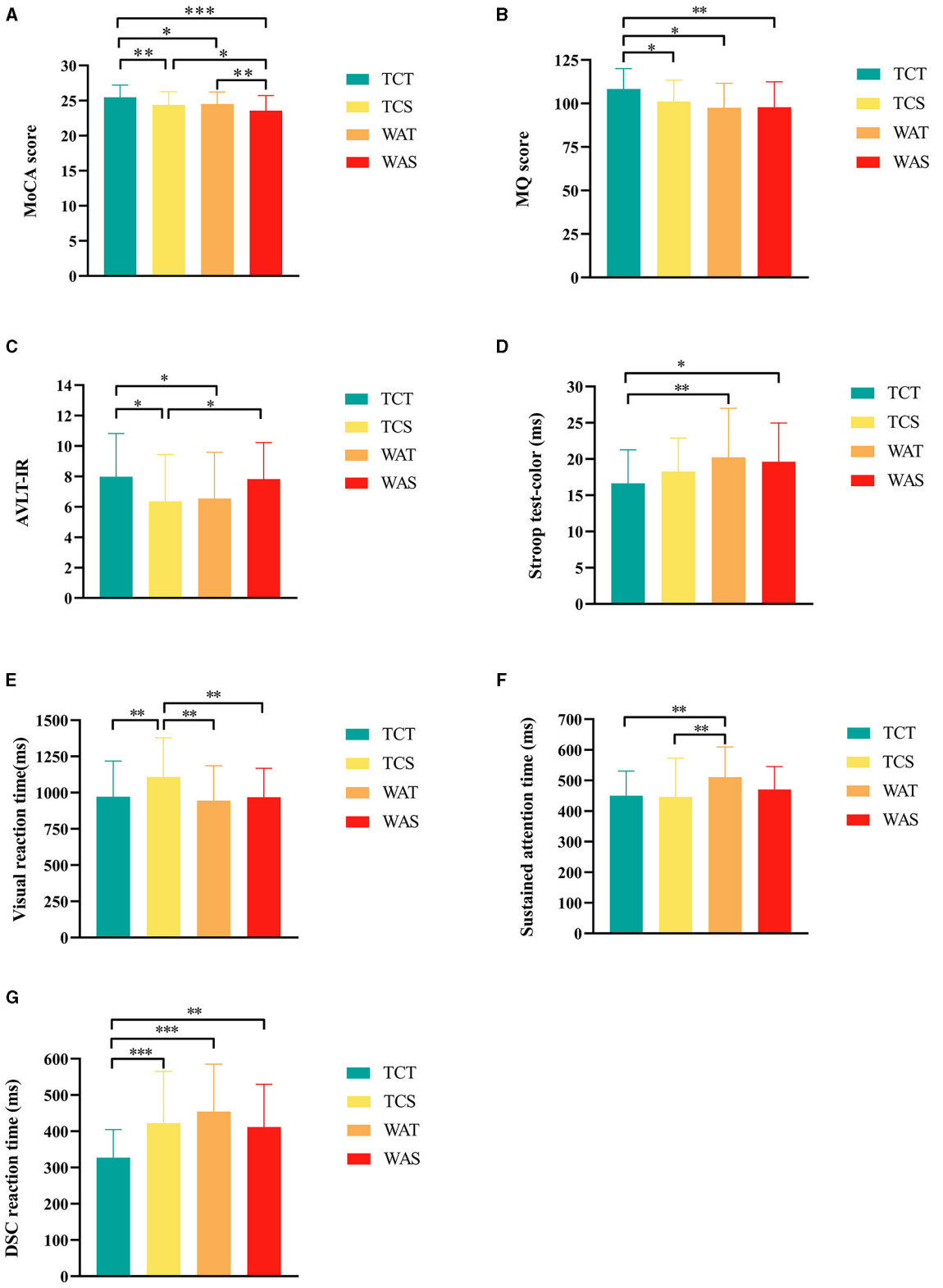

FIGURE 2
Further *post-hoc* analysis results of outcomes among the groups. **(A)** Montreal Cognitive Assessment (MoCA) score, **(B)** memory quotient (MQ) score, **(C)** auditory verbal learning test-immediate recall (AVLT-IR), **(D)** Stroop test-color, **(E)** Visual reaction time; F, Sustained attention time, **(G)** digit-symbol coding task (DSC) reaction time. *indicate differences of a *P*-value of < 0.05, **indicate differences of a *P*-value of < 0.01, ***indicate differences of a *P*-value of < 0.001. TCT, Tai Chi combined with tDCS; TCS, Tai Chi combined with sham tDCS; WAT, walking combined with tDCS; WAS, walking combined with sham tDCS.

the efficiency of the intervention was inevitably affected. Second, no follow-up study was conducted, and whether there is a long-term effect of Tai Chi combined with tDCS remains to be explored. Future large-scale, well-conducted, randomized controlled trials with appropriate comparison groups and follow-up arrangements are required to evaluate the long-lasting effects of Tai Chi combined with tDCS on cognitive health.

Conclusion

This study found that Tai Chi combined with tDCS was more beneficial in improving the global cognitive function, memory function, execution function, and attention in patients with MCI. These non-pharmacological interventions are easy to implement, time- and cost-effective, safe, and have no serious side effects. Therefore, we believe that Tai Chi combined with tDCS is an effective intervention for patients with MCI.

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 Ethics Committee of Rehabilitation Hospital Affiliated to Fujian University of Chinese Medicine. The patients/participants provided their written informed consent to participate in this study.

Author contributions

WL, JT, and JL contributed to the conception, the design of the study, and revised the manuscript. JL, ZL, and JH were responsible for coordinating and monitoring the process. YX and JZ performed the statistical analysis and wrote the first draft of the manuscript. HL, ZQ, and MW managed the recruitment and data analysis. All authors contributed to the manuscript revision, read, 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.

Publisher's note

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Correlation among sleep quality, physical frailty and cognitive function of the older adults in China: the mediating role

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Objective: To explore the correlation among sleep quality, physical frailty, and cognitive function in the older adults in community, and to explore the mediating role of sleep quality.

Methods: A total of 1,182 community-based older adults were investigated with frailty phenotype (FP), Pittsburgh sleep quality index (PISQI), Montreal cognitive assessment (MoCA) and self-made general information questionnaire.

Results: The incidence of physical frailty among the older adults in the community was 25.8% and the incidence of cognitive decline was 19.5%. Cognitive function was negatively correlated with physical frailty ($r = -0.236$, $p < 0.01$) and sleep quality ($r = -0.558$, $p < 0.01$). Sleep quality was positively correlated with physical frailty ($r = 0.337$, $p < 0.01$).

Conclusion: The physical frailty of the older adults has a direct prediction effect on cognitive function, and is regulated by the mediating role of sleep quality. Sleep quality partially mediates the relationship between cognitive dysfunction and physical frailty, which is a new insight into the study of cognition and physical frailty in the older adults. In the future, we can take measures to improve the sleep quality of the older adults, so as to reduce the occurrence of cognitive dysfunction and physical frailty of the older adults.

KEYWORDS

community, the older adults, physical frailty, sleep quality, cognitive function

1. Introduction

Auyeung et al. study found physical frailty was associated with cognitive decline over four years period (1). Physical frailty is a state of increased vulnerability and reduced responsiveness to stressors, which can lead to fall, hospitalization, disability, and mortality (2). Cognitive function is a process in which individuals actively understand the world through psychological activities after contact with the outside world, including memory and delayed memory, attention, language, execution and other fields. When

damage occurs in one or more fields, it is cognitive dysfunction, which will affect the social function and quality of life of individuals to different degrees. In severe cases, it may even lead to death (3). Changes in cognitive function are associated with physical frailty, with the growth of age, the older adults will inevitably face a series of decline and loss of body function (4). Therefore, the prevention and early treatment of cognitive decline and physical frailty have important scientific and social significance.

The research by Brigola et al. (5) showed that physical frailty was a strong risk factor for cognitive decline in the older adults. The cognitive ability of the frailty older adults was lower than that of the non-frailty older adults. Canevelli et al. (6) found in their research that decreased cognitive function also increases the risk of physical frailty, and older adults with decreased cognitive function or dementia are more likely to be frailty. Physical frailty and cognitive decline in the same older adults often occur together, and their incidence increases with age (2). Studies have shown that cognitive decline can be predicted by physical frailty, and the risk of cognitive decline in the older adults with physical frailty will be increased (7). Longitudinal studies abroad have found that the cognitive function of the older adults with physical frailty declines faster than that of the non-physical frailty older adults. However, the underlying mechanism of the relationship between physical frailty and cognitive function remains unclear.

One possible mechanism is somnipathy, which is a common physiological state in the older adults, which seriously affects the quality of life of the older adults and increases the incidence of physical frailty to a certain extent (8). In recent years, sleep disorder, as a risk factor for physical frailty, has gradually attracted extensive attention by researchers (9). According to statistics, the prevalence of sleep disorders in the older adults aged 60 and over is 42.3% (10). At the same time, the prevalence of sleep disorders in patients with cognitive decline is also high. Sleep disorders not only accelerate cognitive decline and lead to an increase in the mortality rate, but also increase the economic and psychological burden of caregivers (11).

Sleep disorders, physical frailty and cognitive decline are common among the older adults and are often overlooked. Although they are not directly life-threatening, their long-term existence can lead to an increased risk of dementia in the older adults, affect the quality of life of the older adults, and have an interaction with the health status of the older adults (12). At present, the relationship between sleep quality and cognitive function and physical frailty of the older adults is still unclear.

Most previous studies focused on the relationship between cognitive function and physical frailty, but few studies explored the potential mechanism of this relationship. In order to make up this gap, this study aims to explore the mediating role of sleep disorder in the relationship between cognitive function and physical frailty of the older adults in the Chinese community. To this end, we have the following specific goals. First, we will determine the prevalence of frailty and cognitive impairment among the older adults in the Chinese community. Secondly, we will study the relationship between sleep disorder, cognitive function and physical frailty of the older adults. Finally, we will verify the mediating role of sleep disorder between cognitive function and physical frailty.

2. Methodology and methods

2.1. Sampling method

In this study, stratified cluster sampling was used to investigate the older adults in the community in China. According to the economic development level of each district and county, we randomly divided three districts, five counties and one county-level city in Yancheng City, Jiangsu Province, China into three groups. Using random table method, each group selects one district and county, each district and county randomly selects two streets, and each street randomly selects two communities. A total of 12 communities were investigated, and the older adults who met the inclusion criteria in this community were investigated. The sample collection time of our study is from May 1st to June 1st, 2022.

2.2. Participants

Inclusion criteria: ① Age ≥ 60 years old; ②Informed consent and voluntary participation in research. Exclusion criteria: ① severe cognitive impairment; ② those with severe hearing and hearing impairment; ③ Those who have serious diseases and cannot cooperate. All participants obtained informed consent and signed the informed consent form. At the same time, this research was approved by the Ethics Review Committee of China Shanghai University of Medicine & Health Sciences (no. 2021-SMHC-01-015).

2.3. Survey method

We will take 12 community health service centers sampled by stratified cluster as survey sites, and each service center will set up an office as the survey point, and our investigators will conduct a unified questionnaire survey on the older adults in the community who meet the requirements. We have five investigators, including one attending doctor, two nurses and two graduate students, who passed the unified training before taking part in this study. The training content includes the definitions and standards of sleep, physical frailty and cognition, as well as matters needing attention in the process of sample collection. A total of 1,200 older adults in the community were investigated in this study. Among them, 18 older adults refused to cooperate with the investigation midway, and 1,182 older adults were eligible for the study.

2.4. Instruments and measurements

1. General information questionnaire: including gender, age, marital status, length of education, exercise, intellectual activity, social contact, fall history, and live in solitude, etc.
2. Montreal cognitive assessment (MoCA): this phenotype was prepared by Nasreddine et al. (13), in 2004 and included seven items, which were as follows: ① visuospatial skills; ② naming; ③ attention; ④ Language; ⑤ Abstraction; ⑥ Memory and delayed memory; ⑦ Calculation and orientation, the total score ranged from 0 to 30, and the higher the score, the better the cognitive function would be. A score of ≥26 indicates normal cognitive function and < 26 indicates cognitive decline. If the

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participant's educational year is less than 12, the total score will be increased by 1 point.

3. Frailty phenotype (FP): FP was proposed by Freid et al. (14), and includes five phenotypes, as follows: ① unexplained weight loss; ② Self-incriminating fatigue; ③ Slow walking speed; ④ weak grip strength; (5) less physical activity. Total score of 0 ~ 5, the higher the score, the more serious the frailty. Score ≥ 3 is considered frailty, score of 1 ~ 2 is considered pre-frailty, 0 points are considered no frailty.
4. Pittsburgh sleep quality index (PSIQ): PSIQ compiled by Buysse et al. (15). The scale consists of 18 self-rated items and consists of 7 components, including ① subjective sleep quality; ② sleep latency; ③ sleep duration; ④ sleep efficiency; ⑤ sleep disorder; ⑥ use of hypnotic drugs; ⑦ daytime dysfunction, the scores of each component are 0 ~ 3, and the total score is 0 ~ 21. The higher the PSIQ score, the worse the sleep quality.

2.5. Statistical analysis

The database was established using EpiData 3.1 software. All data were entered and checked by two people. If there was any disagreement between the two people, the third person would check the data. SPSS 25.0 software was used for statistical analysis. The Kolmogorov–Smirnov test was used to determine the normality of continuous variables. Measurement data subject to normal distribution were described with mean ± standard deviation (SD), and t test was used for inter-group comparison. The non-normal distribution was described by the median and quartile, and Mann–Whitney U test was used for inter-group comparison, the correlation between variables was analyzed by Spearman's correlation coefficient. Enumeration data were described by frequency and percentage, and inter-group comparison was performed by Chi-square test. PROCESS v4.1 was used to analyze the mediating role and the Bootstrap program in the software was used to test the mediating role of sleep quality in the relationship between physical frailty and cognitive function. A difference of $p < 0.05$ was statistically significant.

3. Results

The older adults in the community investigated in this study were aged 60–97, including 462 (39.09%) aged 60–70, 490 (41.46%) aged 70–80, 218 (18.44%) aged 80–90, and 12 (1.02%) aged over 90. Among them, 618 female (52.28%) and 184 unmarried (15.57%); 55 people (4.65%) have never received education. See Table 1 for other general information.

The incidence rate of physical frailty, cognitive decline and sleep quality among the older adults in our survey is 30.37, 19.54, and 11.68%, respectively. According to Spearman's correlation analysis, there is a significant negative correlation between MoCA score and FP score and PSQI score. There was a significant positive correlation between FP score and PSQI score. See Table 2 and Table 3 for details.

The total scores of cognition function from 0 to 30. ≥26 indicates normal cognitive function, and < 26 indicates cognitive decline. The Chi-square test showed that cognitive function was not significant for

TABLE 1 General information of 1,182 participants [*n* (%), *M* (P25, P75)].

Variable	Frequency (%)
Age	73 (67.79)
Gender	
Female	618 (52.28)
Male	564 (47.72)
Marital status	
Married	666 (56.35)
Unmarried	184 (15.57)
Divorce	162 (13.71)
Widowed	170 (14.38)
Years of education	
0	55 (4.65)
1–6	357 (30.20)
6–12	649 (54.91)
>12	121 (10.24)
live in solitude	
Yes	686 (58.04)
No	496 (41.96)
Exercise	
Never	242 (20.47)
Average 1–3 times/week	387 (32.74)
Average 3–6 times/week	278 (23.52)
Every day	275 (23.27)
Intellectual activity	
Yes	687 (58.12)
No	495 (41.88)
History of falls	
Yes	531 (44.92)
No	651 (55.08)
Social contact	
Yes	815 (68.95)
No	367 (31.05)

TABLE 2 Score of sleep quality and cognitive function and physical frailty.

Variable	*M* (P_{25},P_{75})	Score	Frequency	Percent (%)
MoCA score	27 (26,28)	26–30	951	80.46
		0–25	231	19.54
PSQI score	12 (9,14)	16–21	138	11.68
		11–15	586	49.58
		6–10	418	35.36
		0–5	40	3.38
FP score	2 (1,3)	3–5	359	30.37
		1–2	518	43.82
		0	305	25.80

Live in Solution ($p > 0.05$), but significant for Gender, Age, Marital status, Years of education, Exercise, Intellectual activity, social contact, history of falls, sleep quality and physical frailty ($p < 0.05$) (Table 4).

In the mediating role test, FP score has a significant influence relationship on MoCA score in Model 1 ($\beta = -0.390$, $p < 0.01$), indicating that the total effect is valid. In the test of model 2, FP score had a significant effect on PSQI score ($\beta = 0.348$, $p < 0.01$), while in the test of model 3, FP score had a significant effect on MoCA score ($\beta = -0.230$, $p < 0.01$), and sleep quality had a significant effect on cognitive function ($\beta = -0.460$, $p < 0.01$), therefore, the mediating role of sleep quality in the model is established, and it is part of the mediating role. See Table 5 and Figure 1 for details.

The mediating role of health responsibility in the model is tested by Bootstarp technology, and it can be seen that the indirect effect value is −0.510, and the 95% confidence interval (−0.352, −0.234) does not contain 0, which means that the indirect effect is established, so the sleep quality plays a significant mediating role in the model, and the confidence interval of the direct effect test results is (−0.510, −0.329). According to the calculation results of effect ratio, it can be seen that the effect ratio of sleep quality is 72% (Table 6).

TABLE 3 Correlation between sleep quality and cognitive function and physical frailty.

Variable	MoCA score	FP score	PSQI score
MoCA score	1		
FP score	−0.236**	1	
PSQI score	−0.558**	0.337**	1

TABLE 4 Comparison of cognitive function with different characteristics.

Variable		Cognitive function (%)		χ^2	p
		Decline	Normal		
Gender	Male	80 (34.63)	484 (50.89)	19.701	0.000**
	Female	151 (65.37)	467 (49.11)		
Age	60–70	69 (29.87)	393 (41.32)	31.635	0.000**
	70–80	106 (45.89)	384 (40.38)		
	80–90	47 (20.35)	171 (17.98)		
	>90	9 (3.90)	3 (0.32)		
Marital status	Married	81 (35.06)	585 (61.51)	59.566	0.000**
	Unmarried	62 (26.84)	122 (12.83)		
	Divorce	49 (21.21)	113 (11.88)		
	Widowed	39 (16.88)	131 (13.77)		
Years of education	0	42 (18.18)	13 (1.37)	188.947	0.000**
	1–6	108 (46.75)	249 (26.18)		
	6–12	81 (35.06)	568 (59.73)		
	>12	0 (0.00)	121 (12.72)		
Exercise	Never	98 (42.42)	144 (15.14)	128.193	0.000**
	1-3times/week	86 (37.23)	301 (31.65)		
	3-6times/week	5 (2.16)	273 (28.71)		
	Every day	42 (18.18)	233 (24.50)		
Intellectual activity	No	112 (48.48)	383 (40.27)	5.149	0.023*
	Yes	119 (51.52)	568 (59.73)		
Social contact	No	98 (42.42)	269 (28.29)	17.353	0.000**
	Yes	133 (57.58)	682 (71.71)		
History of falls	No	107 (46.32)	544(57.20)	8.896	0.003**
	Yes	124 (53.68)	407 (42.80)		
live in solitude	No	85 (36.80)	411 (43.22)	3.146	0.076
	Yes	146 (63.20)	540 (56.78)		
Sleep quality	Very good	0 (0.00)	40 (4.21)	343.430	0.000**
	Good	19 (8.23)	399 (41.96)		
	Not bad	108 (46.75)	478 (50.26)		
	Bad	104 (45.02)	34 (3.58)		
Physical frailty	No frailty	133 (57.58)	226 (23.76)	110.828	0.000**
	Pre-frailty	44 (19.05)	474 (49.84)		
	Frailty	54 (23.38)	251 (26.39)		

*$p < 0.05$; **$p < 0.01$.

4. Discussion

4.1. Comparison of cognitive function with different characteristics

The MoCA score ≥ 26 indicates normal cognitive function, and score < 26 indicates cognitive decline. The chi-square test showed that cognitive function was not significant for live in solution ($p > 0.05$), which was different from the results in previous studies (16). Previous studies have considered that living in solution is an independent risk factor for the cognitive decline in the older adults, which may be related to the better autonomy and self-care ability of the older adults living in solution. However, different cognitive functions showed significant differences in gender, age, marital status, years of education, exercise, intellectual activity, social contact, history of falls, sleep quality, and physical frailty ($p < 0.05$). With the increase of age, the cognitive function of the older adults inevitably declines, while the younger the age, the less the accumulation of β-amyloid protein in the brain, and the better the cognitive function of the brain, which is similar to the research results of Bae (17). Wada found that the longer the education time, the greater the total brain capacity of patients with mild cognitive impairment (MCI) (18). Although the education level of the older adults cannot be changed, they can learn through the acquired continuing education. For example, the older adults can take part in community universities for the older adults for further study when their own financial ability permits. Dong found in their research that exercise such as light housework helps the older adults maintain healthy cognitive function, and exercise is a protective factor for cognitive decline (19). The older adults with cognitive decline can be allowed to take appropriate physical activities to maintain their cognitive function. Su found that a healthy lifestyle with a wide range of interests is a protective factor for cognitive dysfunction (20). Therefore, the community should build a healthy and beneficial environment, cultivate the interests and hobbies of the older adults, and encourage the older adults to do whatever intellectual and physical activities they can at home. For the older adults in the

TABLE 5 Test results of mediating role by distribution regression method.

Model	Model 1		Model 2		Model 3	
Variable	MoCA score		PSQI score		MoCA score	
Notation	β	t	β	t	β	t
FP score	−0.390**	−14.558	0.348**	12.733	−0.230**	−9.120
PSQI score					−0.460**	−18.182
R^2	0.152		0.121		0.338	
Adjust R^2	0.152		0.120		0.337	
F	211.945**		162.134**		300.870**	

* $p < 0.05$; ** $p < 0.01$.

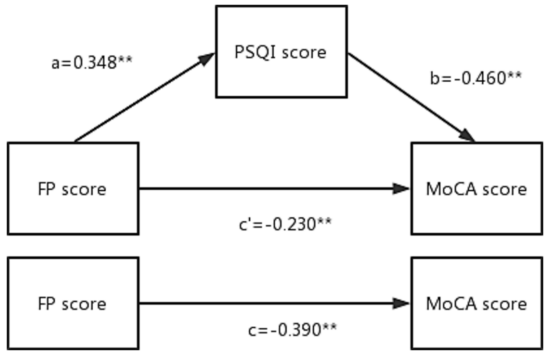

FIGURE 1
Mediating role test model diagram.

TABLE 6 Bootstrap test results.

Effect relation	Effect value	LLCI	ULCI	Proportion of effect
Total effect	−0.710	−0.806	−0.615	
Direct effect	−0.420	−0.510	−0.329	59%
Indirect effect	−0.510	−0.352	−0.234	72%

community, we can intervene in many aspects, such as exercising and cultivating hobbies, so as to prevent, detect and intervene cognitive decline early.

4.2. Status of sleep quality, physical frailty and cognitive function

A total of 1,182 older adults in the community were surveyed in this study. Pittsburgh's sleep quality scores ranged from 0 to 21, and those with PSQI scores ranging from 16 to 21 were considered to have poor sleep quality. In this study, 138 older adults with poor sleep quality accounted for 11.68%, which was consistent with some domestic research results (21). Sleep disorders will not only reduce the quality of life of the older adults, but also lead to or complicate physical and mental diseases and increase the risk of death. Therefore, the sleep problems of the older adults should be throughout our community care process. The incidence of physical frailty in this survey is 30.37%. The proportion of female physical frailty is higher than that of male. The main reason may be the rapid loss of estrogen in postmenopausal women, which has a negative impact on muscle strength, neuromuscular function and posture stability, leading to the increased incidence of senile female physical frailty. Among the older adults investigated in this study, 231 people (19.56%) have cognitive decline, which is lower than 31.3% reported by some domestic research institutes (22), which may be related to the differences of research subjects. Studies have also shown that cognitive function is related to educational level (23, 24). The older adults in this study have a relatively high educational level, so the detection rate of cognitive function decline is relatively low.

4.3. Correlation among sleep quality, physical frailty and cognitive function

Studies have pointed out that sleep quality is closely related to physical frailty and cognitive decline (25). This study found that the rate of cognitive decline of the older adults with poor sleep quality is higher than that of those with good sleep quality, and the rate of physical frailty of the older adults with poor sleep quality is also higher than that of the older adults with good sleep quality. According to Spearman correlation analysis, the correlation coefficient between FP score and MoCA score is −0.236, $p < 0.01$, which indicates that there is a significant negative correlation between physical frailty and cognitive function, that is, physical frailty may increase the risk of cognitive function decline, which is consistent with previous research results (26). Physical frailty may lead to the limitation of the older adults' activities and the reduction of social communication, which may easily lead to problems such as loneliness and social isolation, while the reduction of external stimulation will also increase the risk of cognitive decline or even damage of the older adults. In addition, although physical frailty is not a disease, it is often related to arthritis, stroke, chronic pulmonary edema and other diseases, and diseases may bring adverse effects to blood circulation and nervous system, thus inducing cognitive impairment (27). The correlation coefficient between PSQI score and MoCA score was −0.558, and $p < 0.01$, indicating that the worse the sleep quality was, the higher the risk of cognitive decline would be. Sleep itself is a modifiable lifestyle factor that can be used as a protective factor against cognitive decline. The correlation coefficient between PSQI score and FP score was 0.337, and $p < 0.01$, indicating that the higher PSQI score was, the higher the FP score was, namely, the poorer the sleep quality was, the higher the risk of physical frailty was. This result is consistent with that of Chinese scholar Liu et al. (28). Paying attention to the relationship between sleep disorder and physical frailty in the older adults can provide a theoretical basis for early

identification of high-risk factors for physical frailty, early prevention of the occurrence and development of physical frailty, and early implementation of nursing intervention.

4.4. The mediating role of sleep quality in the physical frailty and cognitive decline

The results of this study show that sleep quality plays a partial mediating role in the relationship between the older adults' physical frailty and cognitive function. In other words, physical frailty not only directly affects the cognitive function of the older adults, but also indirectly affects the cognitive function by changing the sleep quality. The sleep quality reflects the individual's ability to adapt to the use of internal and external resources (29). When the older adults face physical, psychological and social frailty, their self-confidence and sense of control decline and they cannot effectively use internal and external resources (30). As a result, the quality of sleep is reduced, leading to an increased risk of cognitive decline. Sleep quality can improve individual autonomy in daily living ability, promote physical recovery, alleviate depression symptoms, maintain mental health, enhance happiness, and improve quality of life (31). When facing the physical frailty, the older adults need to constantly make adjustments from physical, psychological and social aspects to adapt (32). The older adults with poor sleep quality are more likely to have a sense of helplessness and thus affect cognitive function due to the lack of internal and external resources available (33). Conversely, the older adults with good sleep quality were more energetic and able to maintain better cognitive function. It could be seen that sleep quality played an important buffer role between the physical frailty and cognitive function in the older adults.

4.5. Limitations

This study is a cross-sectional study, and the survey results can only represent the state of the respondents at that time. It is suggested that in the future, a large sample size, multi-center research on the cognitive function of the older adults in the community should be carried out, and longitudinal follow-up should be carried out to compare the differences of cognitive function with time.

5. Conclusion

The sleep quality of the older adults can be improved through health knowledge promotion, exercise, nutrition intervention, and group psychological counseling. Good sleep quality can enhance their resilience and strength to deal with adverse environment or negative events, thereby improving or even reversing physical frailty state of the older adults and avoiding the decline of their cognitive function.

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 study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Review Committee of the Shanghai University of Medicine and Health Sciences (no. 2023-hxxm-01-612,401,197,903,300,537) Shanghai, China. Informed consent was obtained from all participants in the study.

Author contributions

SP and PZ: conceptualization and visualization. YaW and XL: methodology. YC: software. SP, YC, JL, YaW, XL, YiW, SG, MP, and PZ: validation, investigation, and supervision. SP, YC, JL, YiW, SG, MP, YaW, and PZ: formal analysis. SP: resources. YaW, XL, and MP: data curation. SP, YC, PZ, and SG: writing—original draft preparation and writing—review and editing. YC and SP: project administration and 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.

Publisher's note

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Tai Chi for fall prevention and balance improvement in older adults: a systematic review and meta-analysis of randomized controlled trials

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Background and objective: As the population ages, the health of older adults is becoming a public health concern. Falls are a significant threat to their health due to weakened balance. This study aims to investigate the beneficial effects of Tai Chi on fall prevention and balance improvement in older adults.

Methods: We conducted a systematic review and meta-analysis of randomized controlled trials related to Tai Chi, falls, and balance ability, searching PubMed, Embase, and Cochrane Library databases from their establishment until December 31, 2022. Two independent reviewers performed the search, screening of results, extraction of relevant data, and assessment of study quality. This study followed the PRISMA guidelines for systematic review and meta-analysis.

Results: Totally 24 RCTs were included for meta-analysis, and the results showed that Tai Chi can effectively reduce the risk of falls in older adults (RR: 0.76, 95% CI: 0.71 to 0.82) and decrease the number of falls (MD [95% CI]: −0.26 [−0.39, −0.13]). Tai Chi can also improve the balance ability of older adults, such as the timed up and go test (MD [95% CI]: −0.69 [−1.09, −0.29]) and the functional reach test (MD [95% CI]: 2.69 [1.14, 4.24]), as well as other balance tests such as single-leg balance test, Berg balance scale, and gait speed ($p < 0.05$). Subgroup analysis showed that Tai Chi is effective for both healthy older adults and those at high risk of falls ($p < 0.001$), and its effectiveness increases with the duration and frequency of exercise. In addition, the effect of Yang-style Tai Chi is better than that of Sun-style Tai Chi.

Conclusion: Tai Chi is an effective exercise for preventing falls and improving balance ability in older adults, whether they are healthy or at high risk of falling. The effectiveness of Tai Chi increases with exercise time and frequency. Yang-style Tai Chi is more effective than Sun-style Tai Chi.

Systematic review registration: https://clinicaltrials.gov/, identifier CRD42022354594.

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KEYWORDS

Tai Chi, fall, balance, older adults, meta-analysis

1. Introduction

The global population is currently experiencing an aging trend, and it is predicted that by the mid-21st century, individuals aged 60 years and above will constitute approximately 20% of the total population (1, 2). As individuals age, physiological changes are inevitable, leading to challenges such as decreased balance ability, weakened muscle strength, and a higher risk of falling (3). Falls are a primary cause of injuries among the older adult, which can result in severe consequences such as fractures, head injuries, and even death, placing a significant burden on the public health system (4). Annually, between 28 and 35% of individuals aged 65 years and older experience falls worldwide, with rates reaching 32–42% among those over 70 years of age (5). Therefore, preventing falls has become a critical global objective for the older adult population.

Tai Chi is a distinctive form of exercise that involves movements primarily performed in a semi-squatting position. These movements require a continuous shift in the body's center of gravity, incorporating posture control, trunk rotation, weight transfer, and strength training. All these features are advantageous for improving balance and strength, reducing the risk of falling and the fear of falling (6–8). In comparison to other types of exercise, Tai Chi practice has fewer requirements for equipment, venues, and caregivers, making it a more accessible form of exercise to promote (9).

However, previous recommendations regarding Tai Chi as an effective tool for reducing the risk of falling may be limited due to a small number of selected studies, a lack of subgroup analysis on factors such as Tai Chi style, exercise time and frequency, and balance ability analysis (10, 11). Considering the insufficient information available on the impact of Tai Chi on fall prevention among the older adult, this current systematic review aims to explore the recent randomized controlled trials (RCTs) that analyze the effective reduction of fallers, fall rates, and improvement of balance ability in the older adult through the practice of Tai Chi. This systematic review provides valuable insights for using Tai Chi as an intervention for fall prevention in the older adult.

2. Methods

Our systematic review was performed following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (12) and was registered with PROSPERO using the registration number CRD42022354594.

2.1. Search strategy

We conducted a search of databases such as PubMed, EMBASE, and the Cochrane Library using a specific search strategy for each database, covering literature from inception up to December 31, 2022. Additionally, we conducted a review of the references of each included study to ensure that no relevant papers were missed during the search. The full search strategy is available in Supplementary Table S1.

2.2. Inclusion criteria for the study

(1) Participants: older adult people aged ≥60 years, as defined by the World Health Organization (13, 14).

(2) Inventions: any form of Tai Chi exercise.

(3) Controls: receiving either exercise that is stretching or other low-level exercises, usual care, or wellness education.

(4) Outcomes: the number of fallers (participants who experienced at least one fall), average number of falls per person, and balance assessment indicators including the timed up and go (TUG) test, functional reach test (FRT), single leg balance test (SLB), Berg balance scale (BBS), short physical performance battery (SPPB) score, fall efficacy scale (FES), and gait speed assessment. Among these, FRT is a simple, practical, and widely used clinical tool to assess an individual's balance capability and risk of falling. In this test, the maximum distance an individual can reach forward while maintaining a fixed support base in a standing position is measured.

(5) Study: only include RCTs in English.

2.3. Management of the study and retrieval of data

After eliminating duplicate studies using Endnote software, two reviewers (W.C. and M.L.) independently selected eligible studies and extracted relevant data. In case of any discrepancies, the reviewers reached a consensus through discussion and negotiation. The collected data included the author's name, year of publication, sample size, older adult population, health status, age, Tai Chi style, frequency, total exercise time, and follow-up time and outcomes.

2.4. Assessment of study quality

The assessment parameters for the evaluation of study quality included random sequence generation, allocation concealment, blinding of participants and assessors, handling of incomplete outcome data, selective reporting, and other biases. Each item was assessed as having "low risk," "unclear risk," or "high risk." Two reviewers (W.C. and M.L.) independently assessed the data using the Cochrane Risk of Bias tool (15) and resolved any discrepancies through mutual discussion based on justifications.

2.5. Data analysis

The effect size of binary variables was represented by the risk ratio (RR) with a 95% confidence interval (CI), and the effect size of continuous variables was represented by the mean difference (MD) with a 95% CI, evaluated using a random-effects model. The I^2 statistic was used to evaluate the heterogeneity among studies, where $I^2 < 50\%$ indicated low heterogeneity and $I^2 \geq 50\%$ indicated significant

heterogeneity. Subgroup analysis was performed on exposure time, Tai Chi style, weekly frequency, risk of fall, and follow-up time.

Sensitivity analysis was performed by using the one-by-one exclusion method and excluding studies with a small number of participants to test the stability of the outcomes. For each result that included 10 or more original trials, we used funnel plots to test for publication bias, and assessed the symmetry of the funnel plot using Egger's test and Begg's test (16, 17). If the funnel plot was asymmetric, we used the trim-and-fill method for adjustment (18). A two-tailed $p < 0.05$ was considered statistically significant. All analyses were conducted using RevMan 5.3 and Stata 14.0 software.

3. Results

3.1. Study selection and characteristics

A total of 1948 articles were initially searched, of which 837 duplicates and 25 articles without titles were excluded automatically. An additional 828 articles were excluded by reading titles and abstracts. From the remaining 258 articles, 88 were conference papers, other reports, and reviews. Further exclusions were made for 33 non-RCT, 85 articles with incomplete data or unrelated research content, and 28 articles for other reasons. In the end, 24 articles (with one or more outcomes) were included for analysis (7, 8, 19–40) (Figure 1).

Among the 24 articles, 6 reported participants with a history of falls (7, 24, 27, 29, 30, 36), and 5 reported patients with a history of neurological diseases such as stroke or Parkinson's disease (8, 21, 35, 37, 38). The Tai Chi styles used in the interventions were mainly Sun-style (19, 25, 33, 34, 36, 39) or Yang-style (7, 21, 23, 24, 26, 32, 35, 37, 40), with one article using Chen-style (30) and others not specifying. Exercise frequency ranged from one to three times a week, with one article reporting five times a week (23). Total exercise time was mainly within 72 h, with one article reporting 96 h (19) and another reporting 144 h (40). Follow-up periods were ≤ 3 months in 6 articles (25, 30, 32–35), 3–6 months in 9 articles (8, 20, 23, 26–28, 36, 37, 39), 6–12 months in 7 articles (7, 19, 21, 22, 29, 38, 40), and > 12 months in 2 articles (24, 31) (Table 1).

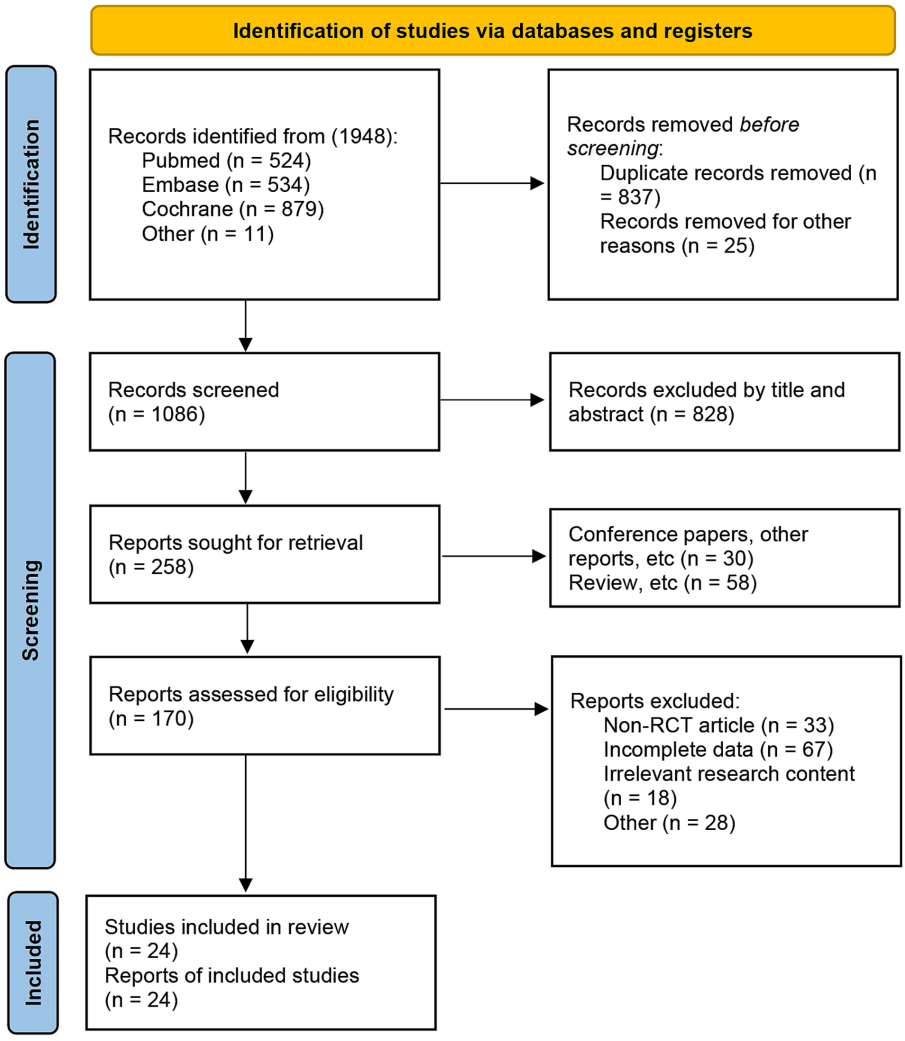

FIGURE 1
PRISMA study selection flowchart.

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TABLE 1 Characteristics of included studies.

Study year	Country	Risk of falls	Age	Tai Chi/Control (n)	Intensity	Exposure Time (h)	Follow-up time
Day et al. (19)	Australia	Non-high risk	77.6	Sun style Tai Chi (205)	Twice a week for 48 weeks, 60 min per session.	96	12 months
			77.8	Stretching (204)			
Faber et al. (20)	Netherlands	Non-high risk	84.4	Tai Chi (80)	Once a week for 4 weeks, followed by twice weekly for 16 weeks. 90 min per session	54	5 months
			85.4	Functional walking (66)			
			84.9	No intervention (92)			
Gao et al. (21)	American	Parkinson's disease and history of falls[#]	69.54	Yang style Tai Chi (40)	Three sessions per week for 12 weeks, 60 min per session.	36	12 months
			68.28	Usual care (40)			
Huang et al. (22)	China	Non-high risk	71.40	Tai Chi (31)	Three sessions per week for 20 weeks,60 min per session.	60	12 months
			71.50	No Tai Chi (47)			
Huang et al. (23)	China	Non-high risk	>60	Yang style Tai Chi (62)	Five sessions per week for 8 weeks, 60 min per session.	40	6 months
				Cognitive Intervention (62)			
				No intervention (62)			
Hwang et al. (24)	China	History of falls	72.0	Yang style Tai Chi (182)	Once a week for 6 months, 60 min per session.	24	18 months
			72.7	Balance training (175)			
Kim et al. (25)	South Korea	Non-high risk	71.4	Sun style Tai Chi (23)	Twice a week for 12 weeks, 60 min per session.	24	3 months
			70.9	Taekwondo (23)			
Li et al. (26)	American	Non-high risk	77.4	Yang-style Tai Chi (125)	Three times per week for 6 months, 60 min per session.	72	6 months
			77.4	Stretching (131)			
Li et al. (8)	American	Parkinson's disease[¥]	68	Tai Chi (65)	Twice a week for 24 weeks, 60 min per session.	48	6 months
			69	Resistance (65)			
			69	Stretching (65)			
Li et al. (27)	American	History of falls	77.5	Tai Chi (224)	Twice a week for 24 weeks, 60 min per session.	48	6 months
			77.8	Multimodal Exercise (223)			
			77.8	Stretching (223)			
Li et al. (28)	American	Non-high risk	76.13	Tai Chi (15)	Three sessions per week for 24 weeks, 60 min per session.	72	6 months
			76.20	Stretching (15)			
Logghe et al. (29)	Netherlands	History of falls	77.5	Yang-style Tai Chi (138)	Twice a week for 13 weeks, 60 min per session.	26	12 months
			76.8	Usual care (131)			
Ni et al. (30)	American	History of falls	70.27	Chen-style Tai Chi (11)	Twice a week for 12 weeks, 60 min per session.	24	3 months
			77.80	Balance training (15)			
Nowalk et al. (31)	American	Non-high risk	82.8	Tai Chi (38)	Three times per week	–	24 months
			85.5	FNBF exercise (37)			
			85.9	Basic enhanced program (35)			
Penn et al. (32)	China	Non-high risk	75.3	Yang-style Tai Chi (15)	Three sessions per week for 8 weeks, 30 min per session.	12	2 months
			73.4	Wellness education (15)			
Pluchino et al. (33)	American	Non-high risk	69.3	Sun-style Tai Chi (14)	Twice a week for 8 weeks, 60 min per session.	16	2 months
			76.0	Standard balance item (14)			

(Continued)

TABLE 1 (Continued)

Study year	Country	Risk of falls	Age	Tai Chi/Control (n)	Intensity	Exposure Time (h)	Follow-up time
Son et al. (34)	South Korea	Non-high risk	72.8	Sun-style Tai Chi (21)	Twice a week for 12 weeks, 60 min per session.	24	3 months
			71.5	Balance training (24)			
Taylor et al. (36)	American	Post-stroke¥	72.8	Yang-style Tai Chi (12)	Three sessions per week for 12 weeks, 50 min per session.	30	3 months
			64.5	Usual care (16)			
Taylor et al. (35)	New Zealand	History of falls	75.3	Sun-style Tai Chi (223)	Once/twice a week for 20 weeks, 60 min per session.	20	5 months
			74.4	Sun-style Tai Chi (220)		40	
			73.7	Low-level exercise (231)			
Taylor et al. (37)	American	Post-stroke	71.5	Yang-style Tai Chi (30)	Three sessions per week for 12 weeks, 60 min per session.	36	5 months
			69.6	Usual community-based exercise (31)			
			68.2	Usual care (28)			
Tousignant et al. (38)	Canada	Frail older adults* and history of falls	79.1	Tai Chi (76)	Twice a week for 15 weeks, 60 min per session.	30	12 months
			80.7	Conventional physical therapy (76)			
Voukelatos et al. (39)	Australia	Non-high risk	Mean 69 year	Sun (83%) or Yang-style Tai Chi (353)	Once a week for 16 weeks, 60 min per session	16	4 months
				No Tai Chi (349)			
Wolf et al. (7)	American	History of falls	80.9	Yang-style Tai Chi (145)	Twice a week for 48 weeks, 30 ~ 45 min per session	48–64	12 months
			80.9	Wellness education (141)			
Woo et al. (40)	China	Non-high risk	68.9	Yang-style Tai Chi (60)	Three times per week for 12 months，60 min per session.	144	12 months
			68.8	Resistance training (60)			
			68.1	No intervention (60)			

*Types of diagnoses varied from stroke/neurological diseases, musculoskeletal and gait disorders.
#At least one fall in the past 12 months.
¥Occurred in the past 6 months.

3.2. Evaluating the risk of bias

Due to the appropriate methods used in random sequence generation and allocation concealment, 22 (8, 19–31) or 17 (8, 19, 20, 23–28, 31, 33, 35–40) articles were considered low risk, respectively. In addition, only 7 articles (7, 8, 20, 26, 29, 36, 38) were considered low risk due to the difficulty in blinding participants, while 19 articles used blinding well in assessing outcomes (7, 8, 19–21, 23–29, 32, 34–37, 39, 40). In terms of incomplete outcome data and selective reporting, 21 (8, 19–21, 23–35, 37–40) and 22 (8, 19–27, 29–32) articles were considered low bias, respectively (Figure 2 and Supplementary Figure S1).

3.3. Number of fallers

A total of 18 studies provided data on the number of fallers (7, 8, 19–24, 26–29, 31, 36–40), and meta-analysis found that Tai Chi exercise could significantly reduce the number of fallers (1,041/2766 VS. 1,321/2703; RR: 0.76, 95% CI: 0.71–0.82, I^2: 25%, $p < 0.001$) (Figure 3A). Sensitivity analysis was performed by sequentially excluding each trial or removing studies with fewer than 100 participants, and the results showed that there was no significant change in statistical significance and heterogeneity. Subgroup analysis showed that Tai Chi could prevent falls in any population at risk, regardless of the overall duration of Tai Chi exercise, follow-up time, or Tai Chi style (Sun or Yang) (all $p < 0.01$). However, in terms of exercise frequency, exercising twice (7, 8, 19, 20, 27, 29, 36, 38) or ≥ 3 times (21–23, 26, 28, 31, 37, 40) per week showed more significant benefits than exercising once a week (RR [95% CI] were 0.78 [0.73, 0.84] and 0.67 [0.58, 0.79], respectively) (Table 2).

3.4. Rate of falls

According to 15 articles providing the total number of falls, the Tai Chi group had a lower incidence of falls compared to the control group (1816/2539 VS. 2,681/2475, IRR, 0.66) (see Supplementary Table S2) (7, 8, 19–21, 23, 24, 26–29, 36–39). Among them, 9 articles provided mean and standard deviation information (7, 20, 21, 23, 24, 27, 28, 38, 39). Tai Chi significantly reduced the number of falls per person (MD [95%CI]: −0.26

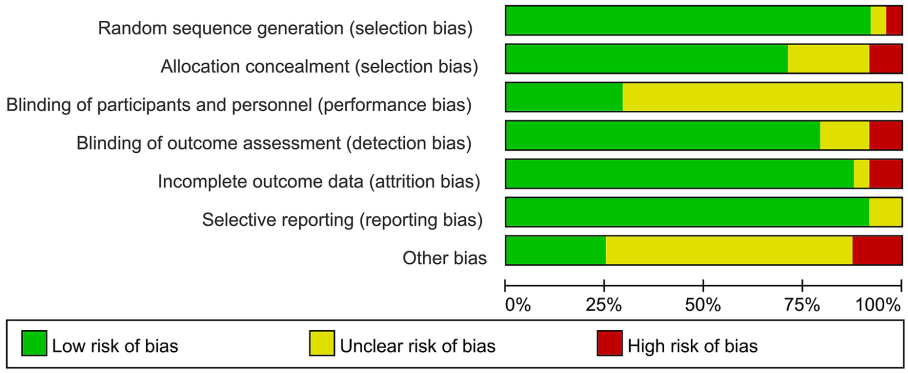

FIGURE 2
Risk of bias graph.

[−0.39, −0.13], $I^2 = 61\%$, $p < 0.001$) (Figure 3B). Excluding the Li et al. study effectively reduced heterogeneity ($I^2 = 49\%$), but did not significantly affect the results (−0.12 [−0.17, −0.06], $p < 0.001$) (7, 20, 21, 23, 24, 28, 38, 39). Moreover, studies excluding fewer participants did not significantly change the results (−0.12 [−0.18, −0.07], $p < 0.001$) (7, 20, 23, 24, 38, 39). Subgroup analysis showed that Tai Chi is more effective in reducing falls per person with longer exercise time ($p = 0.15$, 0.02, and < 0.01, respectively), and that Yang-style Tai Chi is more effective than Sun-style Tai Chi ($p < 0.01$ and $= 0.09$, respectively). Furthermore, regardless of the exercise follow-up duration (≤6 months, 6 ~ 12 months, or > 12 months), Tai Chi exercise was found to significantly reduce the number of falls per person ($p = 0.01$, <0.01, and < 0.01, respectively) (Supplementary Table S3). These findings can be used to design better Tai Chi interventions for fall prevention.

3.5. Timed up and go test

Meta-analysis of 12 studies showed that Tai Chi can significantly reduce TUG time (MD [95%CI]: −0.69 [−1.09, −0.29], $p < 0.001$) (Figure 4A) (8, 21, 22, 25–28, 30, 32–34, 36). Sensitivity analysis was conducted by sequentially deleting each trial and excluding studies with smaller sample sizes, and the significance and heterogeneity of the results remained unchanged. With increasing exercise time and frequency, Tai Chi was more effective in reducing TUG time ($p = 0.93$, 0.01, and <0.001; $p = 0.76$, 0.28, and <0.001, respectively). Yang-style Tai Chi was more effective than Sun-style Tai Chi ($p < 0.01$ and $= 0.66$, respectively). In addition, Tai Chi can shorten TUG time in older adult people with falls related diseases ($p = 0.02$) (Supplementary Table S4) (21, 38).

3.6. Functional reach test

Meta-analysis of 9 studies providing FRT data has shown that the functional reach distance of practicing Tai Chi was significantly greater than that of the control group (MD [95%CI]: 2.69 [1.14, 4.24], $p < 0.001$) (Figure 4B) (8, 22, 25–27, 30, 32–34). Sensitivity analysis, conducted by sequentially excluding each study or studies with smaller sample sizes, did not significantly alter the results (all $p < 0.01$). Subgroup analysis revealed that Yang-style Tai Chi was more effective than Sun-style Tai Chi ($p < 0.001$ and 0.82, respectively), and practicing Tai Chi twice a week had a better effect ($p < 0.001$). Furthermore, Tai Chi was found to be particularly effective in improving FRT test scores in older adult individuals with a history of falls or fall-related diseases ($p = 0.003$ and < 0.001, respectively) (Supplementary Table S5).

3.7. Other outcomes

Through a meta-analysis of other fall or balance ability tests, it was found that Tai Chi can effectively lengthen SLB test times (including with eyes open and closed) (MD [95% CI]: 9.63 [5.87, 13.40], $p < 0.001$) (25, 26, 30, 33, 34), increase BBS scores (MD [95% CI]: 1.80 [0.09, 3.51], $p = 0.04$) (21, 26, 29, 32), and improve gait speed (MD [95% CI]: 9.26 [1.00, 17.52], $p = 0.03$) (8, 25, 26, 34). In addition, Tai Chi did not have a significant effect on overall SPPB scores (27, 35, 37) or FES scores (24, 29, 34) (MD [95% CI]: −0.07 [−1.07, 0.93], 0.17 [−0.49, 0.83]; $p = 0.89$, 0.61; respectively) (Table 3).

3.8. Publication bias

Publication bias analyses were conducted on the results of more than 10 studies on fallers and TUG. It was found that there was a significant publication bias in the Fallers results (Begg's test: 0.014 and Egger's test: 0.003) (Figure 5A). The trim-and-fill method was used to adjust for publication bias, and the outcome still showed statistical differences ($p < 0.001$). In addition, there was no significant publication bias in the TUG results (Begg's test: 0.092, Egger's test: 0.315) (Figure 5B).

4. Discussion

In the meta-analysis, Tai Chi exercise can effectively decrease the rate of fallers and number of falls in older adults, including those with a high risk of falling, while also improving their balance, as measured by TUG, FRT, SLB, BBS score, or gait speed. The effectiveness of Tai Chi

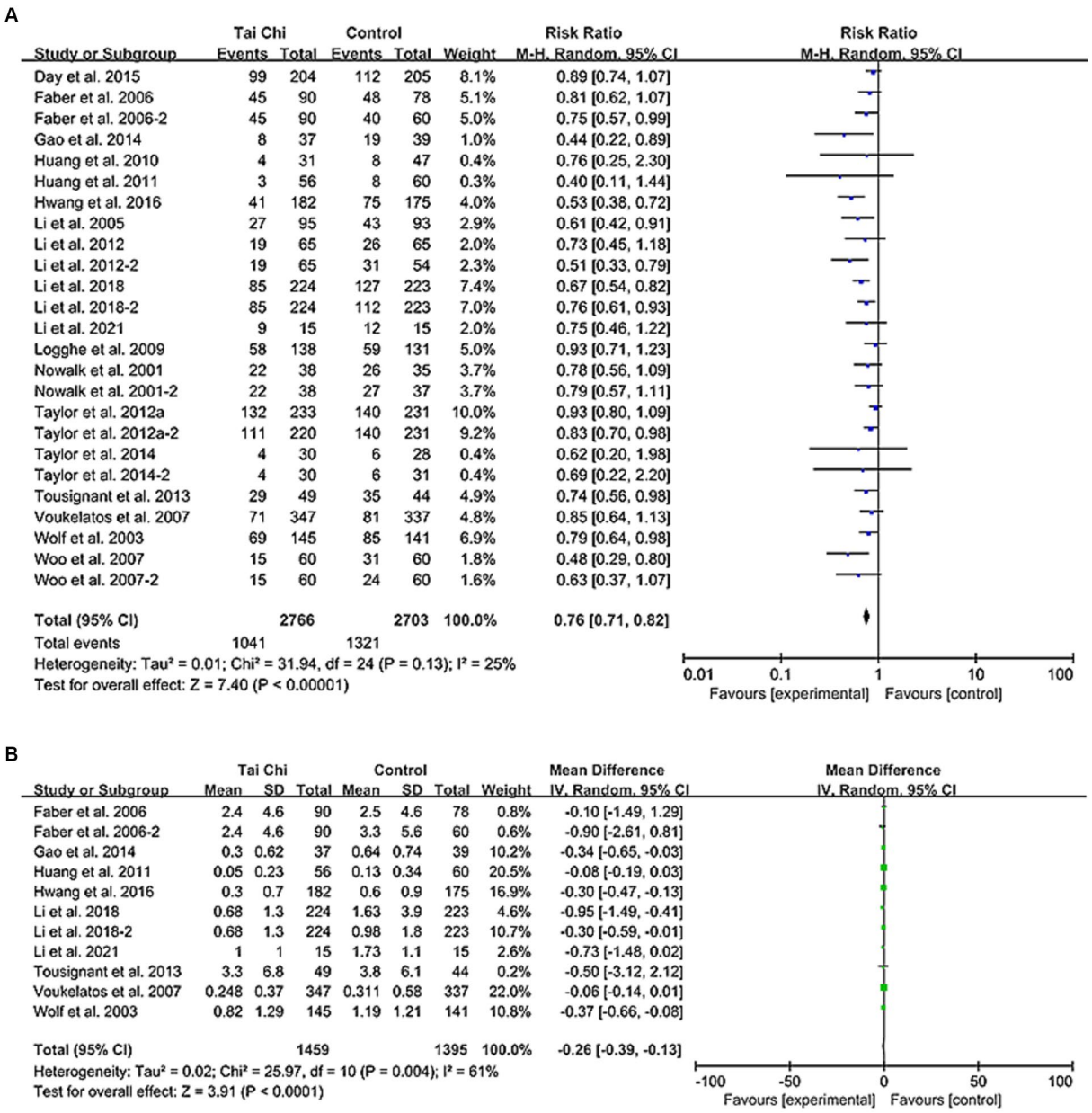

FIGURE 3
Forest plot comparing Tai Chi with control group. **(A)** Number of fallers. **(B)** Rate of falls. CI, confidence interval; RR, risk ratio.

increases with the duration and frequency of exercise. Furthermore, Yang-style Tai Chi was found to be more effective than Sun-style Tai Chi. Sensitivity analysis by excluding individual studies and those with small sample sizes did not significantly alter the outcomes.

The importance of Tai Chi for older adults is increasingly recognized in research. Past meta-analyses have found that Tai Chi can improve cognitive abilities (41), enhance the quality of life and alleviate symptoms related to cancer (42), and relieve chronic pain (43), among other benefits. Our study results, in comparison to previous systematic reviews, consistently find that Tai Chi is indeed effective in preventing falls among the older adult. However, there is a lack of exploration regarding the results of improving balance and the relationship between improving balance and preventing falls (4, 44, 45). By including more RCTs, our research not only investigates Tai Chi's role in fall prevention but also explores whether it is related to enhancing balance abilities. Moreover, our study adds more nuances to these findings. For example, the differences in various Tai Chi practices, exercise durations, and frequencies, could guide future Tai Chi exercise instructions more effectively.

Compared to other exercise interventions or non-interventions, Tai Chi is an effective fall prevention method for the older adult and has been validated in previous studies (10, 11, 44). This study included more updated randomized controlled trials and examined the impact of Tai Chi on balance ability. The fall prevention effect of Tai Chi may stem from its ability to improve balance (7, 21, 26). The study found that Tai Chi can not only improve static balance (e.g., SLB), but also dynamic balance (e.g., TUG and gait speed), and enhance postural control (e.g., FRT). Tai Chi exercise conforms to the statics balance theory, where the

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TABLE 2 Subgroup analysis of fallers.

Subgroup	Included studies	Tai Chi group positive/ total	Control group positive/ total	Heterogeneity (I^2)	RR [95% CI]	*p*	Test for subgroup difference
Exposure time (h)							0.69
≤24	4 (23, 24, 37, 39)	247/818	304/803	75%	0.74 [0.53, 1.02]	0.06	
24 ~ 48	7 (8, 21, 27, 29, 36–38)	422/1082	561/1069	15%	0.74 [0.68, 0.82]	<0.001	
>48	7 (7, 19, 20, 22, 26, 28, 40)	328/790	403/759	0	0.76 [0.69, 0.85]	<0.001	
Tai Chi style							0.004
Sun	3 (19, 37, 39)	413/1004	473/1004	0%	0.88 [0.81, 0.97]	0.008	
Yang	9 (7, 21, 23, 24, 26, 29, 37, 40)	244/833	829/1822	36%	0.76 [0.68, 0.86]	<0.001	
Weekly frequency							0.22
Once	3 (24, 36, 39)	244/762	296/743	81%	0.76 [0.55, 1.06]	0.11	
Twice	8 (7, 8, 19, 20, 27, 29, 36, 38)	664/1514	815/1455	4%	0.78 [0.73, 0.84]	<0.001	
≥Three times	8 (21–23, 26, 28, 31, 37, 40)	133/490	210/505	0	0.67 [0.58, 0.79]	<0.001	
Risk of fall							0.18
Non-high risk	9 (19, 20, 22, 23, 26, 28, 31, 39, 40)	377/1124	460/1087	0	0.78 [0.71, 0.86]	<0.001	
History of falls only	5 (7, 24, 27, 29, 35)	581/1366	738/1355	62%	0.78 [0.69, 0.89]	<0.001	
Falls related diseases	4 (8, 21, 37, 38)	83/276	123/261	0	0.42 [0.54, 0.80]	<0.001	
Follow-up time							0.71
≤6 months	9 (8, 20, 23, 26–28, 36, 37, 39)	659/1784	820/1729	15%	0.77 [0.71, 0.84]	<0.001	
6 ~ 12 months	7 (7, 19, 21, 22, 29, 38, 40)	297/724	373/727	32%	0.77 [0.67, 0.89]	<0.001	
>12 months	2 (24, 31)	85/258	1228/247	56%	0.69 [0.51, 0.91]	0.009	

RR, risk ratio.

main factors affecting human balance are the size of the support surface and the height of the center of gravity (46). Therefore, Tai Chi can improve the ability of the older adult to control their center of gravity and adjust their posture, thereby improving balance ability (47, 48).

Tai Chi movements require a semi-squat position and involve concentric and eccentric contractions of leg muscles at varying degrees during practice, which has been reported to significantly enhance lower limb strength and endurance in the older adult (49, 50). Tai Chi practice also provides moderate aerobic exercise and flexibility training, which can improve cognitive function in older adults (41, 51). The enhancement of muscle strength is associated with the improvement of physical fitness and mental quality of life in the older adult (52). Compared to stretching training, Tai Chi's precise joint control and muscle coordination helps achieve better balance control (53). Additionally, Tai Chi's unique meditation component can improve attention and cognitive function, enhancing body control and balance ability in older adults (54). Therefore, Tai Chi's unique exercise characteristics are an important factor in its success in fall prevention among the older adult, reducing hospitalization rates associated with falls in the community (55). These mechanisms may explain Tai Chi's role in enhancing balance ability and preventing falls, with significant effects observed over certain follow-up periods. Although some studies have suggested that the protective effect of Tai Chi on fall prevention in the short-term appears to be greater than in the long-term, indicating a potential loss of effectiveness over time (11), this may be due to inconsistencies in the duration of Tai Chi exercise and follow-up time in some studies. It was discovered in our study that Tai Chi's improvement in balance ability and fall prevention effectiveness increases with longer exercise duration and frequency. A meta-analysis showed that the optimal

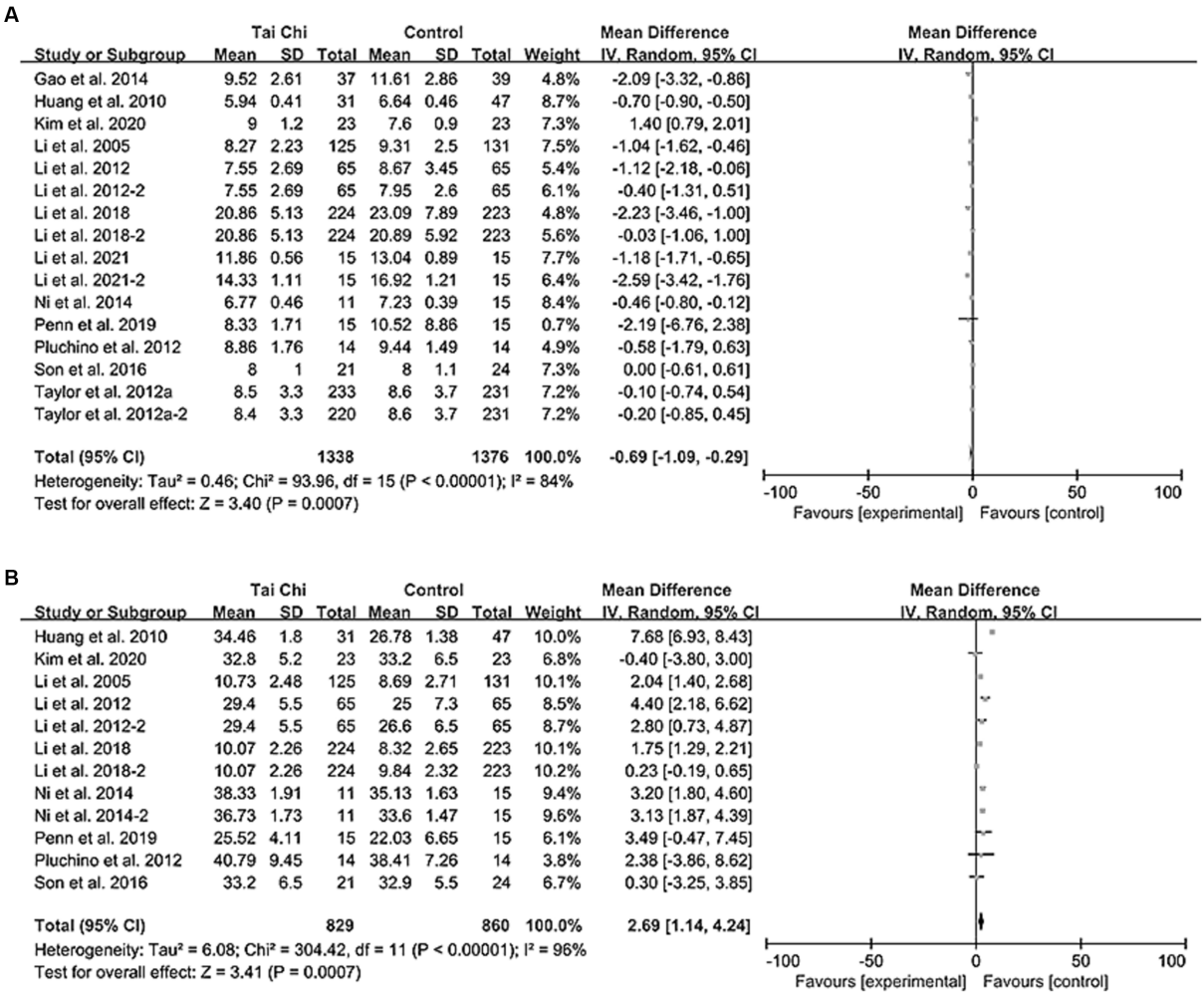

FIGURE 4
Forest plot comparison of balance ability between Tai Chi group and control group. **(A)** TUG. **(B)** FRT. CI, confidence interval; MD, mean difference; TUG, timed up and go; FRT, functional reach test.

TABLE 3 Other outcomes.

Outcomes	Included studies	Tai Chi group	Control group	Heterogeneity (I^2)	MD [95% CI]	*p*
SLB	5 (25, 26, 30, 33, 34)	330	353	69%	9.63 [5.87, 13.40]	<0.001
BBS	4 (21, 26, 29, 32)	315	316	65%	1.80 [0.09, 3.51]	0.04
Gait speed	4 (8, 25, 26, 34)	299	308	91%	9.26 [1.00, 17.52]	0.03
SPPB scores	3 (27, 35, 37)	524	517	90%	−0.07 [−1.07, 0.93]	0.89
FES	3 (24, 29, 34)	334	320	10%	0.17 [−0.49, 0.83]	0.61

MD, mean difference; CI, confidence interval; SLB, single leg balance test; BBS, Berg balance scale; SPPB, short physical performance battery; FES, fall efficacy scale.

total exercise time is between 50 and 72 h with 3 exercise sessions per week (56). However, the optimal exercise frequency and duration per week remain unclear. This necessitates further in-depth research on our part.

This study found that Tai Chi is effective not only for healthy older adults but also for those at high risk of falling. In studies on stroke and Parkinson's disease patients, Tai Chi was found to improve balance ability and prevent falls after stroke, and Tai Chi training was effective in improving the motor ability of stroke patients (48, 56). Further research is needed to evaluate Tai Chi as an adjunctive rehabilitation method, an effective alternative rehabilitation option, or a maintenance strategy. Additionally, Tai Chi can improve cognitive function and immunity in

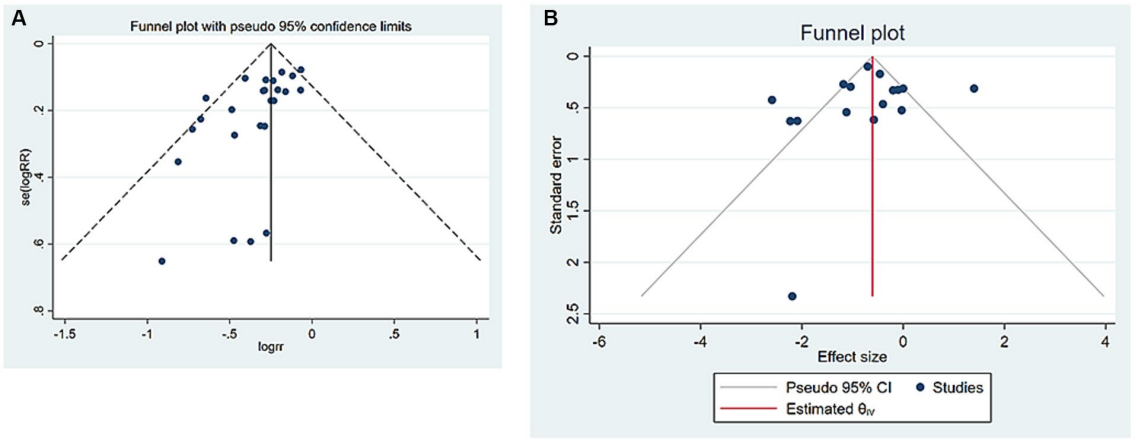

FIGURE 5
Publication bias. **(A)** Number of fallers. **(B)** TUG. CI, confidence interval; RR, risk ratio; TUG, timed up and go.

older adults (57, 58). Cost–benefit studies of fall prevention strategies have shown that Tai Chi is the most cost-effective exercise among older adults living in the community (59). Therefore, Tai Chi's role in the older adult population is universal.

The strengths of our study lie in the inclusion of more recent RCT studies for analysis, the implementation of multiple subgroup analyses based on study characteristics, and the strict execution of sensitivity analyses. However, our study is not without limitations. Firstly, our selection of only English-language literature and specific criteria-based studies may have introduced selection bias. Secondly, the results of our research are only applicable to standard Tai Chi classes, not personalized courses, indicating a need for further investigation into the effects of personalized Tai Chi courses on older adult rehabilitation. Thirdly, despite conducting sensitivity and subgroup analyses, potential heterogeneity across studies may still impact the stability of our results. Lastly, our study only compares Tai Chi exercises with traditional non-Tai Chi exercises, yet a myriad of emerging technologies designed to enhance the quality of life for the older adult warrant further comparative research and exploration in the future (60).

Overall, Tai Chi exercise has a good preventive effect on falls in the older adult (both healthy and high-risk for falls) and enhances their balance ability. However, there is a relatively small number of studies on balance ability, and further research is needed in this area. Additionally, we need to increase the frequency of follow-up observations to observe the process of the Tai Chi intervention's effectiveness. Furthermore, due to limitations in the number and quality of included studies, the above conclusions still require further high-quality verification.

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

WC and ML made equal contributions to this study, including designing the search strategy for retrieving and screening articles, conducting data extraction and analysis. WC and HL wrote the manuscript, while YL and ZF managed the project and reviewed the manuscript. All authors have read and approved the final 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.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1236050/full#supplementary-material

SUPPLEMENTARY FIGURE 1
Risk of bias summary.

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Projecting the burden of dental caries and periodontal diseases among the adult population in the United Kingdom using a multi-state population model

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Objectives: With the aging United Kingdom population, oral diseases are expected to increase. Exploring credible projections is fundamental to understanding the likely impact of emerging population-level interventions on oral disease burden. This study aims at providing a credible, evidence-based projection of the adult population in the United Kingdom with dental caries and periodontal diseases.

Methods: We developed a multi-state population model using system dynamics that disaggregates the adult population in the United Kingdom into different oral health states. The caries population was divided into three states: no caries, treated caries, and untreated caries. The periodontal disease population was disaggregated into no periodontal disease, pocketing between 4 and < 6 mm, 6 and < 9 mm, and 9 mm or more. Data from the 2009 dental health survey in the United Kingdom was used to estimate age and gender-specific prevalence rates as input to the multi-state population model.

Results: Of the population 16 years and older, the number with carious teeth is projected to decrease from 15.742 million in the year 2020 to 15.504 million by the year 2050, representing a decrease of 1.5%. For individuals with carious teeth, the older adult population is estimated to constitute 62.06% by 2050 and is projected to increase 89.4% from 5.079 million in 2020 to 9.623 million by 2050. The adult population with periodontal pocketing is estimated to increase from 25.751 million in 2020 to 27.980 million by 2050, while those with periodontal loss of attachment are projected to increase from 18.667 million in 2020 to 20.898 million by 2050. The burden of carious teeth and periodontal diseases is anticipated to shift from the adult population (16–59 years) to the older adult population. The older adult population with carious teeth is estimated to rise from 32.26% in 2020 to 62.06% by 2050, while that for periodontal disease is expected to increase from 42.44% in 2020 to 54.57% by 2050.

Conclusion: This model provides evidence-based plausible future demand for oral health conditions, allowing policymakers to plan for oral health capacity to address growing needs. Because of the significant delay involved in educating and training oral health personnel, such projections offer policymakers the opportunity to be proactive in planning for future capacity needs instead of being reactive.

KEYWORDS

oral diseases, caries, periodontal diseases, system dynamics, United Kingdom, projections

Introduction

Oral diseases are among the most prevalent non-communicable diseases (NCD) globally, affecting 3.5 billion people in 2019 (1). They encompass a range of diseases and conditions that include dental caries, periodontal disease, tooth loss, oral cavity cancer, dental trauma, noma, and congenital anomalies such as cleft palate and lip (2). The estimated number of cases of oral diseases globally is approximately 1 billion more than the combined number of cases of the five main NCDs: cardiovascular disease, diabetes mellitus, chronic respiratory diseases, mental disorders, and cancers (2). Among these oral diseases, dental caries in permanent teeth and severe periodontitis are the most common and major causes of tooth loss. Untreated dental caries in permanent teeth stand out as the most prevalent disease on a global scale, with 2.3 billion people having it, followed by severe periodontitis, which affects approximately 1 billion people globally (3). Furthermore, oral diseases impose a high economic burden and are the fourth most expensive group of diseases to treat globally (4). In 2015, the estimated direct and indirect costs of oral diseases amounted to $356.80 and $187.61 billion, respectively, totaling the global economic burden of oral diseases to $544.41 billion (5). Despite oral diseases being wildly prevalent, largely preventable, and having a substantial economic burden, they are rarely prioritized in global health policy.

In the United Kingdom, the prevalence trends of untreated caries indicate a sharp decline in dental caries among adults between 1998 and 2009, from 54 to 31% (6). In contrast, trends in periodontal status vary, with only 17% of British adults having healthy periodontal status. More severe periodontal disease among British adults increased from 6% in 1998 to 9% in 2009, while mild and moderate periodontal disease affecting 37% of adults has decreased (6). Despite these trends, the expected increase in the aging population and other demographic shifts are anticipated to increase the cumulative burden of oral diseases substantially. The projected increase in the burden of oral diseases is supported by epidemiological evidence. Between 1990 and 2019, there was a significant global increase in estimated cases of oral diseases, surpassing 1 billion, representing a 50% increase (2, 7). This increase was higher than the population growth of around 45% during the same period. Furthermore, in high-income countries, the case numbers for oral diseases rose by 23%, outpacing demographic growth in those countries (7).

In recent years, there has been growing interest in oral health burden projections, which have shown to be valuable in estimating future trends and informing public health policies. Nevertheless, the application of projection analysis in oral health research remains limited and scattered in scope, projection method, and target population, particularly when considering the utilities this approach offers. Few studies have projected the prevalence of dental caries and caries-free in primary and permanent dentitions among different age groups, as well as projections of other oral conditions such as edentulism and oral cancers. Jordan et al. (8) projected trends in dental caries in permanent dentition among children aged 12 years, adults aged 35–44 years, and older adults aged 65–74 years in Germany until 2030 using log-linearization and a linear regression model. The authors reported decreases in the cumulative caries experience from 1.1 billion DMFT in 2000 to 867 million in 2015 and projected a further decrease to 740 million in 2030 (8). Conversely, a projection analysis was conducted in Thailand and used a system dynamics model to forecast dental caries in permanent teeth among adults and older adults (≥ 15 years old) until 2040 under different policy options (9). The study projected an increase in dental caries experiences among Thai adults and older due to the aging population (9). Furthermore, caries experience among younger age groups was examined in a 2017 study where a shorter-term-projection analysis using an autoregressive integrated moving average (ARIMA) model and a gray predictive model (GM) to forecast early childhood caries prevalence among children aged 5 years from 2014 to 2018 was conducted in China (10). While in Malaysia, the caries-free prevalence among schoolchildren aged 6, 12, and 16 years old was projected from 2020 to 2030 using three time-series models: double exponential smoothing (DES), autoregressive integrated moving average (ARIMA), and the error, trend, and seasonal (ETS) model, and reported that, caries-free prevalence to increase steadily in 6- and 12-year-old schoolchildren from 2020 to 2030 (11). Projection analyses have also been conducted in other oral health conditions such as edentulism and oral and oropharyngeal cancer mortalities (12, 13). Schwendicke and colleagues used Monte Carlo simulations to forecast the prevalence of tooth loss among older adults (aged 65–74 years) in Germany until 2030 (13). Infante Cossio et and colleagues used the Nordpred program to generate a predictive model to predict Oral cavity cancer (OCC) and oropharyngeal cancer (OPC) mortality rate in Spain until 2044 (12). The predictive model projected a higher mortality rate in females than in males for OCC in the period 2040–2044, while deaths for OPC were projected to decrease in males and gradually increase in females (12). However, none of these studies were conducted in the United Kingdom, attempted to project the burden of periodontal diseases or incorporated the demographic changes into projecting the burden of caries and periodontal disease, clearly indicating a gap.

In the context of rapid population aging, in the United Kingdom, it is projected that the number of people aged 85 years and above will increase from 1.7 million in 2020 (2.5% of the United Kingdom population) to an estimated 3.1 million by 2045 (4.3% of the United Kingdom population) (14). To manage the future demands of this aging population, it is crucial to quantify the burden of major oral diseases. This will help estimate and optimize resource allocation for prevention and treatment needs. Additionally, it will aid in planning future demands for dental health services, capacity planning, and workforce requirements. This study aims to use a multi-state population model to project the burden of dental caries and periodontal diseases among the adult population in the United Kingdom and to provide evidence to support population-level intervention evaluation.

Methods

Based on the 2009 dental health survey (ADHS) data from the United Kingdom, the systems science methodology of System Dynamics was used to develop a multi-state population simulation model (15–18) for projecting the adult population of the United Kingdom with dental caries and periodontal diseases. System dynamics models consist of interacting sets of differential, and algebraic equations developed from a broad range of relevant empirical data (19, 20). The simulation models developed are used to understand the underlying dynamics, complex systems, or structures that cause the problems. The system dynamics

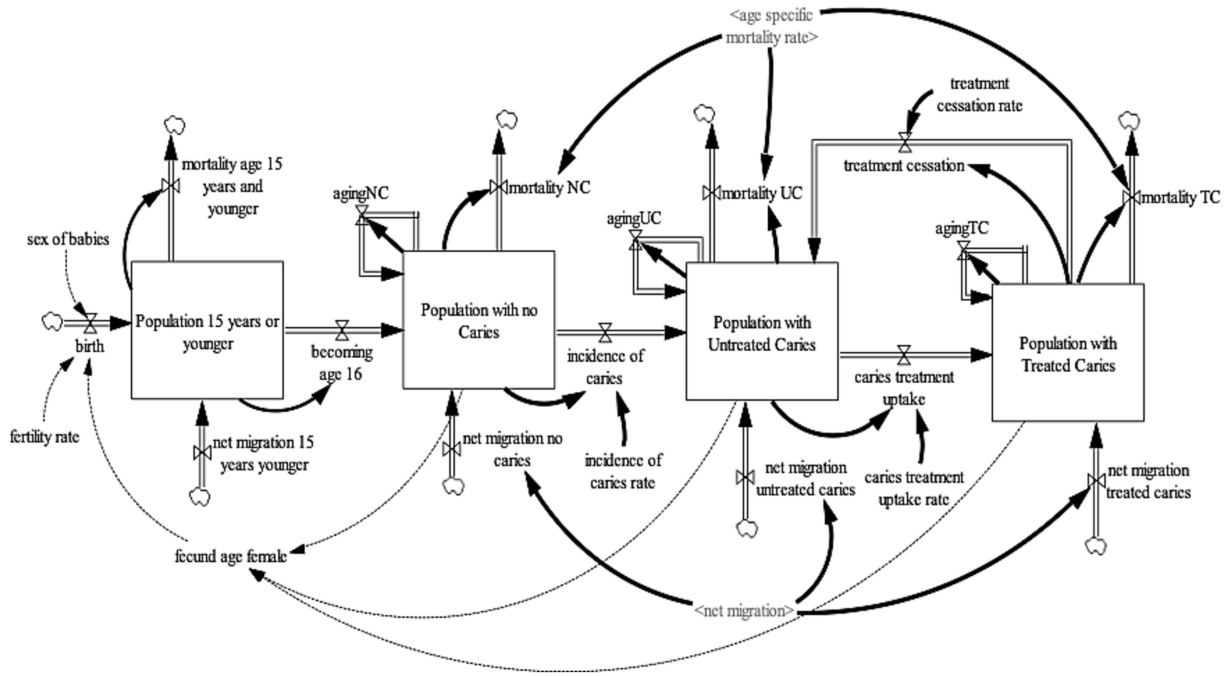

FIGURE 1
Caries sub-model.

method has been used to address complex health issues in healthcare (21–24). There is limited application of the system dynamics method in oral health (25–28), and this research study adds to the limited application to demonstrate its utility to oral public health.

Model structure

The oral health model consists of two sub-models: dental caries sub-model and the periodontal diseases sub-model. The periodontal disease sub-model was further divided into two sub-models (a) the periodontal pocketing sub-model and (b) the periodontal loss of attachment (LOA) sub-model. The oral health model presented herein was developed as follows: first, a validated dynamic multi-state population model that simulates outcomes of interest using available data and information from literature was developed. Next, the multi-state population model was presented to clinician scientists with expertise in dentistry to verify the model structure and its assumptions regarding causal relationships and its consistency with existing evidence. The model was refined in an iterative process until it was considered adequate concerning its realism, clarity, and ability to capture important issues of interest to the purpose of the model. Following the experts' review and revision of the model structure consistency with experts' knowledge, the model was parameterized, and simulated to generate evidence-based projections of dental caries and periodontal diseases in the United Kingdom.

Dental caries sub-model

The caries sub-model (Figure 1) projects the United Kingdom adult population (age 16 years and older) with carious teeth. To project the United Kingdom adult population with carious teeth, the United Kingdom population 16 years and older was disaggregated into three health states—no-caries, untreated caries, and treated caries. These health states were further disaggregated by age (single age cohorts from age 16 to age 100 and older) and gender (male, female). For the purpose of this model, the "no caries" health state refers to individuals with teeth with no visible decay or restoration of any kind, including those such as veneers and crowns, which are not always placed to manage the disease (29). It also includes teeth with sealants that were sound or fractured but with no evidence of caries (29). The "untreated caries" health state refer to individuals with teeth with visual caries or cavitated caries or teeth that were so broken down, possibly with pulpal involvement, that they were unrestorable (29). It includes teeth that had restorations with recurrent caries (29). Lastly, "treated caries" health state refers to individuals with teeth in which a filling has been placed but which are now sound with no active decay and no damage to the filling (29). To ensure consistency and validity of the model output, an additional state that accounts for the population age 15 years or younger was included. This ensures that individuals aged 15 transitions to the adult population with no caries health state. To establish a consistent aging process, the population aged 15 years or younger was divided into single age cohorts (age 0–15 years).

The population 15 years or younger increases through births and net migration and decreases by mortality and becoming age 16. Births were estimated by fecund female population (age 15–49) and fertility rate (30); while net migration is estimated by calibration. Likewise, mortality is determined by age-gender-specific mortality rates from life tables (31). At the end of each year, the surviving population in each age cohort flows to the subsequent cohort, except the final age cohort, age 100 and older. The population with no-caries increases with individuals becoming age 16 and net migration of individuals

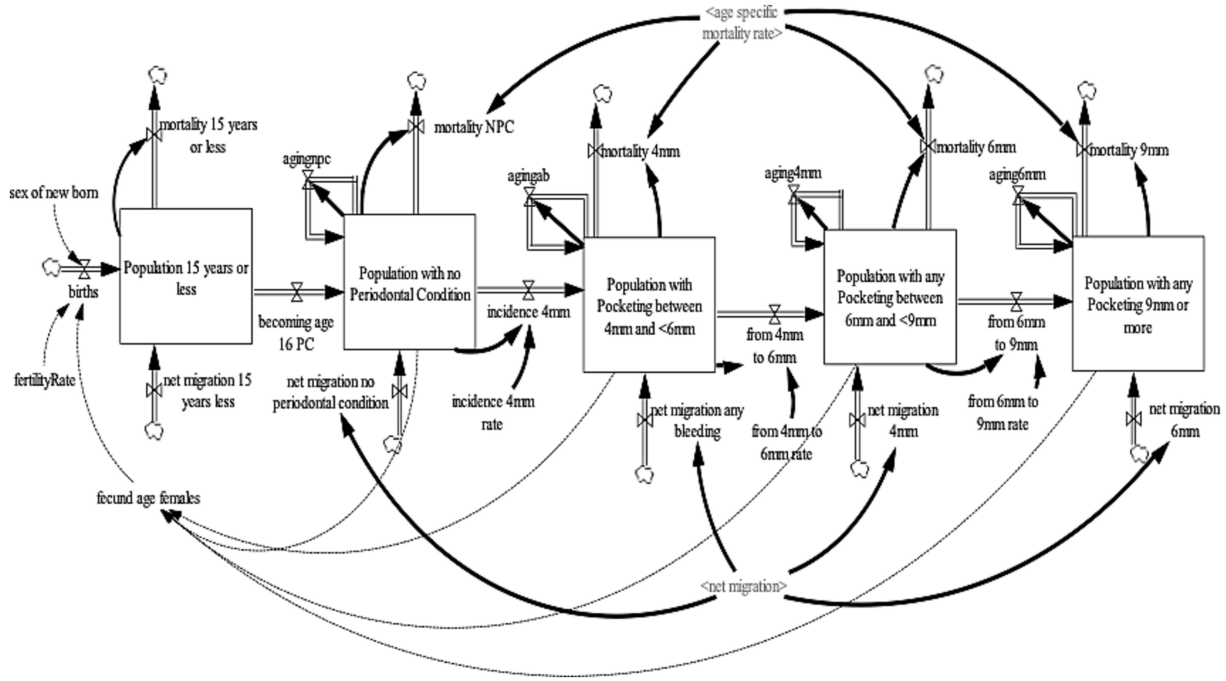

FIGURE 2
Periodontal pocketing sub-model.

with no-caries and decreases via incidence of caries and mortality from the population with no-caries. The incidence rate of caries development is estimated by calibration. The population with untreated cries increases by the incidence of caries, net migration of individuals with untreated caries, and caries treatment cessation of individuals with treated caries; and decreases by caries treatment uptake and mortality among the population with untreated caries. Caries treatment uptake rate and caries treatment cessation rate are estimated *via* calibration. Lastly, the population with treated caries increases by caries treatment uptake and net migration of individuals with treated caries and decreases by caries treatment cessation and mortality among the population with treated caries.

Periodontal disease sub-model

The periodontal diseases sub-model projects the United Kingdom adult population (age 16 years and older) with periodontal diseases. The periodontal disease sub-model was further divided into two sub-models (a) the periodontal pocketing sub-model (Figure 2) and (b) the LOA sub-model (Figure 3). For the periodontal pocketing sub-model, the adult population of the United Kingdom was disaggregated into four health states—no-periodontal condition, any pocketing 4 to <6 mm, any pocketing 6 to <9 mm, and any pocketing 9 mm or more—to project the periodontal disease in the United Kingdom. These health states were further disaggregated by age (single age cohorts from age 16 to 100 and older) and gender (male, female). For the purpose of this model, periodontal pocketing is defined as a pathologically deepened gingival sulcus measured from the gingival margin to the base of the pocket (29). Pockets deeper than 3.5 mm were recorded to give an indication of disease and are reported here at thresholds of 4, 6, and 9 mm. The 4, 6, and 9 mm pockets can be classified as mild, moderate, and severe periodontal pocketing, respectively (29). To ensure consistency and validity of the model output, an additional state that accounts for the population aged 15 years or younger were included to ensure that individuals aged 15 transitions to the adult population with a no-periodontal condition health state. To ensure a consistent aging process, the population aged 15 years or younger was divided into single age cohorts (age 0–15 years).

The population of 15 years or younger increases through births and net migration and decreases by mortality and age 16. Births were estimated by fecund female population (age 15–49) and fertility rate (30), while net migration was estimated by calibration. Likewise, mortality is determined by age-gender-specific mortality rates from life tables (31). At the end of each year, the surviving population in each age cohort flows to the subsequent cohort, except the final age cohort, age 100 and older. The population with the no-periodontal condition increases as individuals become age 16 years and the net migration of individuals with the no-periodontal condition and decreases by the incidence of 4 mm pocketing and mortality of the population with the no-periodontal condition. The population with pocketing 4 to <6 mm increases by the incidence of 4 mm pocketing and net migration of individuals with 4 to <6 mm pocketing and decreases by the transition from 4 to 6 mm pocketing and mortality of the population with pocketing 4 to <6 mm. The population with pocketing 6 to <9 mm increases by the transition from 4 to 6 mm pocketing and net migration of individuals with 6 to <9 mm pocketing and decreases by the transition from 6 to 9 mm pocketing and mortality of the population with pocketing 6 to <9 mm. Lastly, the population with any pocketing of 9 mm or more increases by the transition from 6 mm to 9 mm pocketing and net migration of

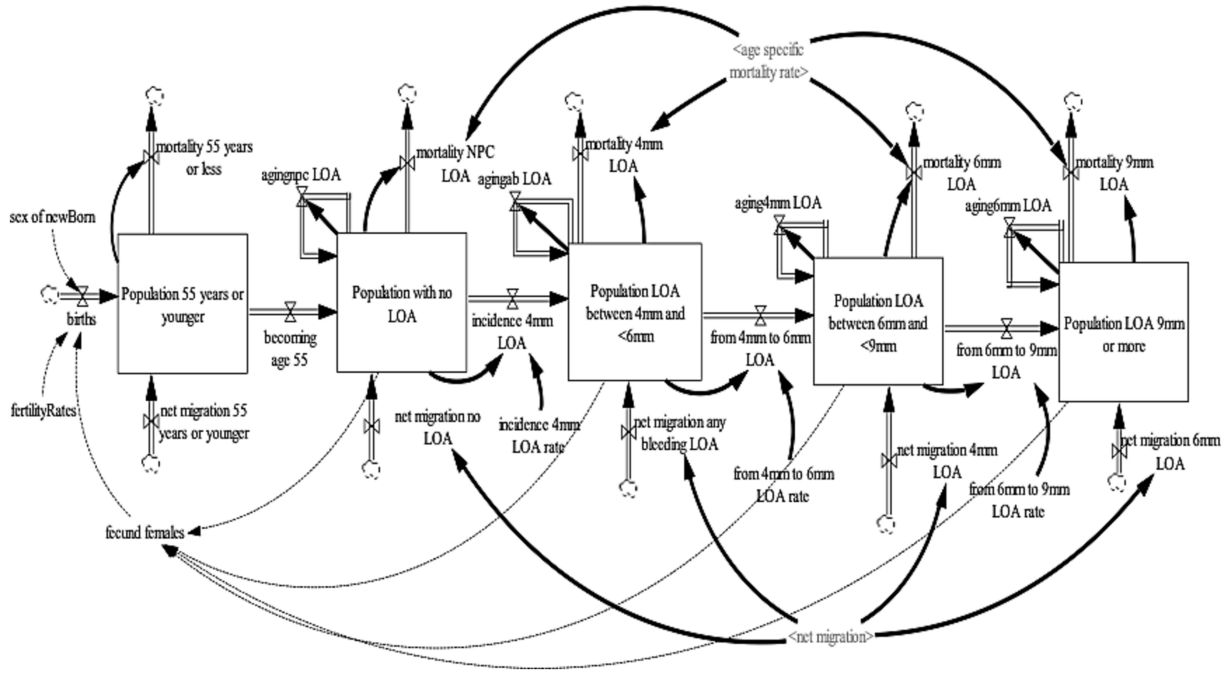

FIGURE 3
Periodontal loss of attachment sub-model.

individuals with 9 mm pocketing and decreases by the mortality of the population with pocketing of 9 mm or more.

In the 2009, ADHS LOA was only assessed for subjects aged 55 years old or over (29). Therefore, the LOA sub-model projects individuals 55 years or older with periodontal LOA in the United Kingdom. The LOA sub-model was disaggregated into four health states—no-loss of attachment, LOA 4 to <6 mm, LOA 6 to <9 mm, and LOA 9 mm or more. These health states were further disaggregated by age (single age cohorts from age 16–100 and older) and gender (male, female). To this model, loss of attachment is defined as damage over a lifetime that takes into account gum recession (which will often occur alongside pocketing). It is measured with the periodontal probe as the distance from the cementoenamel junction (CEJ) to the base of the pocket. As with periodontal pocketing, the worst score for each sextant was recorded and the thresholds of 4, 6, and 9 mm were used, and were classified as mild, moderate, and severe LOA, respectively (29, 31, 32). To ensure consistency and validity of the model output, an additional state that accounts for the population age 54 years or younger were included to ensure that individuals aged 54 transitions to the population 55 years and older with a no-LOA health state. To ensure a consistent aging process, the population aged 54 years or younger was divided into single age cohorts (age 0–54 years).

The population 54 years or younger increases through births and net migration and decreases by mortality and becoming age 55. Births were estimated by fecund female population (age 15–49) and fertility rate (30); while net migration is estimated by calibration. Likewise, mortality is determined by age-gender-specific mortality rates from life tables (31). At the end of each year, the surviving population in each age cohort flows to the subsequent cohort, except the final age cohort, age 100 and older. The population with the no-LOA increases as individuals become age 55 years and the net migration of individuals with no-LOA and decreases by the incidence of 4 mm LOA and mortality of the population with the no-loss of attachment. The population with a LOA of 4 to <6 mm increases by the incidence of 4 mm LOA and net migration of individuals with 4 to <6 mm LOA and decreases by the transition from 4 to 6 mm LOA and mortality of the population with 4 to <6 mm loss of attachment. The population with a LOA of 6 to <9 mm increases by the transition from 4 to 6 mm LOA and net migration of individuals with 6 to <9 mm LOA and decreases by the transition from 6 to 9 mm LOA and mortality of the population with LOA 6 to <9 mm. Lastly, the population with a LOA of 9 mm or more increases by the transition from 6 to 9 mm LOA and net migration of individuals with 9 mm or more LOA and decreases by the mortality of the population with LOA of 9 mm or more.

Model assumptions

Birth rate and age-gender-specific mortality rates were assumed to be constant over the simulation time. However, it is important to emphasize that these variables were included in the sensitivity analysis and were varied to evaluate their impact on outcomes of interest. Individuals becoming age 16 were assumed to transition directly into the population with no-caries, while a similar assumption was made for individuals 16 years transitioning to no-periodontal condition. For the caries sub-model, the incidence rate of caries, caries treatment uptake rate, and caries treatment cessation rate were assumed to be constant across age. Similarly, for the periodontal sub-model, the incidence rate of 4 mm pocketing, the transition from 4 to 6 mm pocketing, and the transition from 6 to 9 mm pocketing rates were assumed to be constant across age. Also, for the LOA sub-model, the

incidence rate of 4 mm loss of attachment, the transition from 4 to 6 mm loss of attachment, and the transition from 6 to 9 mm LOA rates were assumed to be constant across age. However, all these parameters were included in the sensitivity analysis.

Data

The oral health model used demographic data in the United Kingdom and the 2009 Adult Dental Health Survey (ADHS) data as input for the model, and was accessed with permission from the United Kingdom Data Service (33). The demographic datasets used as input for the sub-models were obtained from the Office of National Statistics (30, 31, 34). Data regarding the prevalence of caries and periodontal conditions were obtained from the 2009 ADHS data (29). The ADHS is a cross sectional study conducted every 10 years. The survey provides oral health status of the population and their access to, and experience of, dental services. The 2009 ADHS comprised of two components: a questionnaire survey and a clinical survey, and used two-stage cluster sampling design, with a sample size of 13,400 households. The 13,400 households comprised 1,150 households from each of the 10 English Strategic Health Authorities, 1,150 from Wales, and 750 from Northern Ireland. The participating households, all adults 16 years or older, were invited for face-to-face interview and individuals with at least one natural tooth were invited to undergo a subsequent dental examination, conducted by NHS salaried dentist who attended study training over 4 days (29, 35). The list of model input parameters is provided in the Appendix A.

Model validation and sensitivity analysis

The typical structure and behavior test (36, 37) of system dynamics models were applied to validate the oral health model. For the validity of the model structure, the oral health model was presented to two clinician-scientists with expertise in dentistry to verify the model structure and its assumptions regarding causal relationships and its consistency with existing literature evidence. Consequently, we are confident that the model is grounded on current knowledge and evidence on the development and progression of caries and periodontal diseases. The behavior test compared simulated model outcomes with available data. Since the 2009 ADHS data is cross-sectional data, we generated a time series data of the prevalence of caries and periodontal diseases and used it to calibrate the incidence and transition rates in caries and periodontal disease sub-models. The time series data was generated by multiplying the age-specific prevalence rates by a validated dynamic population model of the United Kingdom. Appendix B shows the simulation of caries and periodontal diseases as compared to available data. The results suggest that the simulation model output compares favorably with data, indicating that the model performs credibly for the visual fit test.

For the sensitivity analysis, a two-way sensitivity analysis was performed to evaluate the impact of a change in selected model parameters on the outcomes of interest. The parameters included in the sensitivity analysis, where they were varied simultaneously are fertility rate, net migration rate, age-specific mortality rate, incidence of caries rate, caries treatment uptake rate, caries treatment cessation rate, incidence 4 mm pocketing rate, transition from 4 to <6 mm pocketing rate, transition from 6 to <9 mm pocketing rate, incidence of 4 mm LOA rate, transition from 4 to <6 mm LOA rate, and transition from 6 to <9 mm LOA rate. These parameters were varied simultaneously by ±50%, and the model was simulated 500 times. The estimated average and the minimum and maximum values at a 95% confidence interval were used to show the uncertainty around the projected outcomes.

Results

Table 1 shows the results of the projected number of adult 16 years and older with dental caries in the United Kingdom from 2020 to 2050. The number of people in the United Kingdom 16 years and older is projected to increase from 54.709 million (with a 95% confidence interval of 54.670–54.747) in 2020 to 58.356 million (57.804–58.907) by 2050, representing a 6.7% (5.7–7.6%) increase. Due to population aging, the older adult population 60 years and older is projected to increase the most by 33.4% (33.3–33.5%) from 16.884 million (16.803–16.965) in 2020 to 22.526 million (22.404–22.648) by 2050. Due to the low fertility rate, the population of 16–24 years and 25–59 years are projected to decline by 7.7% (10.7–4.7%), and 4.7% (6.1–3.4%) respectively, from the year 2020 to 2050.

Of the population 16 years and older, the number with carious teeth is projected to decrease from 15.742 million (15.666–15.818) in the year 2020 to 15.504 million (15.224–15.784) by the year 2050, representing a decrease of 1.5% (2.8–0.2%). For individuals with carious teeth, the older adult population is estimated to constitute 62.06% by 2050 and is projected to increase 89.4% (88.2–90.7%) from 5.079 million (5.055–5.104) in 2020 to 9.623 million (9.514–9.731) by 2050. The individuals between ages 16 and 24 years with carious teeth are projected to decrease from 0.335 million (0.329–0.340) in 2020 to 0.232 million (0.219–0.44) by 2050, which represents a decrease of 30.7% (33.3–28.2%). Likewise, the number of individuals between the ages 25–59 years with carious teeth is projected to decrease from 10.327 million (10.281–10.373) in 2020 to 5.649 million (5.490–5.808) by 2050, representing a decrease of 45.3% (46.6–44.0%). Of the individuals with carious teeth, the majority are estimated to be treated. The untreated carious teeth are expected to increase from 4.278 million (4.222–4.334) in 2020 to 7.497 million (7.308–7.686) by 2050, representing a 75.2% (73.1–77.3%) increase.

Table 2 shows the results of the projected number of adult 16 years and older with periodontal diseases in the United Kingdom from 2020 to 2050. The number of individuals with mild pocketing (pocketing between 4 and < 6 mm) is projected to increase from 20.676 million (20.552–20.799) in 2020 to 22.495 million (22.036–22.954) by 2050, representing 8.8% (7.2–10.4%) increase, while those with moderate pocketing (pocketing between 6 and < 9 mm) is estimated to decrease from 3.162 million (3.151–3.173) in 2020 to 2.489 million (2.440–2.537) by 2050, which is a decrease of 21.3% (22.6–20.0%). However, the number of people with severe pocketing (pocketing which is 9 mm or more) is projected to increase 56.7% (54.1–59.2%) from 1.912 million (1.883–1.941) in 2020 to 2.996 million (2.902–3.090) by 2050. For individuals with pocketing, by 2050, the older adult population 60 years and older is projected to constitute 54.6% [which is 15.269 million (15.062–15.475)] and is expected to increase by 39.7% (38.4–41.1%) from the year 2020 to 2050.

TABLE 1 Projected number of adult 16 years and older with dental caries in the United Kingdom from 2020 to 2050.

Age cohort	2020	2035	2050	Relative change (2020–2050) %
Population (million)				
16–24 years	6.879 [6.868–6.889]	6.984 [6.817–7.151]	6.349 [6.134–6.564]	−7.7% [−10.7-(−4.7)]
25–59 years	30.945 [30.913–30.977]	30.177 [30.049–30.305]	29.480 [29.025–29.934]	−4.7% [−6.1-(−3.4)]
60+ years	16.884 [16.803–16.965]	21.093 [20.972–21.215]	22.526 [22.404–22.648]	33.4% [33.3–33.5]
Total	54.709 [54.670–54.747]	58.255 [58.079–58.432]	58.356 [57.804–58.907]	6.7% [5.7–7.6]
Caries (million)				
16–24 years	0.335 [0.329–0.340]	0.244 [0.234–0.255]	0.232 [0.219–0.244]	−30.7% [−33.3-(−28.2)]
25–59 years	10.327 [10.281–10.373]	8.241 [8.143–8.338]	5.649 [5.490–5.808]	−45.3% [−46.6-(−44.0)]
60+ years	5.079 [5.055–5.104]	7.863 [7.795–7.931]	9.623 [9.514–9.731]	89.4% [88.2–90.7]
Total	15.742 [15.666–15.818]	16.349 [16.174–16.525]	15.504 [15.224–15.784]	−1.5% [−2. 8-(−0.2)]
Untreated caries (million)				
16–24 years	0.191 [0.186–0.195]	0.193 [0.184–0.201]	0.182 [0.173–0.192]	−4.4% [−7.3-(−1.5)]
25–59 years	2.687 [2.654–2.720]	3.359 [3.292–3.426]	3.559 [3.448–3.670]	32.4% [29.9–34.9]
60+ years	1.399 [1.381–1.417]	2.758 [2.712–2.804]	3.755 [3.686–3.823]	168.3% [166.9–169.7]
Total	4.278 [4.222–4.334]	6.311 [6.189–6.432]	7.497 [7.308–7.686]	75.2% [73.1–77.3]
Treated caries (million)				
16–24 years	0.143 [0.142–0.145]	0.0517 [0.0493–0.0540]	0.0492 [0.0465–0.0520]	−65.7% [−67.3-(−64.1)]
25–59 years	7.639 [7.627–7.652]	4.881 [4.851–4.911]	2.089 [2.041–2.137]	−72.6% [−73.2-(−72.1)]
60+ years	3.680 [3.673–3.686]	5.104 [5.083–5.126]	5.868 [5.827–5.908]	59.4% [58.6–60.3]
Total	11.464 [11.443–11.484]	10.038 [9.984–10.092]	8.006 [7.915–8.098]	−30.2% [−30. 8-(−29.5)]

TABLE 2 Projected number of adult 16 years and older with periodontal diseases in the United Kingdom from 2020 to 2050.

Age cohort	2020 (Projection in million)	2035 (Projection in million)	2050 (Projection in million)	Relative change (2020–2050) %
Periodontal pocketing*				
16–24 years	0.674 [0.659–0.690]	0.664 [0.636–0.693]	0.629 [0.595–0.662]	−6.7% [−9.7-(−4.0)]
25–59 years	14.147 [14.942–14.252]	12.955 [12.733–13.177]	12.082 [11.720–12.444]	−14.6% [−16.5-(−12.7)]
60+ years	10.929 [10.886–10.971]	14.068 [13.946–14.190]	15.269 [15.062–15.475]	39.7% [38.4–41.1]
Total	25.751 [25.588–25.913]	27.689 [27.316–28.061]	27.980 [27.379–28.582]	8.7% [7.0–10.3]
Mild pocketing	20.676 [20.552–20.799]	22.234 [21.953–22.516]	22.495 [22.036–22.954]	8.8% [7.2–10.4]
Moderate pocketing	3.162 [3.151–3.173]	2.867 [2.839–2.894]	2.489 [2.440–2.537]	−21.3% [−22.6-(−20.0)]
Severe pocketing	1.912 [1.883–1.941]	2.587 [2.523–2.650]	2.996 [2.902–3.090]	56.7% [54.1–59.2]
LOA**				
Mild LOA	13.505 [13.448–13.562]	15.037 [14.975–15.100]	15.666 [15.591–15.740]	16.0% [15.9–16.1]
Moderate LOA	4.352 [4.294–4.411]	4.398 [4.290–4.507]	4.278 [4.149–4.406]	−1.7% [−3.4-(−0.1)]
Severe LOA	0.809 [0.798–0.820]	0.916 [0.895–0.938]	0.954 [0.928–0.980]	18.0% [16.3–19.6]
Total	18.667 [18.542–18.792]	20.353 [20.164–20.541]	20.898 [20.672–21.124]	12.0% [11.5–12.4]

*Periodontal pockets severity is classified as follows: mild pocketing between 4 and < 6 mm; moderate pocketing between 6 and < 9 mm; and severe pocketing ≥ 9 mm.
**Loss of attachment (LOA) severity is classified as follows: mild LOA between 4 mm and < 6 mm; moderate LOA between 6 and < 9 mm; and severe LOA ≥ 9 mm.

The number of individuals with periodontal LOA is projected to increase from 18.6767 million (18.542–18.792) in the year 2020 to 20.898 million (20.7672–21.124) by 2050. Of the individuals with LOA, mild LOA is projected to increase from 13.505 million (13.448–13.562) in the year 2020 to 15.666 million (15.591–15.740) by 2050. The number of people with moderate LOA is projected to decrease from 4.352 million (4.294–4.411) in the year 2020 to 4.278 million (4.149–4.406) by 2050. Lastly, the number of people with severe LOA is projected to increase from 0.809 million (0.798–0.820) by the year 2020 to 0.954 million (0.928–0.980) by 2050.

Discussion

A multi-state population model using system dynamics was used to provide, for the first time, a projection of the adult population in the United Kingdom with dental caries and periodontal diseases from 2020 to 2050. The results from the oral diseases burden simulation model show that while the burden of carious teeth is projected to decrease from 2020 to 2050, the periodontal disease burden is projected to increase. However, due to population aging, the older adult population (≥60 years old) is expected to experience the highest burden of carious teeth and periodontal diseases, while a significant decrease in burden is projected from individuals between the ages of 16 and 59 years.

The insights from this 30 years projection are as follows: First, the burden of carious teeth and periodontal diseases is anticipated to shift from the adult population (16–59 years) to the older adult population. The older adult population with carious teeth is estimated to rise from 32.26% in 2020 to 62.06% by 2050. Our forecasting analysis indicating a demographic shift of caries morbidity is in line with findings from a study conducted in Germany, which assessed the trends in dental caries experience in the permanent dentition from 1997 to 2014 and projected caries experience to 2030 (8). The authors reported in their 2030 projection that young seniors (aged 65–74 years) and seniors over 75 years are expected to experience an increase in decayed and filled teeth to some degree, mainly due to the retention of more teeth that are now at risk for caries, while decayed teeth and filled teeth are projected to decrease in younger age groups (8). In terms of decreasing trends of untreated caries among the 16–24 years age group, our findings are in agreement with, those reported by Urwannachotima and colleagues, who reported that the proportion with untreated dental caries is expected to decrease slightly over the simulation time (9). They suggested that the observed increase in dental caries could be explained by the increasing and aging population, which is comparable to our findings (9). Second, the older adult population with periodontal disease is expected to increase from 42.44% in 2020 to 54.57% by 2050. The majority of periodontal diseases (80.39%) are projected to remain as mild periodontal diseases. Lastly, untreated carious teeth are estimated to increase by 75.2% from 2020 to 2050. However, the lack of United Kingdom based projections for dental caries and periodontal diseases, hinders any meaningful comparisons. These are important issues to be addressed in future research. These insights from this study has implications for public health, oral health, and economics. In terms of public health, these insights highlight the importance of continued education and improving health of the public on the causes of oral diseases and actions individuals can take to reduce the risk of developing them. Additionally, they emphasize the need for active engagement with stakeholders to explore innovative ways to address social determinants of health that negatively impact oral health outcomes, as well as the implementation of preventive oral health systems will be needed (38), as socio-behavioral and environmental factors play a significant role in oral disease and health (39–41). As for oral health, this study provides evidence-based projections of plausible future demand for oral health conditions, enabling policymakers to plan for oral health capacity to address the growing needs. By adopting this approach, policymakers can proactively plan for future capacity needs instead of being reactive, which often entails substantial delays in educating and training oral health personnel. Despite the scarcity of studies forecasting oral diseases among adults, a research study has used evidence-based projections of plausible future demand for oral health conditions. The study projected the prevalence of edentulism and its occurrence in 2030 among older Germans (aged 65–74 years) using Monte Carlo simulations. It emphasized the importance of accounting for demographic dynamics in the projection and using credible projections for oral diseases (13). Furthermore, the insight that most of the oral disease burden is projected to affect the older adult individuals, oral healthcare services should pay particular attention to the oral health needs of this population group. Proactively planning to address these projected needs can prevent the reduced quality of life associated with oral diseases (42). In the United Kingdom, there are substantial concerns about oral health inequalities evident across the social spectrum and life course, mainly reflecting socio-economic inequalities in overall health (43, 44). With the anticipated increase in dental caries and periodontal diseases among the older adult population and the rapid population aging, this age-related inequality is expected to become more challenging. Therefore, it should have a greater urgency to address risks that could exacerbate these inequalities (43, 44) If not addressed, it could lead to a decline in the oral health of the population, impeding progress toward achieving long-term health goals for the country. The economic burden associated with oral diseases burden includes the direct cost of treatment, the indirect cost of productivity losses due to absence from work and school, and intangible costs such as pain, the problem with biting, chewing, and eating, and the expression of emotions such as smiling (45). Consequently, policymakers and health systems have the opportunity to prioritize and implement cost-effective interventions that have the potential to reduce the economic cost related to the oral health burden. In the United Kingdom, oral health inequalities are a significant concern that has been extensively documented (46, 47).

The study findings hold significant importance, given the ongoing challenges facing oral healthcare system in United Kingdom (48–51). The oral health system has been struggling to meet the growing oral health needs of the population, especially post-pandemic (48). Dental services have become increasingly limited and strained due to workforce shortages, NHS budget cuts, and an increasing number of older patients (48–51). Unless these challenges are promptly addressed and effectively responded to, the projected oral health picture will worsen. These challenges highlight the need for increased attention and investment in oral health care and integration into the broader healthcare framework to accommodate aging populations and their economic burdens of dental diseases.

One of the main limitations of this study is the assumption that the 2009 ADHS age-specific prevalence rates of caries and periodontal disease remains unchanged over the simulation time. Future studies should use current representative studies to improve the projections of the adult United Kingdom population with caries and periodontal diseases. Also, the incidence of caries and periodontal diseases and the transition to severe periodontal diseases were assumed to be the same across different age cohorts. Lastly, it is essential to emphasize that a global sensitivity analysis, which requires Monte Carlo simulations, was not conducted in this study. Future studies should consider performing this analysis to enhance the robustness of the uncertainties around the projections.

Recommendations

The findings from this study that the older adult population (≥60 years old) is expected to experience the highest burden of carious teeth and periodontal diseases, while a significant decrease in burden is projected from individuals between the ages of 16 and 59 years, dictate the need for a radically different proactive approach to oral health to tackle this impended challenge. These efforts need to

be undertaken alongside broader strategies to better align health systems with the population needs and avert age-related inequalities gaps. These projections also suggest that there are large rooms for improvement in dental caries and periodontal diseases prevention and control in the United Kingdom. We recommend that policymakers prioritize improving oral health in older adults by reorienting healthy aging policies to give greater attention to this area (52), particularly given the challenges faced by the struggling health system.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: SN 6884—Adult Dental Health Survey, 2009 (Internet). 2009 (cited October 7, 2022). Available at: https://ukdataservice.ac.uk/find-data/.

Ethics statement

All methods were carried out in accordance with relevant guidelines and regulations. Original ethical approval for Adult Dental Health Survey (2009) was obtained from the Oxford National Health Service (NHS) Research Ethics Committee for the survey to be conducted and anonymized, individual-level data are freely accessible to registered researchers via the United Kingdom Data Service. Anonymized data are accessible via the UK Data Archive for which no additional ethical approval was required.

Author contributions

AE conceived the study. AE and JA designed the study and conducted the analysis and manuscript writing. JA developed the multi-state population model. 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 potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1190197/full#supplementary-material

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How long were older people expected to live with or without sarcopenia? Multistate modeling of a national cohort study

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Objectives: Sarcopenia is well known to be associated with mortality, but there is a lack of evidence on the estimates of life expectancy (LE) for sarcopenia in China. This study aims to estimate total life expectancy (TLE) and sarcopenia-specific LE in community-dwelling older Chinese adults with and without sarcopenia.

Methods: This study included participants aged 60 years and older who enrolled in the cohort in 2011 and 2013 and at least completed one follow-up until 2015 as part of the China Health and Retirement Longitudinal Study (CHARLS). The criteria for defining sarcopenia were based on the guidelines established by the Asian Working Group on Sarcopenia in 2019. TLE and sarcopenia-specific LE were estimated for the total population and subgroups using continuous-time multistate modeling.

Results: A total of 6,029 participants (49.2% women) with an average age of 68.4 (SD: 6.56) years were included in the study. The baseline prevalence of sarcopenia and possible sarcopenia was 19.5 and 44.9%, respectively. We observed that sarcopenia stages naturally deteriorated to worse stages (including death, by 24.4%) and returned to better stages (17.1%) during a median follow-up of 3.92 years (IQR: 2.00 ~ 4.00). The average TLE at the age of 60 was 20.9 [95%CI: 20.2–21.5] years (22.1 [95%CI: 19.6–24.6] for non-sarcopenic older adults, 20.9 [95%CI: 19.5–22.3] for possible sarcopenic, and 18.7 [95%CI: 16.4–21.1] for sarcopenic). Men, former and current smokers, and those living in northwest China had less TLE. Sarcopenic older adults, those with lower education, those who are unmarried, those with agriculture hukou, and those living in rural and northwest China were expected to live fewer years with non-sarcopenia. Sarcopenic older people, men, those with agriculture hukou, and those living in rural and southwest China were expected to live more years with sarcopenia.

Discussion: The results improved our understanding of the relationship between sarcopenia and life expectancy. We suggested that targeted strategies should be considered in high-risk populations and underdeveloped regions to prevent sarcopenia and improve non-sarcopenic life years for the older population.

KEYWORDS

sarcopenia, possible sarcopenia, life expectancy, multistate model, transitions

Introduction

Sarcopenia is defined as a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength and/or physical performance, associated with advancing aging (1) and with an increased risk of adverse outcomes such as falls (2), physical disability (3), poor quality of life (4), and mortality (5, 6). It has been formally recognized as a disease with the code M62.84 in the 10th version of the International Classification of Disease (ICD-10) (7). In the community, a growing number of older adults have some degree of physical or cognitive impairment because of the aging population and of increasing life expectancy (LE). The underlying decline of muscle mass or strength is often insufficient for a clinical diagnosis of sarcopenia, yet it hinders functional performance. Compared to people of the same age without sarcopenia, there is also an increased economic burden for individuals, families, and healthcare systems associated with sarcopenia due to the increased risk of hospitalization and higher costs during hospital stays (1).

A recent review concluded that the worldwide prevalence of sarcopenia varies widely depending on different assessment criteria, ranging from 9.9 to 40.4%. The average prevalence was 12.9%, according to the European Working Group on Sarcopenia in Older People/Asian Working Group on Sarcopenia (EWGSOP/AWGS) (8, 9), and it increased with age (10). In China, based on the AWGS criterion, the sarcopenia prevalence among older adults was 14.0%, which was a little higher in Chinese women than in men (11). The total life expectancy (TLE) of the Chinese population has increased to 78.2 years in 2021. It is important to determine whether those years are lived in health or whether the additional years of life result in an expansion of unhealthy status among the older population (12). The standard steps revised by EWGS/AWGS for identifying and diagnosing sarcopenia in older adults presented the results for four sarcopenia states: no sarcopenia, possible sarcopenia, sarcopenia, and severe sarcopenia (13, 14). This provides an important basis for three-grade prevention strategies for sarcopenia in older populations. Considering that sarcopenia is a highly prevalent condition among older adults and that it is associated with multiple adverse outcomes (15), it is necessary to identify whether and when older residents will live with possible sarcopenia.

With the growing awareness of the need for early recognition of musculoskeletal degeneration, primary care physicians and family caregivers have an increasingly important role in the intervention of older adults with possible sarcopenia. Studies showing risk factors related to sarcopenia, such as increasing age, unmarried status, living alone, rural residence, smoking, physical inactivity, malnutrition, and chronic diseases (1, 16–18), can provide health education and specific measures for older audiences. Recent research showed that a difference of over 8 years in TLE was attributable to lifestyle factors for Chinese adults (19). Additionally, easily interpretable ways in terms of LE may be additionally helpful for risk communication with older people and their caregivers. LE for a general older population with or without sarcopenia and stratified by modified risk factors is lacking in China. Moreover, estimates of LE stratified by sex, marital status, education, and other characteristics would be informative for vulnerable population identification and more precise risk communications.

This study aimed to estimate the TLE and sarcopenia-specific LE (NSLE: non-sarcopenic life expectancy; PSLE: possible sarcopenic life expectancy; SLE: sarcopenic life expectancy) among sarcopenic and non-sarcopenic older adults based on a nationwide cohort study from China. We additionally examined LE in older Chinese adults stratified by demographics, lifestyle factors, and regions.

Methods

Study design and participants

This study is based on the China Health and Retirement Longitudinal Study (CHARLS), which is a nationally ongoing representative longitudinal survey to examine health and economic adjustments to the rapid aging of the population in China. A more detailed description was published elsewhere (20). Because the CHARLS did not collect physical measures related to sarcopenia assessment for all participants, this study included 6,029 participants aged ≥60 years old who enrolled in the cohort in 2011 and 2013 and at least completed one follow-up until 2015. Given the requirements of the multistate model for sample data, participants were classified into three alive states (no sarcopenia, possible sarcopenia, and sarcopenia) and death in three response waves. Therefore, 6,029, 4,998, and 4,262 participants responded in Wave 1 (survey in 2011–2012), Wave 2 (survey in 2013–2014), and Wave 3 (survey in 2015–2016), respectively. The flowchart of participants is shown in Supplementary Figure S1.

Assessment of the sarcopenia state

According to the AWGS 2019 algorithm (13), the sarcopenia state was classified into "no sarcopenia," "possible sarcopenia," and "sarcopenia," which was assessed by three components: muscle strength, appendicular skeletal muscle mass (ASM), and physical performance. Sarcopenia was defined as low muscle mass plus low muscle strength or low physical performance. Possible sarcopenia was defined as low muscle strength with or without reduced physical performance. Further details about the definitions for sarcopenia components in the CHARLS have been described elsewhere (16).

Muscle strength

Handgrip strength (kg), an indicator of muscle strength, was measured in the dominant hand and the non-dominant hand, with the participant squeezing a YuejianTM WL-1000 dynamometer (Nantong Yuejian Physical Measurement Instrument Co., Ltd., Nantong, China) as hard as possible (20). Every participant was measured twice for both left and right hands by holding the dynamometer at a right angle (90°). The cutoff points for low grip strength were <28 for men and <18 for women, respectively.

The ASM

The ASM was estimated by a validated anthropometric equation in Chinese adults (21): ASM = 0.193*body weight + 0.107*height − 4.15*sex − 0.037*age − 2.631. The height, body weight, and age were measured in centimeters, kilograms, and years, respectively. For sex, the value 1 represented men, and the value 2 represented women. The agreement between the ASM equation model and dual X-ray absorptiometry (DXA) was strong (21). After calculating the ASM, the height-adjusted muscle mass (ASM/Ht^2) was calculated using the ASM divided by the square of the height in

meters. According to the AWGS 2019 (13), the cutoff points for defining low muscle mass were <7.0 for men and <5.4 for women.

Physical performance

The chair stand test measures the amount of time needed for the participants to rise continuously five times while keeping their arms folded across their chest from a chair. Participants who attempted but failed to perform the chair stand text were considered to have low physical performance for analyses. According to AWGS2019 (13), the criteria for low physical performance is a 5-time chair stand test of ≥12 s.

Age calculation

The multistate model used to estimate LE needs not only the exact status of a condition but also the exact age in the specific states. The CHARLS recorded the exact birthday of all participants and the exact year and month of interview for all survivors in each wave. The ages of survivors were calculated by the duration of the interview date and their birthdays. For age at death, the exact death time was recorded in Wave 2. Thus, the age of death for those who were dead during Wave 1 and Wave 2 was calculated by the difference between the specific time of death and birthday. In Wave 3, the exact time of death was not recorded. Referring to the previous method (22, 23), the median of the two follow-up times (the specific wave with death information and its former wave) was calculated as the death time, which was used to calculate the age at death.

Subpopulation identifier

To examine potential factors related to TLE and sarcopenia-specific LE, we classified the whole population into subpopulations by sex (man and woman), education (illiterate, non-formal education, elementary school, and middle school or above), marital status (unmarried and married), and hukou status (agriculture and non-agriculture) by self-reported data in the earliest response. Living residences (rural and urban) and regions (Northeast, East, North, Centre, South, Southwest, and Northwest) were identified according to government office region using *zip* codes in the database. We also examined the effects of behaviors including smoking (no, former, or current) and drinking (yes or no) on TLE and sarcopenia-specific LE.

Statistical analysis

Descriptive statistics for demographic and lifestyle variables are presented as frequency and percentage, and continuous variables are described as means and standard deviation (SD), and the chi-squared test was used to evaluate the difference between the prevalence of sarcopenia by subgroups. Continuous-time multistate models were used to estimate the TLE and sarcopenia-specific LE by the following two steps. In the first step, a general multistate Markov model by the *msm (multi-state model)* package (24) of the R language (25) was used to examine the parameters of yearly transition probabilities and the state distribution obtained from the general multistate Markov model conditioned on age and identifiers of a subpopulation, as defined in Supplementary Figure S2. In the second step, based on the parameters obtained in the first step, a multistate life table (MSLT) method was used to calculate the TLE and sarcopenia-specific LE by the *elect* (*Estimating Life Expectancies in Continuous Time*) package of R (26). In this study, we assumed that the human maximal age was 120 years old when we ran *elect* with the default "*step*" method for the numerical approximation. For each estimate, a standard error was calculated using a bootstrapping method that executed 30 repeated estimates through random draws. The estimation method of life expectancy was shown in the Supplementary material (p. 4–5).

To assess the robustness of the findings, three methods of sensitivity analysis were used. First, we excluded the sample that was newly enrolled in the second wave because a short follow-up period may affect the robustness of the results. Next, we, respectively, reran elect with the alternative "*MiddleRiemann*" and "*Simpson*" methods for the numerical approximation (26). Windows-based Stata version 14.0 and R version 4.2.1 were used for all of the statistical analysis, and a p-value of less than 0.05 was considered to be statistically significant.

Results

Study population and prevalence of sarcopenia

The mean age of the analysis sample was 68.4 years (SD = 6.56), with 49.2% being women. The baseline prevalence of sarcopenia and possible sarcopenia were 19.5 and 44.9%, respectively. As shown in Table 1, older people with sarcopenia had a significantly older age ($p < 0.001$). The prevalence of sarcopenia was significantly different in sex ($p < 0.001$), education ($p < 0.001$), marital status ($p < 0.001$), smoking ($p = 0.006$), drinking ($p < 0.001$), hukou type ($p < 0.001$), living residence ($p < 0.001$), and region ($p < 0.001$).

Transitions in sarcopenia stages

As presented in Figure 1, during a median follow-up of 3.92 years (IQR: 2.00 ~ 4.00), 1,119 of 3,386 older people showed transitions from no sarcopenia to possible sarcopenia (28.2%), sarcopenia (2.0%), and death (2.9%); 1,874 of 4,106 from possible sarcopenia to no sarcopenia (23.1%), sarcopenia (15.8%), and death (6.7%); and 844 of 1,768 from sarcopenia to no sarcopenia (3.5%), possible sarcopenia (32.3%), and death (12.0%), respectively. In general, 24.4% of sarcopenic older adults deteriorated to a worse stage, and 17.1% returned to a better one.

Estimates of LE

As shown in Figure 2, TLE at age 60 was, on average, 20.9 years (95% CI: 20.2–21.5) in China overall and 22.1 years (95% CI: 19.6–24.6) for those with no sarcopenia, 20.9 years (95% CI: 19.5–22.3) for possible sarcopenia, and 18.7 years (95% CI: 16.4–21.1) for sarcopenia, respectively. Sarcopenic older adults exhibited a markedly extended sarcopenia life expectancy (SLE) compared to individuals with possible sarcopenia or non-sarcopenia. Specifically, the SLE for sarcopenic older adults (8.1 years [95% CI: 6.7−9.4]) was more than double that of possible sarcopenic individuals (3.8 years [95% CI: 2.9–4.7]) and five times longer than non-sarcopenic individuals (1.5

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TABLE 1 Prevalence of sarcopenia by participant characteristics at baseline.

Characteristics	Prevalence of sarcopenia, *n* (%)			*p*
	No sarcopenia	Possible sarcopenia	Sarcopenia	
Age, mean (SD)	65.7 (4.73)	68.7 (6.43)	72.7 (7.31)	<0.001
Sex				<0.001
Man	1,286 (42.0)	1,297 (42.4)	479 (15.6)	
Woman	860 (29.0)	1,412 (47.6)	695 (23.4)	
Education				<0.001
Illiterate	495 (21.9)	1,125 (49.8)	641 (28.4)	
Non-formal education	465 (35.7)	589 (45.2)	249 (19.1)	
Elementary school	643 (43.6)	629 (42.6)	204 (13.8)	
Middle school or above	543 (54.9)	366 (37.0)	80 (8.1)	
Marital status				<0.001
Married	286 (21.8)	627 (47.9)	397 (30.3)	
Unmarried	1860 (39.4)	2080 (44.1)	777 (16.5)	
Smoking				0.006
No	697 (37.8)	814 (44.1)	333 (18.1)	
Former	286 (37.9)	341 (45.2)	127 (16.8)	
Current	1,159 (34.0)	1,542 (45.2)	711 (20.8)	
Drinking				<0.001
No	1,325 (32.0)	1947 (47.0)	873 (21.1)	
Yes	697 (46.0)	591 (39.0)	228 (15.0)	
Hukou type				<0.001
Agriculture	1,530 (32.0)	2,217 (46.3)	1,041 (21.7)	
Non-agriculture	591 (49.4)	476 (40.0)	130 (10.9)	
Living residence				<0.001
Rural	1,216 (31.0)	1836 (46.8)	867 (22.1)	
Urban	930 (44.1)	873 (41.4)	307 (14.6)	
Region				<0.001
Northeast	211 (42.2)	212 (42.4)	77 (15.4)	
East	710 (37.9)	822 (43.8)	343 (18.3)	
North	179 (35.4)	245 (48.4)	82 (16.2)	
Centre	348 (36.6)	422 (44.4)	181 (19.0)	
South	177 (30.8)	264 (45.9)	134 (23.3)	
Southwest	393 (33.2)	534 (45.1)	257 (21.7)	
Northwest	128 (29.2)	210 (48.0)	100 (22.8)	

SD, standard deviation.

years [95% CI: 0.6–2.4]). Similarly, sarcopenic older adults had notably shorter non-sarcopenia life expectancy (NSLE) compared to possible sarcopenic individuals and non-sarcopenic individuals. The NSLE for sarcopenic older adults (2.7 years [95% CI: 1.9–3.5]) was approximately half of that for possible sarcopenic individuals (6.4 years [95% CI: 5.7–7.2]) and just a quarter of that for non-sarcopenic individuals (12.1 years [95%CI: 11.0–13.1]).

Stratified LE

Table 2 presents the TLE and sarcopenia-specific LE among demographic, lifestyle, and regional factors. Men (19.3 years [95%CI: 18.4 ~ 20.2]), former smokers (16.7 years [95%CI: 15.3 ~ 18.1]), and current smokers (20.0 years [95%CI: 18.7 ~ 21.2]) were expected to live fewer total life years. Those with lower education (7.1 years [95%CI: 6.5 ~ 7.6] for those with illiterate education and 6.9 years [95%CI: 6.2 ~ 7.6] for those with non-formal education), those who are unmarried (6.8 years [95%CI: 6.1 ~ 7.6]), those with agriculture hukou (7.4 years [95%CI: 7.0 ~ 7.8]), and those living in rural areas (7.4 years [95%CI: 7.0 ~ 7.9]) were expected to live fewer life years with non-sarcopenia. Men (5.5 years [95%CI: 4.8 ~ 6.2]), those with agriculture hukou (4.5 years [95%CI: 4.1 ~ 5.0]), and those living in rural areas (4.8 years [95%CI: 4.3 ~ 5.3]) were expected to live more life years with sarcopenia. In addition, Figure 3 presents the TLE and sarcopenia-specific LE among older Chinese at age 60 by region. Older

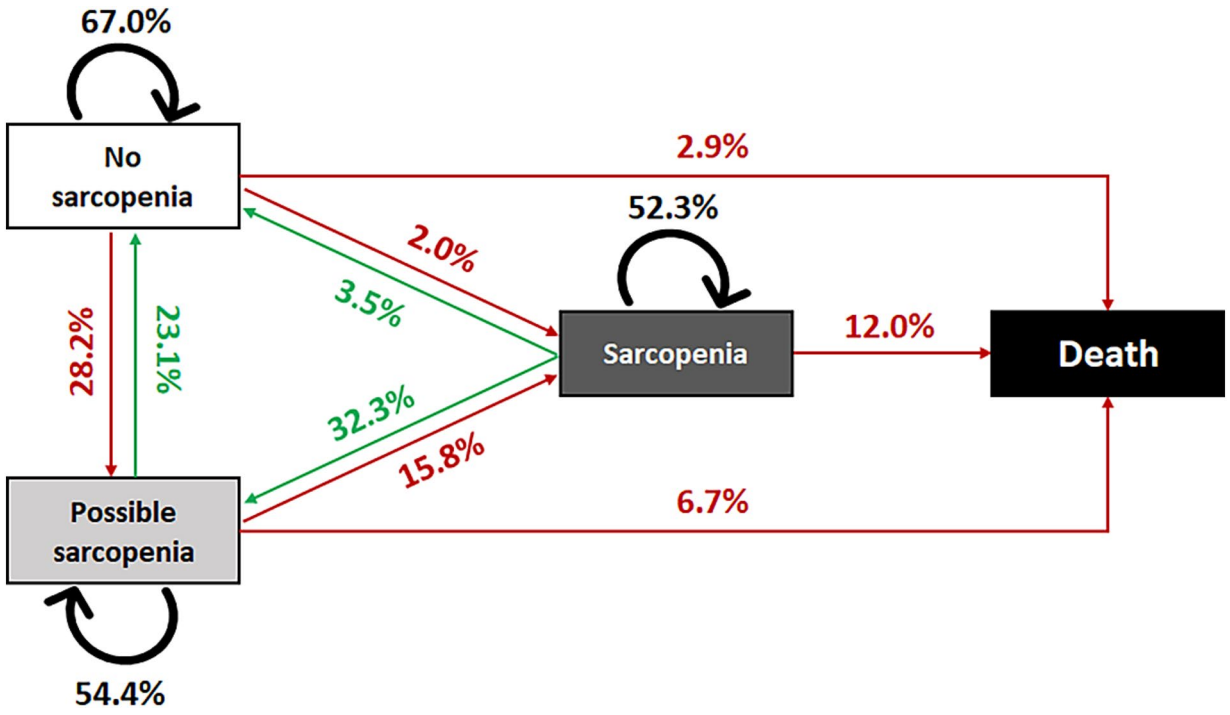
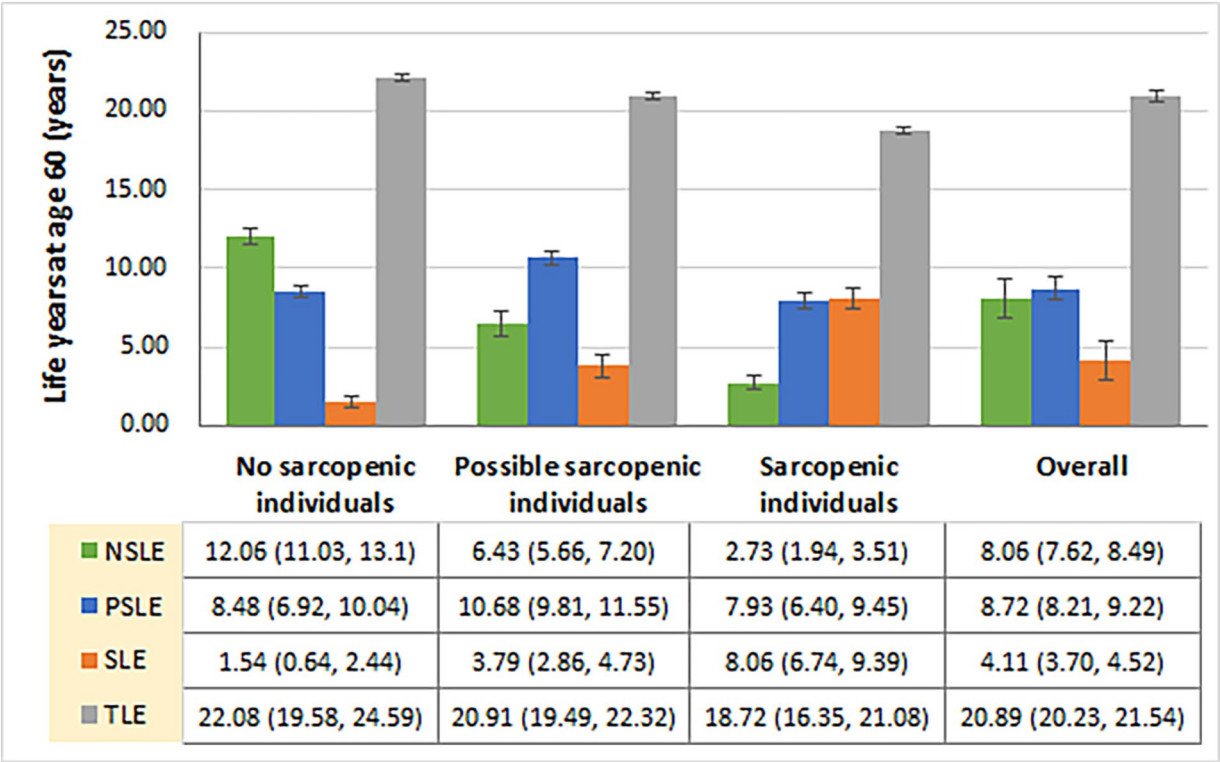


FIGURE 1
Transitions of sarcopenia state, China Health and Retirement Longitudinal Study, 2011–2015.



	No sarcopenic individuals	Possible sarcopenic individuals	Sarcopenic individuals	Overall
NSLE	12.06 (11.03, 13.1)	6.43 (5.66, 7.20)	2.73 (1.94, 3.51)	8.06 (7.62, 8.49)
PSLE	8.48 (6.92, 10.04)	10.68 (9.81, 11.55)	7.93 (6.40, 9.45)	8.72 (8.21, 9.22)
SLE	1.54 (0.64, 2.44)	3.79 (2.86, 4.73)	8.06 (6.74, 9.39)	4.11 (3.70, 4.52)
TLE	22.08 (19.58, 24.59)	20.91 (19.49, 22.32)	18.72 (16.35, 21.08)	20.89 (20.23, 21.54)

FIGURE 2
Total and sarcopenia-specific life expectancies among older Chinese with and without sarcopenia at age 60, China Health and Retirement Longitudinal Study, 2011–2015. NSLE, non-sarcopenic life expectancy; PSLE, possible sarcopenic life expectancy; SLE, sarcopenic life expectancy; TLE, total life expectancy.

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TABLE 2 Total and sarcopenia-specific life expectancies for older Chinese at age 60 by demographic and lifestyle subgroups.

Variables	Total and sarcopenia-specific life expectancy, mean (95%CI)			
	NSLE	PSLE	SLE	TLE
Sex				
Man	8.38 (7.85, 8.92)	7.87 (7.23, 8.50)	3.05 (2.70, 3.39)	19.30 (18.44, 20.15)
Woman	7.71 (7.15, 8.26)	9.62 (9.04, 10.20)	5.51 (4.82, 6.19)	22.83 (21.80, 23.87)
Education				
Illiterate	7.07 (6.53, 7.60)	9.52 (9.00, 10.05)	4.76 (4.18, 5.33)	21.35 (20.55, 22.14)
Non-formal education	6.90 (6.21, 7.60)	8.33 (7.30, 9.35)	4.29 (3.47, 5.10)	19.52 (18.01, 21.02)
Elementary school	9.04 (8.10, 9.98)	8.21 (7.24, 9.19)	3.41 (2.47, 4.36)	20.67 (19.11, 22.23)
Middle school or above	10.03 (9.18, 10.88)	8.88 (7.59, 10.16)	3.22 (2.14, 4.30)	22.12 (19.96, 24.28)
Marital status				
Married	8.41 (7.91, 8.90)	8.67 (8.09, 9.24)	3.96 (3.55, 4.37)	21.03 (20.16, 21.90)
Unmarried	6.85 (6.14, 7.56)	8.95 (8.09, 9.80)	4.47 (3.79, 5.15)	20.26 (19.09, 21.44)
Smoking				
No	8.36 (7.88, 8.83)	9.70 (9.05, 10.35)	5.02 (4.43, 5.61)	23.08 (21.99, 24.16)
Former	8.09 (7.02, 9.16)	6.71 (5.64, 7.77)	1.90 (1.31, 2.48)	16.69 (15.26, 18.12)
Current	7.61 (6.85, 8.36)	8.33 (7.59, 9.08)	4.03 (3.34, 4.71)	19.97 (18.74, 21.20)
Drinking				
No	7.82 (7.35, 8.29)	8.99 (8.55, 9.43)	4.30 (3.87, 4.74)	21.11 (20.37, 21.86)
Yes	8.62 (7.84, 9.41)	7.98 (7.00, 8.96)	3.75 (3.07, 4.44)	20.36 (18.90, 21.82)
Hukou type				
Agriculture	7.36 (6.95, 7.77)	8.86 (8.46, 9.27)	4.52 (4.09, 4.95)	20.74 (20.04, 21.44)
Non-agriculture	10.61 (9.61, 11.61)	7.94 (6.74, 9.15)	2.57 (1.96, 3.18)	21.12 (19.51, 22.74)
Living residence				
Rural	7.43 (6.98, 7.88)	8.80 (8.36, 9.25)	4.83 (4.33, 5.33)	21.07 (20.28, 21.86)
Urban	9.33 (8.59, 10.06)	8.39 (7.49, 9.29)	2.83 (2.39, 3.27)	20.55 (19.36, 21.74)

CI, confidence interval; NSLE, non-sarcopenic life expectancy; PSLE, possible sarcopenic life expectancy; SLE, sarcopenic life expectancy; TLE, total life expectancy.

Chinese living in northwest China (16.4 years [95%CI: 14.5 ~ 18.3]) were expected to live fewer total life years, while those living in the northwest (5.2 years [95%CI: 4.4 ~ 6.0]) of China were expected to live fewer life years with non-sarcopenia, and those living in the southwest of China (5.6 years [95%CI: 4.6 ~ 6.6]) were expected to live more life years with sarcopenia.

Sensitive analysis

The results of sensitive analyses conducted by different methods were almost consistent with the main analysis (Supplementary Tables S2–S7). There were almost no differences from the results of the main analyses, which indicated the robustness of the findings.

Discussion

The findings of our study suggest that sarcopenia stages can transition into each other naturally. Sarcopenia stages can deteriorate to a worse stage (including death, 24.4%) but can also turn back to a better stage (17.1%). The majority stayed in the same stages, which is consistent with the previous study, even with a longer follow-up (27) and more stages (28). These results provide evidence that sarcopenia is a dynamic, reversible, and generally progressive disease similar to frailty (29, 30). Beyond the age of 50, muscle mass and strength started to decline smoothly with age and showed a steep drop over 85 years (1, 14). Possible sarcopenia is a relatively unstable stage, in that approximately half of the patients transition to other stages, indicating a possibility for intervention. For example, nutrition and exercise would provide benefits for sarcopenic patients (13, 31). Therefore, it is probably the healthy lifestyle approach advocated by health authorities in recent years that promotes the recovery of some sarcopenic patients to a certain extent. It is well known that sarcopenia is correlated with a higher risk of mortality (1, 5). We also found that older adults with possible sarcopenia or sarcopenia have an approximately 2.9-fold higher risk of all-cause mortality than those without, which is similar to the newly available evidence from a meta-analysis based on community-dwelling older adults (5).

Our study shows significant differences in TLE and sarcopenia-specific LE between sarcopenic and non-sarcopenic older people. In both absolute and relative terms, at age 60 years, sarcopenic older Chinese expected to live more life years with sarcopenia (8.06 vs.

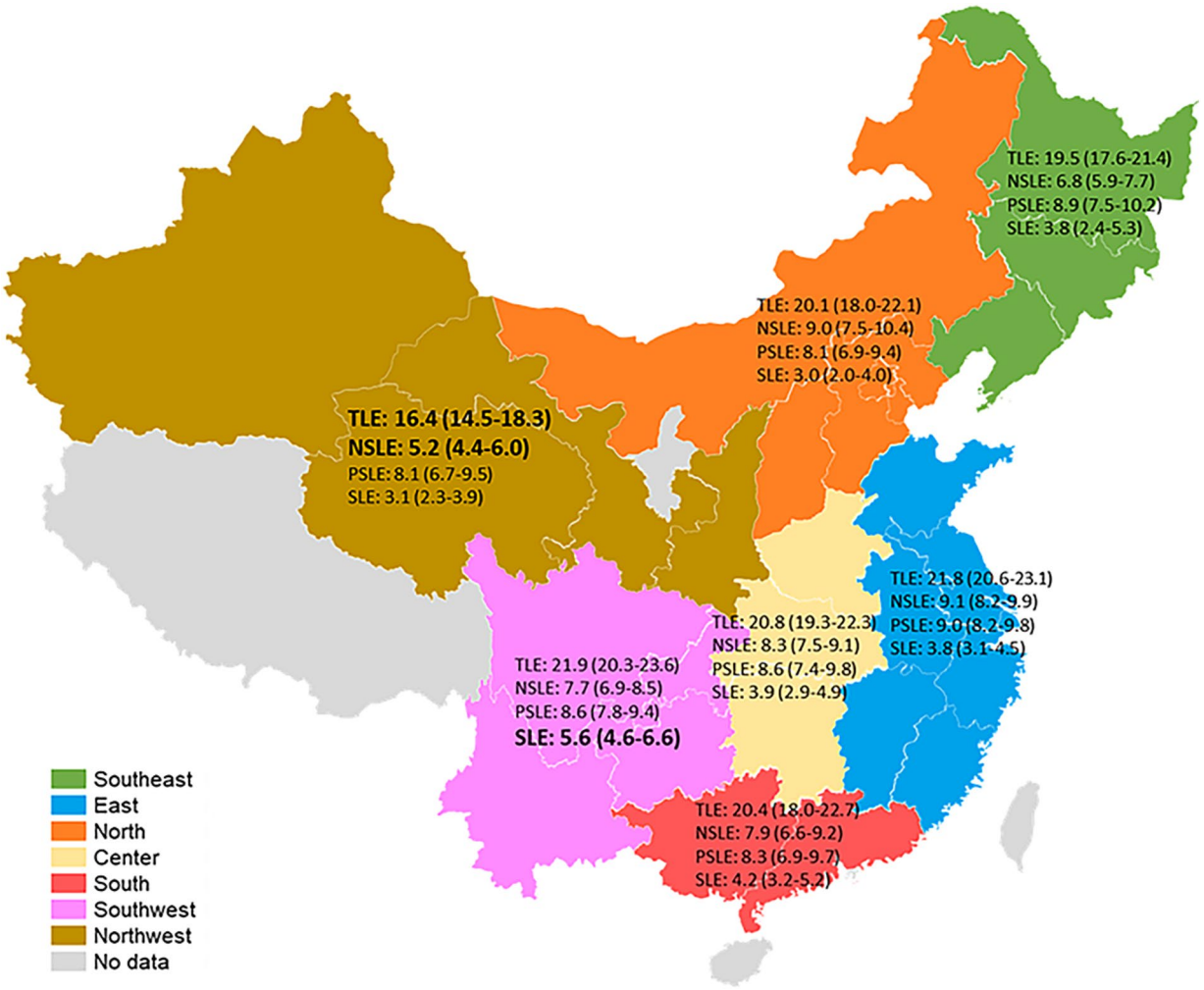

FIGURE 3
Total and sarcopenia-specific life expectancies among older Chinese at age 60 by regions, China Health and Retirement Longitudinal Study, 2011–2015. TLE, total life expectancy; NSLE, non-sarcopenic life expectancy; PSLE, possible sarcopenic life expectancy; SLE, sarcopenic life expectancy.

1.54 years; 43.0% vs. 7.0%), fewer life years with non-sarcopenia (2.73 vs. 12.06 years; 14.6% vs. 54.6%), and fewer total life years (18.72 vs. 22.08 years), compared to non-sarcopenic individuals. Compared to the average level, the findings of a 10.4% reduction in TLE, a double increase in SLE, and an almost two-thirds decrease in NSLE for sarcopenic older adults are amazing but understandable. Sarcopenia has been proven to lead to multiple adverse health outcomes, including falls, frailty, functional decline, poor quality of life, and mortality (1). It is not difficult to understand that these adverse outcomes, in turn, can reduce older patients' physical activity and/or social participation, creating an adverse cycle. Therefore, we suggest that sarcopenic older adults need to be intervened with and treated as soon as possible to reduce the impact on their daily activities.

The life expectancy results for older Chinese at age 60 by population subgroups suggest that women were expected to live more total life years but also more life years with sarcopenia and possible sarcopenia than men. This paradoxical phenomenon was also found in many previous studies that showed that women lived longer but were unhealthy (1, 11, 19). Both former and current smokers were expected to live fewer total years, which is consistent with previous studies (31). In the current study, those who start smoking in early adult life and continue smoking lose approximately 3.11–6.39 years of life. A study conducted in Japan showed that the reduced life years of those smoking people were almost a decade (32). We also found that those with lower education and those who are unmarried were expected to live fewer life years with non-sarcopenia. In common with previous studies, lower education and unmarried status were risk factors for sarcopenia (18, 33).

Poorer population health tends to be present in poorer regions (34). The results of our study also show that older people with agriculture hukou and those living in rural and northwest China were expected to live fewer life years with non-sarcopenia and those with agriculture hukou, those living in rural and southwest China were expected to live more life years with sarcopenia. In China, the development of the regional economy is unbalanced. The eastern region has the fastest economic development, while the economies of

the western regions are relatively backward. It may be explained by the fact that health inequality is closely related to regional economic inequality (34). Hukou type presents an individual's birthplace; that is, agriculture hukou presents the person born in a rural region. Although some people with agriculture hukou live in urban areas, childhood experiences may influence physical function in later life (35). Previous studies have shown that the prevalence of sarcopenia is higher in rural regions (16, 36). This may be due to inadequate medical conditions and a higher incidence of malnutrition in the rural population (36).

The strengths of this study include the national sample and the measurement of sarcopenia according to the AWGS 2019, which enhance the representativeness of the results and their comparability to other studies. TLE and sarcopenia-specific LE were estimated using the multistate model, which can also describe how individuals move through different stages of sarcopenia and can capture the dynamic nature of sarcopenia, compared with the existing methods of calculating LE, such as the Cox model and the Sullivan method. To our knowledge, this study is one of the few to profile the transitions of sarcopenia stages and their end to death and the first to present the relationship between expected life years and sarcopenia in older Chinese adults.

However, several limitations are associated with the measurement of sarcopenia in the current study. First, although this is a large national cohort study, the excluded participants due to missing sarcopenia assessments and the loss of follow-up in the study may lead to potential selection bias. More number of older participants in the excluded sample may lead to an underestimation of the prevalence of sarcopenia because of the positive association between sarcopenia and age (10). Second, we estimated the ASM based on an anthropometric equation instead of the DXA, which was recommended by the AWGS 2019 (13). The equation has been validated and shows high agreement with the measurement of DXA in the Chinese population (21).

Conclusion

The findings of this study present the nature of the transitions of sarcopenia and the estimates of life expectancy with and without sarcopenia. The results improve the understanding of the relationship between sarcopenia and life expectancy, provide a simple measure of health education for older adults, and highlight the importance of early identification and intervention for sarcopenia among older Chinese adults. We suggest that women, older adults with lower education, and those who are unmarried, those with agriculture hukou, and both former and current smokers are particularly susceptible to sarcopenia. Targeted strategies should be taken in rural areas and underdeveloped regions of western China to prevent sarcopenia and improve non-sarcopenic life years for the older population.

Data availability statement

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

Ethics statement

The studies involving human participants were reviewed and approved by Biomedical Ethics Review Committee of Peking University (IRB00001052-11015). The Ethics Committee waived the requirement of written informed consent for participation. This study is a secondary analysis of the publicly available database of CHARLS, and the data have been fully de-identified.

Author contributions

BY analyzed and interpreted the data, drafted and revised the manuscript. JG designed the study, interpreted the data, and revised the manuscript. YW, JX, JJ, and SY contributed to the visualization and revised the manuscript. ZB and JC contributed to interpreting the data. 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.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1203203/full#supplementary-material

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Effects of different types of exercise on hypertension in middle-aged and older adults: a network meta-analysis

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Objective: This study mainly used network meta-analysis to explore the effect of different types of exercise on hypertension in middle-aged and older adults.

Methods: Several databases (e.g., PubMed, Embase, and the Cochrane Library) were used to search for randomized controlled trials on the effects of different types of exercise on hypertension in middle-aged and older adults.

Results: A total of 19 articles and 2,385 participants were included in the analysis. Aerobic exercise interventions [MD = −9.254, $P < 0.05$, 95% CI (−14.810, −3.698)] and static exercise interventions [MD = −10.465, $P < 0.05$, 95% CI (−18.135, −2.794)] had a significant effect on the improvement in systolic blood pressure (SBP). For diastolic blood pressure (DBP), aerobic exercise interventions [MD = −1.4096; $P > 0.05$, 95% CI (−8.2395, 5.4201)] and static exercise interventions [MD = −4.5206, $P > 0.05$, 95% CI (−14.0436, 5.0023)] were not statistically significant. The results of the surface under the cumulative ranking curve (SUCRA) showed that static exercise improved hypertension better than aerobic exercise.

Conclusion: Aerobic exercise and static exercise have been shown to have a good effect on the improvement of hypertension, but the effect on DBP is not significant.

KEYWORDS

hypertension, aerobics, static exercise, middle-aged and older adults, types of exercise

1. Introduction

The increasing prevalence of hypertension in modern times is a cause for worry. Hypertension is characterized by higher-than-normal blood pressure. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of Hypertension (2003 guidelines) stated that blood pressure varies throughout the day, and blood pressure measurements that are always higher than normal may indicate hypertension; the higher the blood pressure level, the greater the risk of other health problems, such as heart disease, heart attack, and stroke (1). The American Society of Cardiology/American Heart Association Guidelines for Prevention, Detection, Evaluation, and Management of Adult Hypertension (2017) indicate that normal blood pressure is below 120/80 mmHg; prehypertensive systolic blood pressure is 120–129 mmHg with diastolic blood pressure <80 mmHg; systolic blood pressure for hypertension is 130 mmHg or higher, and diastolic blood pressure is 80 mmHg or higher (2). The growth rate of the population affected by hypertension gradually increases with age, especially in middle-aged people. For adults aged 45 years without hypertension, the risk of hypertension over the next 40 years was 93% in African Americans, 92% in Hispanic individuals, 86% in white individuals, and 84% in Chinese adults (3). In the Framingham Heart Study, ~90% of all adults aged

55 or 65 years without hypertension developed hypertension during their lifetime (4). Hypertension usually develops over time. It may occur due to unhealthy lifestyle choices, such as insufficient physical exercise, excessive alcohol consumption, or an abnormal diet. Non-pharmacological therapy alone is particularly suitable for preventing hypertension and is used to manage the conditions of adults with hypertension or people with mild hypertension (5).

Non-pharmacological interventions can be performed through lifestyle-changing behavioral strategies and the promotion of physical activity, with the goal of modest BP reduction in the general population or more targeted BP reduction in adults at high risk of hypertension (6). The role of increased physical activity in reducing blood pressure has been repeatedly demonstrated in clinical trials, especially due to dynamic aerobic exercise and static isometric exercise (7, 8). Aerobic exercise is mainly fueled by aerobic metabolism, i.e., when the oxygen supply is sufficient. Generally, the exercise time is longer (more than 30 min), and the main muscle groups of the entire body contribute to the increased oxygen consumption during exercise (9). Quiet isometric stretching also has similar effects on functional improvement and therapeutic rehabilitation (10). Most trials were relatively short in duration, but increased physical activity has been a long-term intervention for lowering blood pressure and preventing hypertension (11). However, there is no main overview of the combined intervention of dynamic and static exercise modes, which needs further discussion and research. A meta-analysis revealed that interventions can prevent or improve the effects of hypertension and reported the effects of regular aerobic exercise on blood pressure, with an average reduction of 2–4 mmHg in SBP in adults with normal blood pressure and 5–8 mmHg in hypertensive patients (12). In addition, a meta-analysis showed that isometric exercise also had significant effects on lowering blood pressure (8). An isometric or static contraction is defined as a sustained muscle contraction (i.e., an increase in tension) with no change in the length of the involved muscle group (13). Isometric exercise might be an effective non-drug intervention for preventing and treating hypertension in older adults (14). There are a variety of active and passive stretches that are essential for the flexibility of older adults. This study mainly used network meta-analysis to explore the influence of different exercise types on hypertension in middle-aged and older adults and to explore the best exercise therapy to reduce hypertension in middle-aged and older adults.

2. Materials and methods

2.1. Inclusion criteria and literature search strategies

The literature search used the Boolean logic algorithm to obtain subject words and free words, searching databases including CNKI, Wanfang, Weipu, PubMed, Embase, Cochrane Library, and Web of Science for articles published up to 23 July 2023. The main subject words were "hypertension, blood pressure, high, high blood pressure, middle age, aerobic training, static training, combined training, and randomized controlled trial." The literature screening applied PICOS strategies, which have been widely used in evidence-based medicine or practice. In the current study, the literature inclusion criteria were as follows: (1) subjects were middle-aged and older adults, with an average age of 45–64 years, without cardiovascular disease or other diseases; (2) randomized controlled experiments; (3) the exercise group only carried out the planned aerobic exercise or static stretching exercise, while the control group received no exercise intervention and no other intervention measures; (4) the intervention lasted more than 4 weeks; and (5) the aim of the study was mainly to compare the mean and standard deviation (SD) of resting blood pressure at baseline and at the end of the study between the control and exercise groups. The studies identified from the literature screening search were mainly those on the effect of exercise on blood pressure in middle-aged and older adults. Once those studies were identified, two investigators independently decided whether they should be included in the analysis. If the two authors disagreed, a third author intervened.

2.2. Data extraction and research quality evaluation

Data extraction was completed with a prespecified data extraction form that extracted relevant data and details related to the study's subject characteristics, interventions, and primary outcomes for systematic analysis. However, the usual PEDro score of two depends on how the study blinded the group and the treatment. In general, it is difficult to blind subjects in studies of exercise interventions. Therefore, these two points were excluded from the study analysis, and the PEDro assessment was based on eight terms, each scoring one point. The authors independently extracted and examined the data and assessed the quality of each study using the PEDro score.

2.3. Statistical analysis

Network meta-analysis was performed using Stata 16 software and RevMan 5.0 software. The outcome indicators selected were continuous variables, and the mean difference (MD) and 95% CI were used as effect size indicators. When $P < 0.05$, the inconsistent model was significant. These data cannot be directly analyzed by the consistency model; if $P > 0.05$, there was no significant difference between the direct and indirect comparisons, and the consistency model was used for analysis. A cumulative ranking probability map (SUCRA) was used to rank and compare the types of interventions. When SUCRA = 1, intervention measures are highly effective, while when SUCRA = 0, intervention measures are highly ineffective (15). According to the SUCRA values of the SBP and DBP indices, a stratified cluster analysis was used to explore the optimal treatment intervention.

3. Results

3.1. Literature screening process

A total of 2,652 relevant articles were screened by a preliminary search of each database, and 19 articles, including 2,385 subjects, were finally included in the preliminary screening of titles and

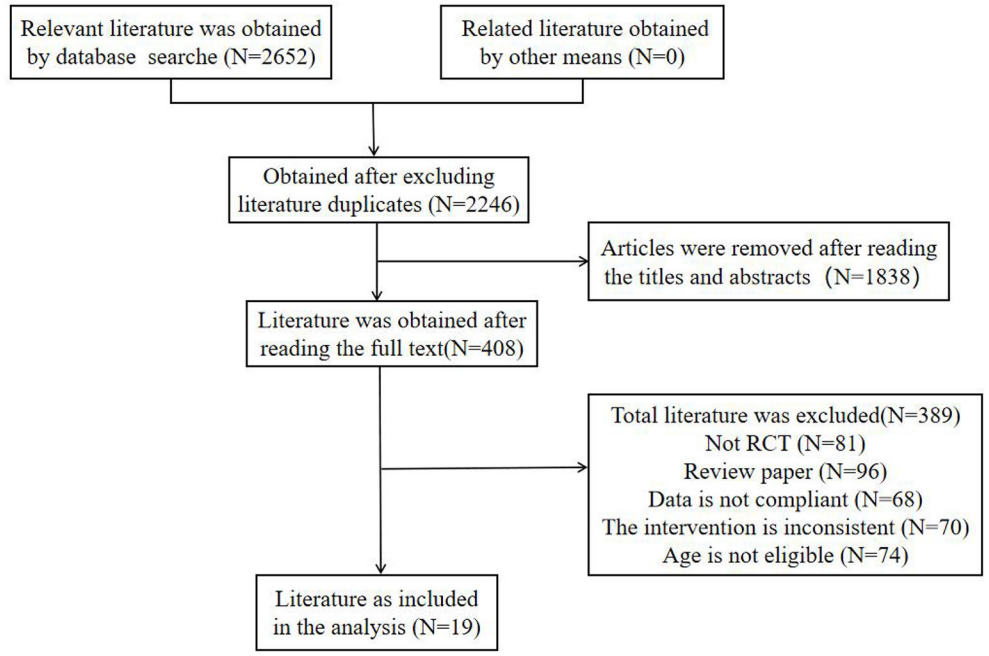

FIGURE 1
Flowchart of literature screening.

abstracts, as well as the rescreening of the full text. The main flow chart of the literature screening is shown in Figure 1.

3.2. The basic characteristics of the included studies and the evaluation of study quality

The 19 included studies mainly focused on hypertension in middle-aged and older adults. All subjects were grouped according to the principle of randomized control and the basic characteristics of the included studies (see Table 1).

All 19 included studies achieved "random assignment," ITT intention-to-treat analysis, "statistical analysis between groups," and "point measurement and variation measurement." It is difficult to assess the overall quality of the study by blinding the subjects and therapists; therefore, these two points were excluded. The PEDro assessment is based on eight factors, and each is worth 1 point. Most PEDro scores were between five and six points, with an average score of ~6 points, and only one study reached a score of eight points. Overall, the results of the quality assessment of the literature were good (see Table 2).

3.3. Consistency analysis results

The inconsistency model test of the 19 RCTs included showed that SBP ($P = 0.228$) and DBP ($P = 0.667$) were not significant. The results of the local inconsistency test by the node splitting method again resulted in $P > 0.05$, and the results of indirect comparison and direct comparison of the two indices were shown to be consistent, indicating that the consistency model should be used for analysis.

3.4. Results of network meta-analysis

A total of 19 studies were included, including 11 studies comparing aerobic exercise with a control group, two studies comparing static exercise with a control group, and six studies comparing aerobic exercise with static exercise with the control group. For the network relationship between SBP and DBP of different exercise interventions, the circle area of aerobic exercise was the largest. The edge between aerobic exercise and conventional exercise was wider, indicating that studies comparing aerobic exercise with conventional exercise appeared most frequently among the included studies (Figure 2). Therefore, the effect of aerobic exercise on the hypertension of middle-aged and older adults is still supported by many studies, thus indicating a strong theoretical basis for its support.

3.5. Network meta-analysis of the effects of different exercise interventions on SBP

The results of the meta-analysis showed the MD value of aerobic exercise intervention [MD = −9.254, $P < 0.05$, 95% CI (−14.810, −3.698)] and the MD value of static exercise intervention [MD = −10.465, $P < 0.05$, 95% CI (−18.135, −18.135); −2.794] were better than those of the control group in improving SBP in hypertension. An indirect comparison between the two exercise modes showed no significant difference in SBP between the two

TABLE 1 Basic characteristics of the included studies.

References	Age (T/C)	Sample (T/C)	Intervention/control measures (T/C)	Intervention cycle	Outcome indicator
Ko et al. (16)	61.9 ± 8.4/61.2 ± 15.0	20/20	ST/AT	8 weeks	SBP; DBP
Nemoto et al. (17)	62.3 ± 11.7/61.2 ± 13.3	27/26	ST/C	16 weeks	SBP; DBP
Lamina et al. (18)	58.27 ± 6.24	140/105	AT/C	8 weeks	SBP; DBP
Ng et al. (19)	50	30/30	AT/C	8 weeks	SBP; DBP
Cornelissen et al. (20)	59	26/22	AT/ST	10 weeks	SBP; DBP
Tsai et al. (21)	48.8 ± 6.3/49.3 ± 7.2	52/50	AT/C	10 weeks	SBP; DBP
He et al. (22)	58 ± 2/57 ± 2/58 ± 2	20/22/20	AT/ST/C	12 weeks	SBP; DBP
Zaleski et al. (23)	52.3 ± 10.8	12/12	AT/C	12 weeks	SBP; DBP
Wong and Figueroa (24)	57 ± 1/56 ± 1	14/14	ST/C	8 weeks	SBP; DBP
Dobrosielski et al. (25)	57 ± 6/56 ± 6	51/63	AT/C	6 months	SBP; DBP
Huiming and Qian (26)	55.7 ± 6.6/56.3 ± 7.5	39/41	AT/C	24 weeks	SBP; DBP
Jin-tao (27)	48.20 ± 7.0/49.62 ± 6.1	50/50	AT/C	3 months	SBP; DBP
Chen et al. (28)	45.77 ± 6.6/45.92 ± 7.2	48/48	AT/C	3 months	SBP; DBP
Hua et al. (29)	52.37 ± 10.45/51.90 ± 10.18	47/46	AT/C	6 months	SBP; DBP
Shengli (30)	50.48 ± 6.3/50.29 ± 6.1	61/61	AT/C	6 months	SBP; DBP
Guirong et al. (31)	50.5 ± 5.6	171/149/149	AT/ST/C	4 weeks	SBP; DBP
Siu et al. (32)	61.0 ± 5.7/62.2 ± 6.6/62.6 ± 6.2	181/181/181	AT/ST/C	12 weeks	SBP; DBP
Dos Santos et al. (33)	63.1 ± 2.3/64.2 ± 3.1/62.6 ± 2.5	20/20/20	AT/ST/C	16 weeks	SBP; DBP
Headley et al. (34)	58.0 ± 8.0; 57.1 ± 9.0	25/21	AT/C	16 weeks	SBP; DBP

groups ($P > 0.05$). The results of the SUCRA ranking showed that the effect of static exercise on SBP in hypertension was better than that of aerobic exercise (Figure 3).

3.6. Network meta-analysis of the effects of different exercise interventions on DBP

The results of the meta-analysis showed that the MD value in the aerobic exercise intervention [MD = −1.4096; $P > 0.05$, 95% CI (−8.2395, 5.4201)] and the MD value in the static exercise intervention [MD = −4.5206, $P > 0.05$, 95% CI (−14.0436, 5.0023)] had no significant effect on DBP improvement in hypertension (all $P > 0.05$). An indirect comparison between the two showed no significant difference in exercise mode between the two groups ($P > 0.05$). The results of the SUCRA ranking showed that static exercise had a better effect on DBP in hypertensive individuals (see Figure 3).

3.7. Detection of publication bias

Compared with the corrected funnel plot, the inverted funnel plot was symmetric, and the scattered points were distributed within the range of the inverted funnel plot (see Figure 4), indicating that there was little possibility of a small-sample effect or publication bias.

4. Discussion

4.1. Intervention effects of aerobic exercise on hypertension in middle-aged and older adults

Many recent studies have found that exercise modes such as isokinetic resistance training, limb stretching exercises, swimming, and running can reduce blood pressure (12, 35). Some studies have shown that aerobic exercise training can lower blood pressure by 5–7 mmHg (36). In this study, aerobic exercise was also found to have a significant effect on lowering SBP in middle-aged and older adults with hypertension, which can reduce the incidence of hypertension to some extent. Engaging in physical activity can also further prevent cardiopulmonary impairment and lower blood pressure (37). The incidence of hypertension increases with age, and the older the individuals are, the more their exercise ability will be affected, and the exercise mode or intensity will be limited (38). The incidence of many chronic diseases, such as cardiovascular disease and hypertension, further increases with age (39, 40). Many forms of aerobic exercise can lower blood pressure in middle-aged and older adults, such as jogging, square dancing, and aerobics, all of which have good effects. Whelton et al. found that aerobic exercise had an overall net effect of reducing SBP and DBP by 3.84 and 2.58 mmHg, respectively (7). Hagberg et al.'s review showed that in hypertensive adults aged 60 or older, SBP and DBP values were reduced by an average of 7.6/8.8 mmHg (41). In this study,

TABLE 2 Quality evaluation of the included studies.

Study	Random allocation	Distribute hide	Baseline similar	Subjects were blinded	Withdrawal rate <15%	ITT intentional treatment analysis	Statistical analysis between groups	Point measurements and variance magnitudes	Total
Ko et al. (16)	1	0	1	0	1	1	1	1	6
Nemoto et al. (17)	1	0	1	0	1	1	1	1	6
Lamina et al. (18)	1	0	1	0	0	1	1	1	5
Ng et al. (19)	1	0	1	0	1	1	1	1	6
Cornelissen et al. (20)	1	0	0	0	1	1	1	1	5
Tsai et al. (21)	1	0	1	0	1	1	1	1	6
He et al. (22)	1	0	1	0	1	1	1	1	6
Zaleski et al. (23)	1	0	1	0	1	1	1	1	6
Wong and Figueroa (24)	1	0	1	0	0	1	1	1	5
Dobrosielski et al. (25)	1	0	1	0	1	1	1	1	6
Huiming and Qian (26)	1	0	1	0	1	1	1	1	8
Jin-tao (27)	1	1	1	0	1	1	1	1	6
Yan (28)	1	0	1	0	1	1	1	1	6
Hua et al. (29)	1	1	1	0	1	1	1	1	7
Shengli (30)	1	0	1	0	1	1	1	1	6
Guirong et al. (31)	1	0	1	0	1	1	1	1	6
Siu et al. (32)	1	1	1	0	0	1	1	1	6
Dos Santos et al. (33)	1	0	1	0	1	1	1	1	6
Headley et al. (34)	1	1	1	0	1	1	1	1	7

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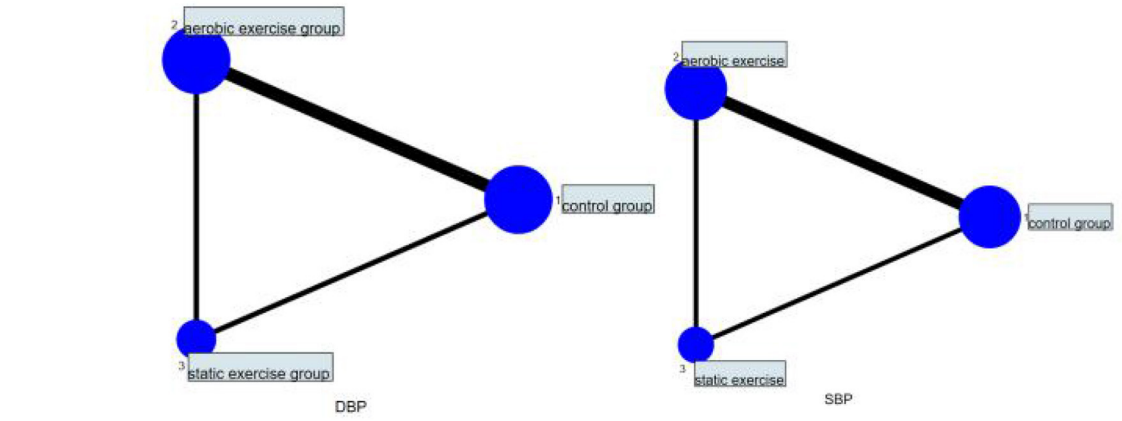

FIGURE 2
Network meta-analysis intervention diagram.

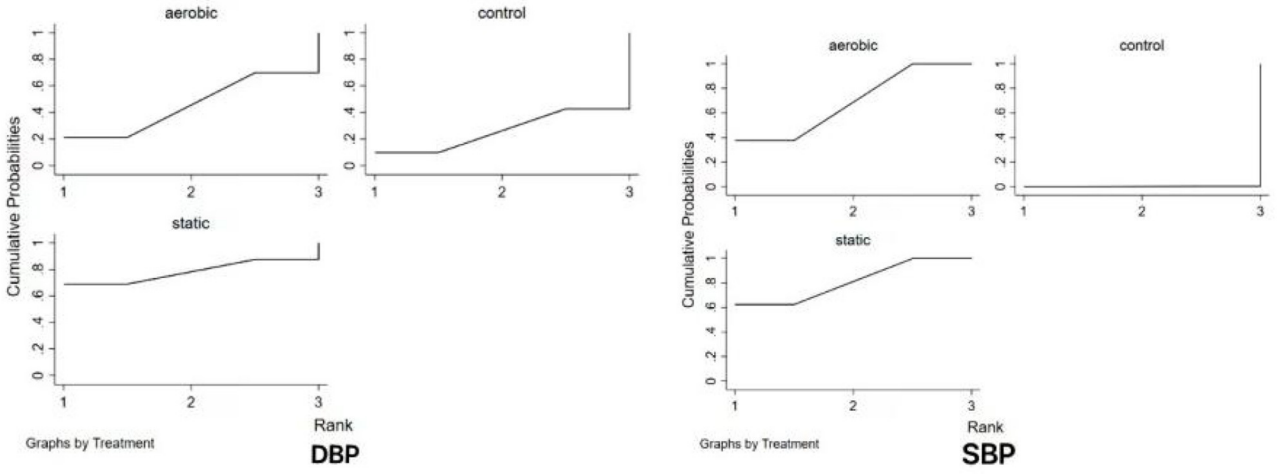

FIGURE 3
Probability ranking plot of different outcome measures of the intervention.

aerobic exercise had a significant effect on SBP but not on DBP. This suggests that in this study, aerobic exercise effectively lowered blood pressure in middle-aged and older adults with hypertension, which has certain clinical significance and value for the health and medical conditions of both middle-aged and older adults.

4.2. Isometric exercise intervention effects on hypertension in middle-aged and older adults

For middle-aged and older individuals, the most common isometric exercises are static stretching exercises, which are primarily defined as sustained muscle contraction (i.e., increased tension) without changes in the length of the involved muscle groups. To date, relatively little attention has been given to the effects of isometric exercise training on resting blood pressure. The results from previous meta-analysis suggest that although the overall sample size is still small, isometric exercise training may produce greater reductions in resting blood pressure (42, 43). The study results also showed that the improvement effect of isometric exercise on the SBP and DBP of middle-aged and older hypertensive individuals was better than that of aerobic exercise on the SBP and DBP of hypertensive individuals, which is similar to the results of the previous meta-analysis. However, middle-aged and older individuals should not excessively perform high-load isometric exercises, as improper training may put pressure on the heart, potentially leading to other diseases. Since isometric exercise is not traditionally recommended for hypertensive subjects, isometric training is generally only applicable to some specific exercise programs. However, small-scale, short-term studies conducted in subjects with normal blood pressure and hypertensive subjects suggest that performing 3–4

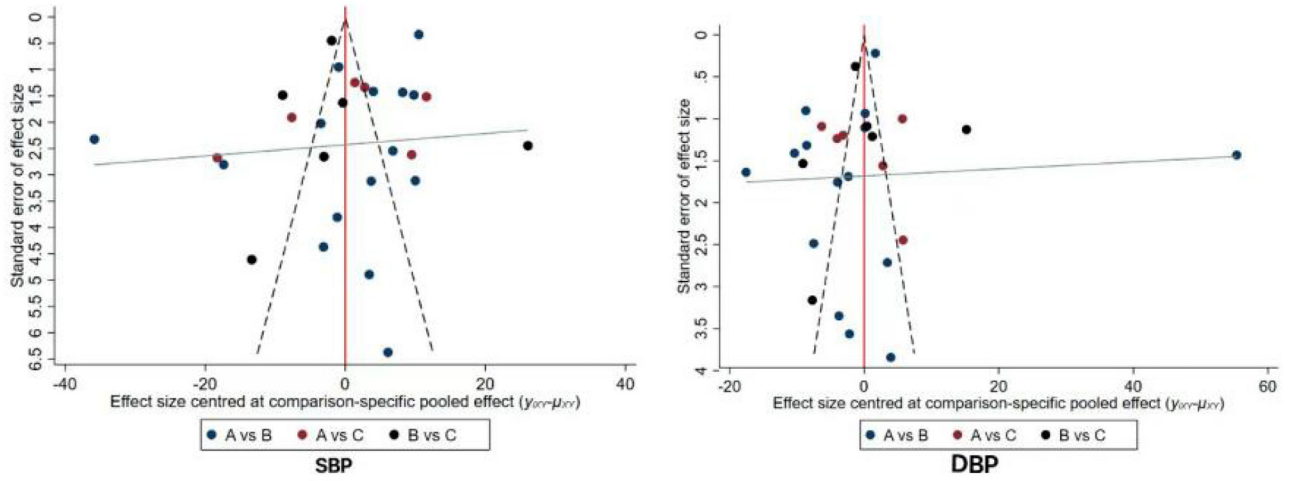

FIGURE 4
Funnel plots of publication bias for outcome measures of included studies. A: control group; B: aerobic exercise; C: static exercise.

short isometric exercises per week can lower systolic and diastolic blood pressure (44). Isometric exercise also has effects on lowering blood pressure in middle-aged and older adults, but its advantages compared to dynamic exercise training (aerobic exercise) may only be limited to blood pressure, and further investigation is still needed regarding other possible aspects. Additionally, middle-aged and older adults need to perform these exercises within their capacity to avoid injuries to the joints and other body parts.

4.3. The impact of different exercise modes on hypertension in middle-aged and older adults

The results of the included literature showed that different exercise intervention modes significantly lower blood pressure in middle-aged and older adults. Aerobic exercise modes such as slow running, hiking, cycling, and brisk walking, as well as static exercises such as stretching, isometric exercises, and combined exercises with low-intensity dynamic and static loading, all have an impact on lowering hypertension in middle-aged and older adults. Currently, international treatment guidelines for primary and secondary prevention of hypertension in China generally recommend lifestyle changes (quitting smoking, weight loss, exercise training, healthy eating, and reducing sodium intake) as the first-line treatment (45). Non-pharmacological treatments can promote the reduction and improvement of blood pressure in middle-aged and older adults, contributing to their physical and mental health development. In daily life, older adults need to engage in reasonable and healthy exercises to cope with the diseases caused by hypertension and provide a suitable and comfortable living environment.

5. Limitations

This study has several limitations. First, it only includes aerobic and static exercise methods, while the effects of other exercise modalities, such as dynamic resistance training, have not been considered. Second, due to the limited number of studies included, there may be a certain degree of selection bias present. Finally, the study incorporates various outcome assessment indicators, and the results of the heterogeneity test suggest that the heterogeneity is relatively high. Therefore, the quality control standards for future clinical trials should be informed by evidence-based medicine standards.

6. Conclusion

Both aerobic exercise and static exercise have significant effects on the reduction of blood pressure in middle-aged and older adults. The effect of both exercise modes on systolic blood pressure, but not diastolic blood pressure, is significant. According to the results of the SUCRA ranking, static exercise is better than aerobic exercise in reducing blood pressure in middle-aged and older adults. Appropriate exercise is effective for middle-aged and older adults with hypertension and has certain benefits in reducing hypertension.

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

WG wrote the article. ML was responsible for data collection and analysis. TH checked and revised the 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.

Publisher's note

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Unmet needs for care for activities of daily living among older adults with functional disabilities in Vietnam

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Background: Given its low-middle-income status, Vietnam is experiencing a rapidly aging population. Along with this demographic trend, the care needs of older adults, particularly those with functional disabilities, have become an emerging policy issue.

Purpose: This study examined the prevalence of unmet needs for care in activities of daily living (ADLs) among Vietnamese older adults with functional disabilities.

Methods: We used data from the Population Change and Family Planning Survey (PCS) in 2021, which was a nationally representative survey. Cross-tabulations and logistic regressions were applied to identify older adults' individual and household factors associated with their unmet care needs.

Results: Overall, 4.80% of older adults with at least one functional disability needing care to perform one or more ADLs suffered from unmet needs, of whom 2.32% did not receive any care and 3.05% received insufficient assistance. Logistic regression results revealed that age, sex, place of residence, ethnicity, marital status, education levels, and self-rated health were significantly associated with unmet needs. The higher risk of having unmet needs is associated with those in middle age (70–79), men, rural residents, ethnic minorities, currently unmarried people, those with less than a primary educational level, and those with normal or poor self-rated health.

Conclusion: Attention should be paid to vulnerable older adults, such as those living in rural areas with poor health status, in order to reduce their unmet needs for ADL assistance.

KEYWORDS

activities of daily living (ADLs), aging, care, older persons, unmet needs, Vietnam

Introduction

Population aging, which has resulted from declining fertility rates and increasing life expectancies, is considered an important demographic trend in the 21st century [United Nations Economic and Social Commission for Asia and the Pacific, (1)]. The United Nations Department for Economic and Social Affairs (2) showed that the world's older population (defined as those aged 60 years and above) is expected to increase from 13% in 2019 to ~25% in 2050, and approximately two-thirds of this population would live in low- and middle-income countries (LMICs). As aging is strongly related to increasing health problems and thus higher risks of disability and chronic diseases, such a demographic trend results in higher care needs for older adults (3–5). Due to underdeveloped healthcare delivery systems

and care-related policies for older adults in LMICs, such demographic aging may generate various challenges in aged care (4, 6). An unmet need for care, particularly among vulnerable older adults, has emerged in policy considerations (7, 8).

As a middle-income country, Vietnam is experiencing a rapid demographic shift from an aging to an aged society. The Vietnamese population was 98.28 million in 2021, and the older population (those aged 60 years and above) was 12.58 million, accounting for 12.80% of the total population (9). The Vietnamese older population is expected to reach 17.28 million in 2029, 22.29 million in 2039, and 28.61 million in 2049, respectively, accounting for 16.53, 20.21, and 24.88% of the total population (10). One of the rising challenges resulting from an aging population is to meet the care needs of older adults.

On the need side, a rapidly aging population leads to a speedy increase in the number and share of older adults, especially those at the oldest ages, and an increasing burden of disease as a result of non-communicable diseases and functional disabilities among older adults [the Ministry of Health and Health Partnership Group (11)]. There were 1.47 million older adults, accounting for 11.7% of the older population, who suffered at least one functional disability (i.e., those who self-assessed as "very difficult" or "could not perform" one of the following functions: seeing; hearing; mobility; cognition; and communication) (9). Older adults with functional disabilities for a prolonged period may face increased difficulties in performing activities of daily living (ADLs), and they need care from other people to fulfill ADLs. Their care needs might be higher than those without functional disabilities. The number of older adults with functional disabilities is expected to increase from nearly 1 million in 2019 to 2.5 million by 2049 if there is no change in the prevalence of disability in terms of age group (11).

On the provision side, based on the traditional culture of intergenerational relationships, most of the care provision for older adults came from their family members, while other sources of care (such as hospitals and other institutions) were limited (11). Approximately 97% of the care received by Vietnamese older adults was provided by family members, and the main care providers were spouses, children, and grandchildren (12). Nevertheless, such traditional family care has been decreasing due to Vietnam's recent sociodemographic changes: smaller household size, children working away from home for better employment, an increasing labor force participation rate among women who have played a primarily home-based care role for older adults, and an increasing number of older adults living alone (particularly the oldest - those aged 80 years and above), living with their spouse only, or living in skip-generation households. The main source of care for older adults is still family members because the development of a long-term care system and public social assistance programs for older adults is at an initial stage in Vietnam (11, 13).

In terms of unmet need, it has been conceptualized as the gap between the amount of long-term care needed as assessed by an individual and the actual resources an individual has at their disposal to meet that need (14). In other words, a person who needs care but whose care provision is unavailable or insufficient is considered to have an unmet need (15). The unmet need could cause a range of adverse consequences, such as more doctor visits, hospitalizations, poor self-assessed health, poor quality of life, higher risks of institutionalization and death (16), more severe disability (17), and an increasing risk of falls (18, 19).

To mitigate such negative consequences and improve the quality of life for the older population, it is important to identify the prevalence and factors associated with the unmet need for personal assistance with ADLs. Given this crucial phase of an aging population, a limited number of studies have been performed to address this issue in Vietnam. To date, few studies have investigated the unmet need for ADL assistance among Vietnamese people aged 60 years and above by using data from the FilaBavi Demographic Surveillance System. For example, Hoi et al. (20) found that a wide proportion of older adults did not receive enough support for different types of ADLs, from 5.1% (for toilet use) to 14.1% (for transferring). Phi et al. (7) found that ∼16% of older adults receiving care experienced insufficient care, and 25% of older adults did not receive any care when needed. The Ministry of Health (21) revealed that 3.3% of older adults faced insufficient care.

To our best knowledge, no study has investigated the prevalence and its association with underlying factors of unmet needs among Vietnamese older adults with functional disabilities. As such, this study, using data from a national survey, namely the Population Change and Family Planning Survey 2021 (or PCS 2021), filled such a research gap by providing analyses on unmet needs and their associated factors for Vietnamese older adults with functional disabilities to provide evidence-based policy discussion to the Government of Vietnam.

Materials and methods

Materials

This study used the data from the Vietnamese Population Change and Family Planning Survey (PCS) in 2021, which was conducted under Decision No. 1903/QD-TCTK dated 30 December 2020 by the GSO Director General. PCS is an annual survey collecting information about the Vietnamese population, comprising basic characteristics of the population, population changes, and the extent to which family planning methods have been used. A total of 1,083,160 participants were recruited for the final survey sample.

For the first time, a new module on older adults and their issues was included in PCS 2021. In the final sample of PCS 2021, there were 148,413 older adults (defined as those aged 60 years and above). A variety of information on older adults was included in the PCS 2021, such as self-rated health status, functional disabilities, activities of daily living (ADLs), and care receipts. These sets of information have been standardized and widely employed by international and local organizations (such as GSO, VWU, and UNFPA) in sociodemographic and health surveys that allowed us to answer the research questions of this study. Particularly, for disability measures, PCS 2021 applied the Washington Group Short Set on Functioning Questions (22), which was also used in the first national survey on disabilities in Vietnam in 2016 (23).

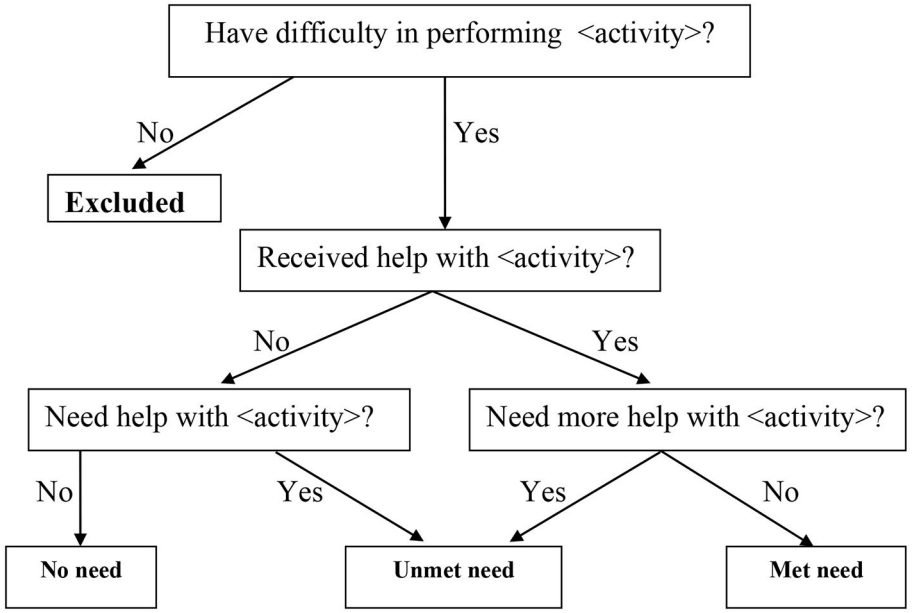

FIGURE 1
Determination of unmet care need. Source: Desai et al. (24).

Data analysis

Data analysis was conducted using the Stata 14.1 software package (College Station, Texas, 77845, USA). A one-way ANOVA test was employed to examine the association between unmet needs and independent variables. A multivariable logistic regression analysis was used to identify significant risk factors for unmet needs.

In all calculations, we used the sample weight to have representative results for all older adults and their sub-groups (such as those by age, sex, ethnicity, and place of residence).

Variable measures

Measure of functional disabilities

The PCS 2021 incorporated questions to collect a variety of information to assess older adults' functional disabilities. Older adults were asked about their functional abilities, including (i) seeing (even with glasses), (ii) hearing (even with a hearing aid), (iii) mobility (walking or climbing a staircase), (iv) cognition (remembering or concentrating); and (v) communicating in a common language (understanding or being understood). They were asked to self-assess the difficulty levels when performing these functions by selecting one of the following answers: (i) not difficult at all, (ii) a bit difficult, (iii) very difficult, and (iv) could not perform.

In this study, we applied the same definition of a disabled person as that outlined in GSO (23) for an older person, i.e., an older person was considered to have a disability in a function if they chose "very difficult" or "could not perform" for that function. An older person was regarded as having at least one functional disability if they had one or more of the functional disabilities listed above.

Measure of care need

A crucial factor influencing the care needs of older adults was how well they could perform activities of daily living (ADLs), including (i) eating, (ii) putting on and taking off clothes, (iii) bathing and washing, (iv) getting up when lying down; and (v) getting to and using the toilet. The PCS 2021 included questions to ask for information on older adults' difficulty levels in ADLs. They were asked to self-assess the difficulty levels when performing the ADLs mentioned above by selecting one of the following answers: (i) not difficult at all; (ii) a bit difficult; (iii) very difficult; and (iv) could not perform.

This study defined that an older person needed care if they were self-assessed to be very difficult or could not perform any of the above ADLs. This definition of care need is consistent with that used in GSO et al. (9).

Measures of unmet needs for care

Figure 1 illustrates unmet needs for care among older adults. Two indicators of unmet needs were analyzed.

The first indicator ("unmet type 1") showed a situation where an older person needed personal assistance in ADLs from others, and they received it, but it was insufficient. It was a dichotomous variable describing whether or not the care recipient reported that their personal care was adequate.

The second indicator ("unmet type 2") showed a situation where an older person needed personal assistance in ADLs from others but did not receive it. This type was also measured as a dichotomous variable, demonstrating whether or not the respondent needed personal care.

TABLE 1 Prevalence of care needs among older adults with at least one functional disability.

Characteristics	1+ ADL disabilities $n = 18,409$	
	%	*P*-value
Total	**50.59**	
Age		0.0000
60–69	38.98	
70–79	42.41	
80+	60.59	
Sex		0.0000
Male	48.97	
Female	51.52	
Residence		0.0404
Urban	51.58	
Rural	50.11	
Ethnicity		0.0000
Kinh	50.97	
Non-Kinh	47.70	
Marital status		0.0000
Currently married	46.24	
Widowed	55.44	
Other (single, divorced, separated)	42.42	
The highest education level		0.000
Less than primary	53.37	
Primary or above	48.99	
Self-rated health status		0.0000
Good	18.04	
Normal	20.40	
Poor	59.74	

Source: Own calculations, using data from PCS 2021.

A person was considered to have an unmet need if they experienced "unmet type 1" or "unmet type 2". The PCS 2021 contained full information on care receipts and whether they were enough for a receiver, allowing us to determine who had an unmet need.

Independent variables

In this research, two categories of independent variables present the sociodemographic and health characteristics of older adults.

Sociodemographic variables included age, sex, place of residence, ethnicity, marital status, and the highest education level. *Age* was divided into three sub-groups (60–69, 70–79, and 80 years and over). *Sex* was a binary variable identifying whether the respondent was male or female. *Place of residence* was a dichotomous variable confirming whether the respondent was living in a rural or urban area at the time of the survey. *Ethnicity* was a binary variable to identify whether the respondent was Kinh (Vietnamese majority) or non-Kinh (other ethnic minorities). *Marital status* was divided into three sub-groups: currently married, widowed, and other statuses (single, divorced, or separated). *The highest education level* was measured as a binary variable showing whether the respondent had less than the primary level (i.e., never schooling or incomplete primary education) or completed primary education or above.

Health characteristics were presented by self-rated health status, which was divided into three sub-groups to reveal whether the respondent was in poor, normal, or good health status.

Results

Sample characteristics

Table 1 shows that 50.59% of Vietnamese older adults have at least one functional disability. In terms of characteristics, the one-way ANOVA test revealed statistically significant differences between care needs and sociodemographic and health statuses. The rate of older adults needing care increased with more advanced age groups (38.98, 42.41, and 60.59% for 60–69, 70–79, and 80 and over, respectively, $p < 0.0001$). Older women had higher care needs than older men (51.52 vs. 48.97%, $p < 0.0001$). Urban older adults reported a slightly higher care needs rate than their rural counterparts (51.58 vs. 50.11%, $p < 0.05$). Kinh people had a significantly higher rate of care needs than their non-Kinh counterparts (50.97 vs. 47.70%, $p < 0.0001$). Older adults with widowed status had the highest prevalence of care needs (55.44%), followed by the currently married group (46.24%) and the other (single, separated, or divorced) (42.42%, $p < 0.0001$). The percentage of older adults with less than a primary education level experienced higher care needs than those with a primary or above education level (53.37 vs. 48.99%, $p < 0.0001$). Older adults with worse self-rated health status had higher care needs than those with better status: 18.04, 20.40, and 59.74% for good, normal, and poor health status, respectively ($p < 0.0001$).

Factors associated with the care needs of older adults with functional disabilities

Table 2 describes the results of the logistic regression model in which sociodemographic and health variables were used to predict the probability of the need for ADL assistance among older adults with functional disabilities.

The results show that the likelihood of needing care increased with more advanced age (OR = 1.059 for 70–79; OR = 1.984 for 80 and over, $p < 0.0001$), men (OR = 1.081, $p < 0.0001$), urban residents (OR = 1.132, $p < 0.0001$), Kinh people (OR = 1.062, $p < 0.0001$), those who were widowed or in other marital statuses (OR = 1.101 for the widowed; OR = 1.064 for the other statuses, $p < 0.0001$), those with less than primary education level (OR = 1.026, $p < 0.0001$), and those with worse self-rated health

TABLE 2 Odds ratios and two-tailed *p*-value from binary logistic regression models predicting care needs among older adults with at least one functional disability.

Variables	Odds ratios ($n = 18,409$)	*P*-value
Age		
60–69 (ref.)		
70–79	1.059	0.000
80+	1.984	0.000
Sex		
Female (ref.)		
Male	1.081	0.000
Residence		
Rural (ref.)		
Urban	1.132	0.000
Ethnicity		
Non-Kinh (ref)		
Kinh	1.062	0.000
Marital status		
Currently married (ref.)		
Widowed	1.101	0.000
Other statuses	1.064	0.000
Education levels		
Primary or above (ref.)		
Less than primary	1.026	0.000
Self-rated health status		
Good (ref.)		
Normal	1.098	0.000
Poor	5.943	0.000

Source: Own calculations, using data from PCS 2021.

status (OR = 1.098 for the normal health; OR = 5.943 for the bad health, $p < 0.0001$).

An unmet need for care and its associated factors among older adults with functional disabilities

The rates of unmet need for ADL assistance are presented in Table 3. The overall rate of unmet needs for ADLs among older adults with at least one functional disability was 4.08%, in which the percentages of "unmet need type 1" (received care but not enough as expected) and "unmet type 2" (did not receive any care when needed) were 3.05 and 2.32%, respectively.

When examining sociodemographic and health characteristics, the one-way ANOVA tests indicated statistically significant differences between unmet care needs and some characteristics. More advanced age groups were associated with a lower rate of unmet need type 1 (4.04%; 3.52%; 2.61% for 60–69; 70–79; 80 and over, respectively, $p < 0.01$). Rural residents had a higher rate of "unmet need type 2" compared to their urban counterparts (2.48 vs. 2.00%, $p < 0.05$). The percentage of Kinh people had a lower percentage of "unmet need type 1" than their counterparts (2.91 vs. 4.19%, $p < 0.05$). Currently married people had the lowest rate of "unmet need type 1" and "unmet need type 2" (3.08 and 1.98%, respectively), followed by widowed people (2.79 and 2.45%, respectively), and the highest rate was for those with other marital statuses (6.41 and 4.02%, respectively) ($p < 0.01$). However, the prevalence of "unmet need type 1" did not significantly vary by sex, residence, the highest education level, or self-rated health status. For "unmet need type 2", age, sex, ethnicity, the highest education level, or self-rated health status did not significantly vary.

In terms of general unmet need status (by combining "unmet need type 1" and "unmet need type 2"), the results showed that rural residents had statistically significantly higher rates than their urban counterparts (5.32 vs. 3.75%, $p < 0.05$). For marital status, older adults with other statuses (single, separated, or divorced) had a significantly higher unmet need rate than those who were currently married or widowed (8.47 vs. 4.43 and 4.78%, respectively, $p < 0.0001$). In contrast, the one-way ANOVA tests indicated that the prevalence of unmet needs insignificantly varies by age, sex, ethnicity, the highest education level, and self-rated health status.

A logistic regression was employed to determine factors associated with the unmet need for ADL assistance among older adults with functional disabilities. The results are presented in Table 4. The likelihood of having unmet needs increased among middle-aged people (70–79) (OR = 1.197, $p < 0.001$); men (OR = 1.189, $p < 0.001$); those who were widowed or had other marital statuses (OR = 1.186 and OR = 2.241, respectively, $p < 0.001$); those with less than primary education level (OR = 1.137, $p < 0.001$), and those with worse self-rated health status (OR = 1.250 for those with normal health; OR = 1.458 for those with poor health, $p < 0.001$), compared with their respective reference groups.

In contrast, the likelihood of having unmet care needs decreased among the "oldest old" (those aged 80 years and above) (OR = 0.956, $p < 0.01$), urban residents (OR = 0.701, $p < 0.001$), and Kinh people (OR = 0.812, $p < 0.001$).

Discussion

The first aim of this study was to investigate the prevalence of the unmet need for ADL assistance among older Vietnamese people with functional disabilities. Using the data from the PCS 2021, we found that 4.80% of older adults reported having unmet needs, in which 3.05% received assistance but not as expected ("unmet need type 1") and 2.32% did not receive any care ("unmet need type 2"). Yet, it is hard to compare estimates of unmet need for ADL across studies because of considerable differences in the study methods, the sample characteristics, and the definitions of disability, care need, and unmet care need (24). For example, this study identified an older person needing care if they self-assessed as "very difficult to perform ADLs" or "unable to perform ADLs," while Phi et al. (7) defined a person with a need for ADL assistance if they had ADL

TABLE 3 Prevalence rates of unmet needs among older adults with at least one functional disability.

Characteristics	Type 1 (%) $n = 7,621$	*P*-value	Type 2 (%) $n = 9,387$	*P*-value	Total (%) $n = 9,387$	*P*-value
Total	3.05		2.32		4.80	
Age		0.0095		0.4382		0.1648
60–69	4.04		1.83		4.83	
70–79	3.52		2.71		5.49	
80+	2.61		2.33		4.53	
Sex		0.6536		0.6855		0.8904
Male	3.15		2.42		5.00	
Female	2.99		2.27		4.69	
Residence		0.2174		0.0182		0.0107
Urban	2.21		2.00		3.75	
Rural	3.45		2.48		5.32	
Ethnicity		0.0129		0.6723		0.0570
Kinh	2.91		2.28		4.66	
Non-Kinh	4.19		2.62		5.92	
Marital status		0.0002		0.0075		0.0000
Currently married	3.08		1.98		4.43	
Widowed	2.79		2.45		4.78	
Other statuses	6.41		4.02		8.47	
Education levels		0.1366		0.6810		0.4312
Less than primary	3.54		2.21		5.11	
Primary or above	2.73		2.39		4.61 |	
Self-rated health status		0.3535		0.3470		0.9164
Good	1.59		2.37		3.38	
Normal	2.34		2.62		4.24	
Poor	3.11		2.29		4.87	

Source: Own calculations, using data from PCS 2021.

difficulty at any level. Moreover, our study examined the status of unmet needs among older adults with functional disabilities instead of the entire older population.

Our estimates might be similar to the prevalence rate previously reported by MOH et al. (21), where 3.3% of older adults suffered from "unmet need type 1". However, the rate of unmet needs obtained in this study might be relatively low compared to other studies conducted in Vietnam. For example, the rate of Vietnamese older adults who did not receive enough care for ADLs varied from 5.1 to 14.1% for specific ADLs (20). By using data from the 2011 Vietnam Aging Survey, Phi et al. (7) found that around 16% of older Vietnamese received inadequate support, and 25% of those did not receive any care when needed. Using data from a cross-sectional survey of 695 individuals aged 60 years and older conducted in Thanh Hoa City and Hoang Hoa district (Vietnam), Nguyen and Assanangkornchai (25) found that 11.6% of the respondents reported difficulties in performing basic ADLs. Individuals with worse self-reported health, two or more chronic diseases, hearing impairment, cognitive impairment, unemployment, and living in rural areas were more likely to be disabled in basic ADLs than their counterparts. Vu et al. (26), examining 412 patients aged 60 years and older with type 2 diabetes mellitus, showed that 79.4% of those had depressive symptoms, and the increased likelihood of having depressive symptoms was related to an impairment of IADLs. Utilizing cross-sectional data with 251 individuals aged 80 years and older in Soc Son district (Vietnam), Nguyen et al. (27) showed that 11.2% of them were considered frail, and 64.5% of them had three or more IADL impairments. Among the frailty components, low walking speed and low physical activity were significantly associated with an increased likelihood of having three or more IADL impairments (which was considered a functional disability). Nguyen et al. (28) indicated that patients who were in the American Spinal Cord Injury Association (ASIA) scale group A (complete dysfunction) had the lowest ADL and IADL index.

In Asian countries, there have been few studies specifically examining this issue. For example, using data from a cross-sectional survey of 2,695 community-dwelling older individuals aged 60 years or above living in five rural Asian towns (Indonesia: 411; Vietnam: 379; Japan: 1,905) between June 2002 and July 2003, Wada et al. (29) showed that those with depression had significantly

TABLE 4 Odds ratios and two-tailed *p*-value from binary logistic regression models predicting unmet needs among older adults with at least one functional disability.

Variables	Odds ratios—OR ($n = 9,387$)	*P*-value
Age		
60–69 (ref.)		
70–79	1.197	0.000
80+	0.956	0.006
Sex		
Female (ref.)		
Male	1.189	0.000
Residence		
Rural (ref.)		
Urban	0.701	0.000
Ethnicity		
Non-Kinh (ref.)		
Kinh	0.812	0.000
Marital status		
Currently married (ref.)		
Widowed	1.186	0.000
Other statuses	2.241	0.000
Education levels		
Primary or above (ref.)		
Less than primary	1.137	0.000
Self-rated health status		
Good (ref.)		
Normal	1.250	0.000
Poor	1.458	0.000

Source: Own calculations, using data from PCS 2021.

lower scores for each item of the ADL than those without depression in all three countries. Momtaz et al. (19) indicated that 18.3% of functionally disabled older Malaysians (those aged years 60 and above) experienced unmet needs of both ADLs and IADLs (Instrumental Activities of Daily Living). Phetsitong and Vapattanawong (30) showed that rates of Thai older adults in households with an unmet need for caregivers were 14.6% in 2007, 17.5% in 2011, 26.5% in 2014, and 22.9% in 2017, which were observation units of households having at least one older person who needed ADL care. Gu and Vlosky (31) showed that ∼60% of the Chinese older population (aged 60 years and above) could not meet their ADL assistance needs. Chen et al. (32) showed that the highest prevalence rate of unmet needs for care for Chinese older adults (aged 60 years and above) ranged from 4.6 to 77.2% for different ADL tasks. Analyzing the data from the 2018 Chinese Longitudinal Healthy Longevity Survey, Cao et al. (33) showed that disabled older adults (65 years and over) experiencing unmet needs had a lower likelihood of obtaining a higher level of healthy aging. Yau et al. (34), using the data from 34 studies conducted in the ASEAN region, performed a systematic literature search to analyze the functional disabilities (ADL and/or IADL disability) status of older adults (aged 60 years and above) and its impact. The result revealed that the pooled rate of ADL disability was 21.5%, and that of IADL disability was 46.8%. Higher rates were for those of more advanced age and women. The increased years of life with disability and poor health-related quality of life had adverse impacts.

Studies carried out in other regions of the world also showed higher percentages of unmet needs. For example, 34.6% of the older population (aged 65 years and above) in the United States with chronic disabilities did not get care to perform ADLs (35). Desai et al. (24) showed that 20.7% of older Americans (aged 70 years and above) needing ADL help had an unmet need. Using the data obtained from the Survey of Health, Aging, and Retirement in Europe, Pego and Nunes (36) indicated that 39.5% of the respondents aged 65 years and above with functional dependence (limited in at least one ADL or IADL) did not receive informal care.

The second aim of this study was to investigate sociodemographic and health characteristics associated with unmet needs among older Vietnamese people with functional disabilities. The results from logistic regression showed that age, sex, residence, ethnicity, marital status, the highest education level, and self-rated health status were significantly associated with unmet needs. Our finding was not consistent with a number of studies reporting an insignificant association between unmet needs and age (19, 24, 31, 37, 38) but was consistent with the finding that the oldest old (those aged years 80 and above) had less likelihood to report an unmet need for care compared to the youngest old (aged 60–64 years) (39).

Our results also indicated that men were ∼19% more likely than women to report unmet needs, and this is consistent with the finding from Peng et al. (38). This result, however, was inconsistent with studies reporting that women had a higher risk of unmet needs than men (15, 19, 39) or showing that there was no gender-significant difference (31, 32, 37).

In this study, urban respondents were ∼30% less likely to have unmet needs than their rural counterparts, which is similar to the findings of other studies (31, 40). But this finding was in contrast with that of Gibson and Verma (17), who found that urban respondents had higher levels of unmet need than their rural counterparts. In between, an insignificant association between residence and unmet needs was found in other studies (18, 41).

Kinh people had an ∼19% lower risk of unmet needs than their counterparts. This finding is similar to the finding from other studies [such as (38)], which found that Han ethnicity was 32% less likely to have unmet needs than non-Han counterparts in the case of China. However, no significant association between race and unmet needs was found in various studies (15, 17, 19, 24, 42).

We found a higher likelihood of unmet needs among older adults who were widowed or in other marital statuses (single, divorced, or separated) than currently married people, particularly those with other marital statuses, who were 2.241 times more likely to experience unmet needs than currently married people. Some previous research examined the correlation between marital status and unmet need for ADL but found an insignificant correlation (15, 19, 31, 32).

Older adults with less than a primary education level had a higher likelihood of unmet needs (1.137 times) than those with a primary or above degree. Other studies found that the highest education level did not have a significant relationship with unmet needs (24, 31, 32, 38, 39, 41, 43, 44).

Compared to those in good health, the risk of unmet needs for those in normal and poor health was higher at 1.250 and 1.458 times, respectively. This finding is consistent with those found in other studies [such as (38, 44)]. However, Otero et al. (43) found that self-rated health was not significantly associated with unmet needs.

Conclusion

The findings from this study indicated that many older Vietnamese people had functional disabilities. Among these people, those with other marital statuses (single, separated, or divorced) had the lowest rate of care needs but the highest rate of unmet needs. Those living in rural areas and those with poor health status experienced higher unmet need rates than their urban counterparts and those with normal or good health status. It is suggested that the most vulnerable groups need more attention from policymakers in Vietnam to address the gaps in their care needs.

With the rapidly aging population, the care needs of older adults will be rising. However, the traditional care provided by family members is declining due to migration and smaller household sizes, and older adults are generally not affordable for care services in public institutions or private facilities. As such, the development of affordable home-based and community-based care services should be a strategic direction for Vietnam (11).

Although this is the first study to use a nationally representative survey to examine unmet care needs among Vietnamese older adults with functional disabilities, and it adds quantitative evidence to the Asian literature, there are some limitations to consider in future studies. The first limitation is related to the usage of a cross-sectional data set because we could not analyze a causal relationship between dependent and independent variables. The second limitation emerges from the data collected using the self-reporting method because it might underestimate or overestimate the levels of need and unmet needs for care. The third limitation is that, beyond the sociodemographic and health factors of older adults, other related factors concerning household and community characteristics could impact older adults' unmet care needs, but they were not available in the PCS 2021 data. If we could have had comparable data sets to combine with the PCS 2021 data, the propensity score matching (PSM) method could have been applied to further explore the impacts of these factors.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: data set is not allowed to be publicly shared. Requests to access these datasets should be directed to not available.

Author contributions

PP formed the research questions, writing ideas, calculated data, and wrote the draft. LG formed the research questions, checked data and calculations, revised, and finalized the draft. TP supported in data processes and calculations. All authors 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.

Publisher's note

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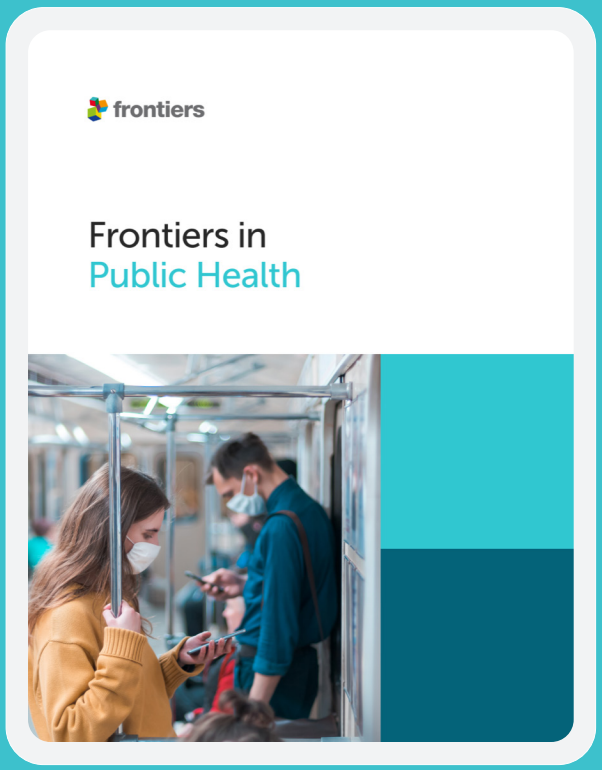

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