frontiers | Research Topics

Metabolic diseases and healthy aging: prevention and public health policy based on risk factors

Edited by
Yun Gao and Xiao Tan

Coordinated by
Xiaohan Tanner Zhang

Published in
Frontiers in Public Health

ISSN 1664-8714
ISBN 978-2-8325-5639-9
DOI 10.3389/978-2-8325-5639-9

About Frontiers

Frontiers is more than just an open access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals.

Frontiers journal series

The Frontiers journal series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the *Frontiers journal series* operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore, Frontiers only applies the most rigorous and unbiased reviews. Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view. By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

What are Frontiers Research Topics?

Frontiers Research Topics are very popular trademarks of the *Frontiers journals series*: they are collections of at least ten articles, all centered on a particular subject. With their unique mix of varied contributions from Original Research to Review Articles, Frontiers Research Topics unify the most influential researchers, the latest key findings and historical advances in a hot research area.

Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers editorial office: frontiersin.org/about/contact

Metabolic diseases and healthy aging: prevention and public health policy based on risk factors

Topic editors
Yun Gao — Sichuan University, China
Xiao Tan — Uppsala University, Sweden

Topic coordinator
Xiaohan Tanner Zhang — Johns Hopkins University, United States

Citation
Gao, Y., Tan, X., Zhang, X. T., eds. (2024). *Metabolic diseases and healthy aging: prevention and public health policy based on risk factors*. Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-5639-9

Table of contents

frontiers | Frontiers in Public Health

TYPE Editorial
PUBLISHED 22 October 2024
DOI 10.3389/fpubh.2024.1502564

OPEN ACCESS

EDITED AND REVIEWED BY
Colette Joy Browning,
Federation University Australia, Australia

*CORRESPONDENCE
Yun Gao
✉ wsgaoyun1982@163.com

RECEIVED 27 September 2024
ACCEPTED 10 October 2024
PUBLISHED 22 October 2024

CITATION
Bai M, Sun X, Tan X and Gao Y (2024) Editorial: Metabolic diseases and healthy aging: prevention and public health policy based on risk factors. *Front. Public Health* 12:1502564. doi: 10.3389/fpubh.2024.1502564

Editorial: Metabolic diseases and healthy aging: prevention and public health policy based on risk factors

Mingxin Bai[1], Xiaodong Sun[2], Xiao Tan[3,4] and Yun Gao[1]*

[1]Department of Endocrinology and Metabolism, Diabetic Foot Care Center, West China Hospital, Sichuan University, Chengdu, Sichuan, China, [2]Department of Endocrinology and Metabolism, Affiliated Hospital of Weifang Medical University, Weifang, China, [3]Department of Neuroscience, Uppsala University, Uppsala, Sweden, [4]Department of Clinical Neuroscience, Karolinska Institutet, Solna, Sweden

KEYWORDS

metabolic diseases, healthy aging, public health, risk factors, prevention strategies

Editorial on the Research Topic
Metabolic diseases and healthy aging: prevention and public health policy based on risk factors

With the rapid global increase in aging populations, healthy aging has become a major challenge to public health worldwide. Healthy aging is defined as the process of maintaining functional ability to enable wellbeing in older age by the World Health Organization (WHO). Aging has been known to significantly increase the susceptibility of older adults to age-related diseases, including metabolic disorders. Additionally, several metabolic diseases, including diabetes, hypertension, and their complications (cardiovascular and renal diseases et al.) impose significant barriers to healthy aging. The development of these metabolic diseases can be attributed to certain risk factors, including smoking, poor dietary habits, obesity and a sedentary lifestyle. Moreover, these risk factors can also affect the aging process itself, by disrupting the balance of metabolic regulation in the body. Prompt and appropriate interventions targeting these risk factors can mitigate the impact of metabolic diseases and promote healthy aging. Therefore, understanding the complex interactions between aging and metabolic diseases is essential for improving public health outcomes in older populations.

This Research Topic focuses on exploring the associations between metabolic risk factors, chronic and metabolic diseases, and healthy aging. We wish to unveil evidence on how to prevent, treat, and manage metabolic risk factors and diseases in older adults, in order to offer recommendations for future research and policy interventions toward healthy aging and public health.

The Research Topic comprised one literature review article and nine original research articles, primarily focusing on risk factors for healthy aging, metabolic risk factors and diseases in older adults and the current state of metabolic diseases and healthy aging. These articles provide valuable insights into effective public health interventions that can bring beneficial outcomes for healthy aging and chronic metabolic diseases.

Yang, Liu et al. utilized Mendelian Randomization to explore the connection between sarcopenia and digestive system illnesses. Their findings suggested that reduced muscle

mass may raise the risk of gastroesophageal reflux disease and non-alcoholic fatty liver through the exacerbation of metabolic disorders.

Mamgai et al. assessed the cardiovascular risk of a large sample from the aging population in India. Their findings indicated that rural, poor, less-educated, and diabetic individuals face higher cardiovascular risks, while regular exercise reduces this risk. Importantly, the study highlighted the need for early detection and management of hypertension, as undiagnosed hypertension poses similar cardiovascular risks.

Chen et al. provided evidence that accelerometer-based physical activity may causally lower the risk of geriatric syndromes, while sedentary behavior may increase the risk of geriatric syndromes (frailty, falls, and dysphagia), emphasizing the significance of strengthening physical activity to improve the quality of life for older adults.

Dąbek et al. conducted a questionnaire survey in Poland, to compare health behaviors between seniors attending and not attending Universities of Third Age (UTA's) classes. They found the positive impact of UTA's classes on seniors' health-promoting behaviors (e.g., physical activity, alcohol consumption, and preventive tests performance).

Wu et al. found that bone mineral density was positively correlated with cardiometabolic index (CMI), suggesting a critical role for lipid metabolism in osteoporosis. CMI may serve as a potential new marker for the diagnosis and prevention of osteoporosis by assessing lipid metabolism levels.

Ravindranath et al. demonstrated patient journeys in primary care for managing hypertension and diabetes in Kerala, India, using Levesque's access framework. They identified several factors influencing access to primary health services for these conditions, highlighting the necessity to enhance timely diagnosis, treatment, and ongoing care within the lower levels of the healthcare system. Furthermore, this study emphasized the necessity of establishing healthcare policies that closely link non-communicable diseases with their social determinants.

Zhou et al. explored the relationship between osteoporosis and multiple special diets through Mendelian Randomization analysis. They identified a significant association between a gluten-free diet and increased osteoporosis risk. Interestingly, the results suggested a hypothesis that in addition to Celiac Disease, a gluten-free diet used for its treatment may also lead to osteoporosis.

Wang et al. revealed the growing demand for "Internet + Traditional Chinese Medicine" home nursing services among older adults with chronic diseases. To provide directed and diversified Chinese medicine home care services, they recommended strengthening demand, improving the service system, and ensuring high-quality care.

Yang, Wang et al. conducted a large-sample study to explore the prevalence and influencing factors of abnormal carotid artery intima-media thickness in Henan Province, China. The results highlighted the significance of early screening for at-risk populations, particularly older men and individuals with hypertension, diabetes, or dyslipidemia.

Zhang et al. conducted an extensive review to explore the complex interaction between environmental and behavioral risk factors with metabolic diseases and their impact on healthy aging. It identified key contributors such as environmental pollutants, diet, physical activity, smoking, alcohol consumption, sleep patterns, and psychological stress, all linked to metabolic disorders and age-related complications. Moreover, they contributed important insights aimed at promoting public health and encouraging healthy aging.

This Research Topic highlights the importance of understanding risk factors associated with metabolic diseases and healthy aging. These findings provide valuable insights into prevention strategies and public health policy to promote healthy aging.

Author contributions

MB: Writing – original draft. XS: Writing – review & editing. XT: Writing – review & editing. YG: Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This study was supported by the Science and Technology Department of Sichuan Province (Grant No. 2022YFS0308), National Natural Science Foundation of China Youth Science Fund Project (Grant No. 81700087), and West China Hospital, Sichuan University (Grant No. ZYGD18025).

Acknowledgments

We thank all the contributors to this Research Topic.

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

frontiers | Frontiers in Public Health

TYPE Review
PUBLISHED 13 October 2023
DOI 10.3389/fpubh.2023.1253506

OPEN ACCESS

EDITED BY
Emiliana Giacomello,
University of Trieste, Italy

REVIEWED BY
Brigitte Le Magueresse-Battistoni,
INSERM U1060 Laboratoire de Recherche en Cardiovasculaire, Métabolisme, diabétologie et Nutrition, France
Giuseppe Sirago,
Université de Lausanne, Switzerland

*CORRESPONDENCE
Xiaodong Sun
xiaodong.sun@wfmc.edu.cn
Chengxia Kan
fykanchengxia@wfmc.edu.cn

†These authors share first authorship

RECEIVED 05 July 2023
ACCEPTED 03 October 2023
PUBLISHED 13 October 2023

CITATION
Zhang K, Ma Y, Luo Y, Song Y, Xiong G, Ma Y, Sun X and Kan C (2023) Metabolic diseases and healthy aging: identifying environmental and behavioral risk factors and promoting public health.
Front. Public Health 11:1253506.
doi: 10.3389/fpubh.2023.1253506

Metabolic diseases and healthy aging: identifying environmental and behavioral risk factors and promoting public health

Kexin Zhang[1,2†], Yujie Ma[3†], Youhong Luo[1,2], Yixin Song[1,2], Guoji Xiong[1,2], Yanhui Ma[4], Xiaodong Sun[1,2*] and Chengxia Kan[1,2*]

[1]Department of Endocrinology and Metabolism, Affiliated Hospital of Weifang Medical University, School of Clinical Medicine, Weifang Medical University, Weifang, China, [2]Clinical Research Center, Affiliated Hospital of Weifang Medical University, Weifang, China, [3]Department of Pathophysiology, School of Basic Medical Sciences, Weifang Medical University, Weifang, China, [4]Department of Pathology, Affiliated Hospital of Weifang Medical University, Weifang, China

Aging is a progressive and irreversible pathophysiological process that manifests as the decline in tissue and cellular functions, along with a significant increase in the risk of various aging-related diseases, including metabolic diseases. While advances in modern medicine have significantly promoted human health and extended human lifespan, metabolic diseases such as obesity and type 2 diabetes among the older adults pose a major challenge to global public health as societies age. Therefore, understanding the complex interaction between risk factors and metabolic diseases is crucial for promoting well-being and healthy aging. This review article explores the environmental and behavioral risk factors associated with metabolic diseases and their impact on healthy aging. The environment, including an obesogenic environment and exposure to environmental toxins, is strongly correlated with the rising prevalence of obesity and its comorbidities. Behavioral factors, such as diet, physical activity, smoking, alcohol consumption, and sleep patterns, significantly influence the risk of metabolic diseases throughout aging. Public health interventions targeting modifiable risk factors can effectively promote healthier lifestyles and prevent metabolic diseases. Collaboration between government agencies, healthcare providers and community organizations is essential for implementing these interventions and creating supportive environments that foster healthy aging.

KEYWORDS

metabolic diseases, healthy aging, risk factors, public health, environment

1. Introduction

Aging is an ongoing and irreversible physiological process that leads to the gradual deterioration of tissue and cellular functions, increasing the susceptibility to age-related diseases, including metabolic disorders (1). While remarkable advancements in modern medicine have improved human health and extended lifespan, metabolic conditions like obesity and type 2 diabetes (T2D) continue to pose significant global public health challenges as populations age (1–5). Understanding the complex relationship between

metabolic diseases and healthy aging is crucial for promoting well-being and preventing disease burden. While genetics play a role in metabolic disease development, environmental and behavioral factors also contribute significantly (6–10). An obesogenic environment, characterized by air pollution, pesticides and exposure to environmental toxins, correlates strongly with the rising prevalence of obesity and its associated comorbidities (8, 10–14). Additionally, research suggests that behavioral factors, such as dietary choices, physical activity levels, and sleep patterns, significantly influence the risk of metabolic diseases throughout aging (15–18).

Effective strategies must be implemented to promote healthy aging and prevent metabolic diseases. This involves understanding the underlying risk factors and their impact on public health, which can then inform the development of targeted interventions and policies that encourage healthier lifestyles. Public health initiatives can address these risks to promote healthier choices among the population by identifying modifiable environmental and behavioral factors (Figure 1).

This review article aims to explore the intricate relationship between metabolic diseases and healthy aging by examining the environmental and behavioral risk factors contributing to their onset and progression. By analyzing current research and existing literature, we will delve into the multifaceted nature of these diseases, considering factors such as diet, physical activity, stress, sleep patterns, and socioeconomic determinants. Furthermore, we will explore the potential of public health interventions to mitigate the impact of metabolic diseases and promote healthy aging (Table 1).

2. The interactions between aging and metabolic diseases

2.1. Aging as a risk factor for metabolic diseases

Aging is a significant risk factor for developing and progressing metabolic diseases in older adults due to various physiological changes that occur with age (19, 20). These changes affect metabolic regulation and contribute to the increased risk of metabolic disorders. One notable change associated with aging is the decline in metabolic rate. If calorie intake remains constant or increases, this decline in metabolic rate can lead to weight gain, obesity and insulin resistance (IR) (21). IR refers to repaired responses to insulin stimulation in specific tissues, primarily the liver, muscles, and adipose tissues. This impairment leads to ineffective glucose utilization, prompting a compensatory increase in β-cell insulin production and ultimately resulting in hyperinsulinemia (22, 23). This age-related decline in insulin sensitivity becomes more prominent as people grow older. Moreover, aging affects body composition, leading to increased adiposity (fat accumulation) and decreased lean muscle mass (24). This shift in body composition, known as sarcopenic obesity, contributes to metabolic dysregulation and raises the risk of metabolic diseases (24, 25). Besides these factors, aging-related hormonal changes play a role in metabolic dysregulation. Aging is accompanied by a natural decline in growth hormone and insulin-like growth factor-1 (IGF-1) levels (26, 27). This reduction increases adiposity, particularly abdominal fat, while decreasing muscle mass. Lower

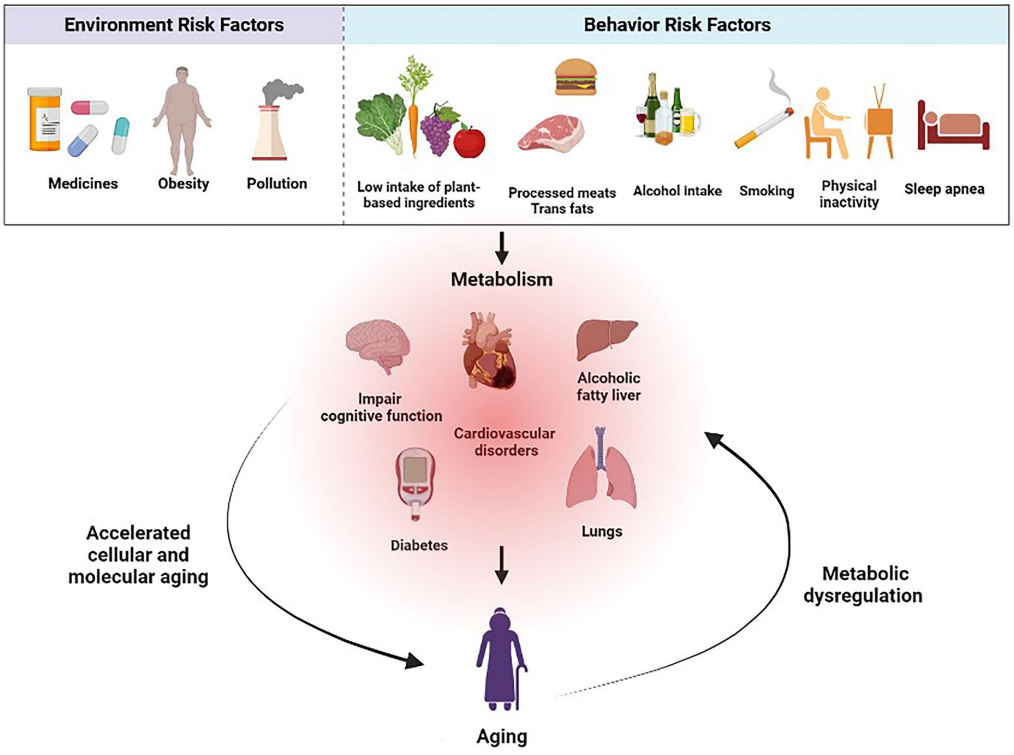


FIGURE 1
The interactions between aging and metabolic diseases.

TABLE 1 Risk Factors and their relationship with metabolic diseases and aging.

Risk factors	Relationship to metabolic diseases	Relationship to aging	Refs
Environmental pollutants	Increase metabolic diseases risk	Accelerate the aging process	(12, 13, 50–52)
Diet and nutrition	Poor dietary choices contribute to metabolic diseases; a healthy diet can maintain optimal metabolic function	Poor diet can aggravate metabolic diseases and aging; healthy diet can maintaining promoting healthy aging	(69–74, 161)
Physical activity and sedentary behavior	Regular physical activity can reduce metabolic diseases risk; Sedentary lifestyle can elevate metabolic diseases risk	Regular physical activity can delay aging; Sedentary can promote aging	(35, 92, 93, 99, 100)
Tobacco smoking	Increase metabolic diseases risk	Accelerate the aging process	(120, 121, 123–128)
Alcohol consumption	Excessive and prolonged alcohol consumption can have detrimental effects on metabolic health	Excessive and long-term alcohol consumption has a negative impact on aging	(131–136)
Sleep patterns and quality	Chronic sleep deprivation, poor sleep quality, and disturbances in sleep patterns elevate metabolic diseases risk	Inadequate sleep can impair cognitive function and accelerates the aging-related complications	(140–146)
Physical stress and mental health	Increase metabolic diseases risk	Accelerate the aging process	(147–153, 162)

hormone levels lead to IR, glucose intolerance (the body's struggle to control blood glucose levels, resulting in elevated levels not yet classified as diabetes), and the potential development of diabetes (28, 29). In women, menopause triggers a substantial decrease in estrogen levels, potentially resulting in IR and an increase in abdominal fat, since estrogen renders tissues more sensitive to insulin (30, 31). Similarly, men experience a gradual decline in testosterone levels with aging, resulting in higher body fat levels, loss of muscle mass, and IR (32). These hormonal changes influence fat metabolism, insulin sensitivity, and energy expenditure, thereby increasing the risk of metabolic diseases in older adults (33, 34).

Furthermore, aging is associated with a higher prevalence of additional risk factors for metabolic diseases. Reduced physical activity, sedentary behavior, underlying genetic predispositions, and cumulative exposure to environmental factors over a lifetime increase risk in older adults (17, 35). When combined with age-related changes in metabolic regulation, these factors contribute to the bidirectional relationship between aging and metabolic diseases (6, 8, 10).

2.2. Impact of metabolic diseases on the aging process

Metabolic diseases, particularly diabetes and hypertension, significantly impact aging by accelerating age-related decline in health and functionality (19, 20). Both conditions foster systemic inflammation and oxidative stress, contributing to cellular and molecular aging (36–39). Chronic inflammation from these diseases elevates reactive oxygen species levels, inflicting cellular damage and disrupting normal functions. It also induces IR, which inhibits glucose uptake by cells and raises blood glucose levels, thereby impairing glucose metabolism and leading to complications like renal disease and cognitive decline (40–43). Diabetes causes microvascular and macrovascular damage, increasing the risk of complications such as diabetic retinopathy, peripheral neuropathy, and cardiovascular issues. These conditions impede sensory and motor functions, limit mobility, and negatively affect overall well-being (44–47). Hypertension, often related to metabolic disorders like obesity and IR, imposes strain on the cardiovascular system, accelerating aging and promoting heart-related complications (38, 39). It also exacerbates organ damage, leading to chronic conditions like kidney disease, dementia, and heart failure, thereby further speeding up the aging process when coupled with metabolic syndrome (42, 43, 48, 49).

3. Environment risk factors

Environmental pollutants, including air pollutants, pesticides, heavy metals, and endocrine-disrupting compounds (EDCs), pose substantial risks to metabolic health and can accelerate aging (12, 50, 51). Air pollution, especially fine particulate matter (PM2.5) and nitrogen dioxide has been linked to IR, inflammation, and an increased risk of metabolic disorders such as obesity, T2D, and cardiovascular disease (CVD) (13, 52). Similarly, pesticides can disrupt metabolic processes and hormonal regulation, increasing the risk of diseases like IR and obesity (12, 14). Heavy metals, such as lead, cadmium, and mercury, can also induce metabolic dysfunction and oxidative stress (50).

EDCs are present in various consumer products and can interfere with the production, transport, or metabolism of hormones. It is estimated that there are more than one thousand different EDCs. EDCs disrupt hormonal action, while metabolic disruptors affect metabolism. It is crucial to clarify that not all metabolic disruptors are EDCs. EDCs specifically pertain to substances that interfere with the hormonal aspects of metabolism (51, 53–56). Therefore, mitigating exposure to these pollutants can help reduce the risk of metabolic diseases and age-related complications.

The term "exposome" encompasses both external and internal environmental factors that impact human health. It includes the ecto-exposome, which pertains to external environmental influences, and the endo-exposome, which relates to the immediate adjacent extracellular environment. Both the ecto-exposome and the endo-exposome are conditions that support cell survival and organ/system function. According to reports, persistent organic pollutants, also known as 'EDCs,' interfere with the endocrine system and are found in the environment, causing lifelong exposure in certain populations (57, 58). Occupational exposure to toxins, including heavy metals, solvents, pesticides, and industrial chemicals, is a significant risk

factor for metabolic diseases and healthy aging (14, 59–61). The heavy use of these toxins in industries such as manufacturing, agriculture, and mining can lead to adverse health effects like IR, dyslipidemia, impaired glucose metabolism, hormonal disruption, and altered lipid metabolism (62–64). Toxic exposure can also influence aging by promoting inflammation, DNA damage, mitochondrial dysfunction, and impairing natural defense mechanisms against oxidation, thereby accelerating cellular aging and increasing the risk of age-related diseases (12, 65–68). However, little is known about how these exposures actually affect humans or potentially affect the onset of metabolic diseases. It is critical to further explore the impact of environmental exposure on health under the concept of exposure and enforce strict safety regulations and promote adequate workplace protection to reduce these risks. Training and regular health screenings can also contribute to early detection and prevention of occupational health issues.

4. Behavior risk factors

4.1. Role of diet in metabolic diseases and healthy aging

Diet plays a significant role in the onset and progression of metabolic diseases, with varying dietary habits yielding distinct impacts on these conditions. A well-balanced diet, rich in fruits, vegetables, whole grains, lean meats, and healthy fats, contributes to weight maintenance, blood sugar regulation, lowered cholesterol levels, and reduced risk of chronic diseases (69–71). Specific dietary factors, such as the overconsumption of sugary beverages and processed foods, elevate the risk of obesity and T2D. Conversely, diets high in fiber, antioxidants and omega-3 fatty acids, along with adequate intake of micronutrients and phytochemicals, can protect against these diseases and age-related decline (72–74). Interestingly, studies in invertebrates and rodents have found that calorie or diet restriction can slow down age-related diseases and prolong life expectancy (75). Simultaneously, Longo et al. (76) demonstrated that dietary interventions, such as intermittent fasting and protein restriction, can attenuate aging and extend a healthy lifespan (73). Furthermore, the Mediterranean diet has been proven to reduce mortality from cardiovascular disease (77, 78).

Moreover, diet significantly influences gut microbiota homeostasis, impacting energy metabolism and fat storage. Imbalances in gut flora, or dysbiosis, can lead to increased energy extraction and fat storage, contributing to obesity and diabetes (79, 80). Specifically, an increase in *Firmicutes* and a decrease in *Bacteroidetes* are commonly observed in these conditions (81, 82). In addition, certain potentially harmful bacterial groups may become overrepresented. For instance, the family *Enterobacteriaceae*, which includes potentially harmful species such as *Escherichia coli*, is often found to increase in metabolic diseases (83). These bacteria can lead to inflammation and further disrupt the balance in the gut microbiota. Conversely, beneficial bacteria may decrease in metabolic diseases. Examples include *Akkermansia muciniphila*, known to help maintain the health of the gut lining and *Bifidobacterium*, a genus often used in probiotics known for its health-promoting effects (84). These bacteria produce short-chain fatty acids that help regulate metabolism and inflammation, and their reduction can exacerbate metabolic issues. Positive dietary interventions, such as increasing the intake of prebiotic fibers and probiotic-rich foods, can help maintain healthy gut microbiota and promote healthy aging (85, 86). Additionally, age-related dysbiosis is linked to inflammation, promoting metabolic disorders and frailty, accelerating aging (87, 88). Understanding the intricate relationship between diet, gut flora, and overall health is crucial for mitigating metabolic diseases and fostering healthier aging outcomes.

4.2. Influence of physical activity and sedentary behavior on metabolic health

Declining activity and unhealthful changes in body composition are linked to aging. Physical activity and sedentary behavior have significant impacts on metabolic health.

Exercise prevents many chronic diseases and mitigates certain undesirable physiological changes brought on by aging. Interestingly, the impact of physical training on the reward system is a topic of growing interest. Engaging in regular physical activity reduces the motivation to seek unhealthy rewards like high-fat, sugary foods, and drugs. Additionally, it changes attitudes toward overeating, making individuals more mindful of their food choices. This transformation promotes healthier lifestyle preferences (89, 90).

Regular exercise also promotes glucose metabolism by increasing cells' sensitivity to insulin, reducing the risk of developing T2D characterized by IR (91–93). Engaging in aerobic exercise training, such as brisk walking, jogging, swimming, wheel running, or cycling, increases energy expenditure, promotes cardiovascular health, and aids in weight management (94–96). Studies in the natural aging mouse model (C57BL/J6) have shown that early lifelong aerobic exercise training is crucial in preventing age-related issues, including muscle loss, decreased motility, and testicular atrophy, along with overall organ pathology (97). Testicular atrophy, the shrinking of testicles, can impact reproductive health. The findings highlight that aerobic exercise, when initiated early in life, can effectively mitigate these age-related challenges. Moreover, early-onset, lifelong running can inhibit inflammation, prevent multiple types of cancer, and prolong the healthy lifespan of naturally aging mice (97). The wheel running exercise can improve insulin sensitivity and treat IR in aging rats by restoring the role of hepatic insulin sensitizing substance. This substance is also known as hepatalin, a liver-produced hormone that enhances insulin sensitivity, particularly in skeletal muscle, promoting glucose storage as glycogen and contributing to the post-meal glucose disposal effect of insulin (53, 98). Resistance training, including weightlifting, improves metabolic health by enhancing muscle strength and mass, leading to an increased resting metabolic rate and insulin sensitivity (99, 100).

The World Health Organization recommends that adults engage in at least 150 min of moderate-intensity aerobic exercise or 75 min of vigorous exercise per week, or a combination of both (101, 102). It is well known that the level and intensity of physical activity decline as humans age, and during long-term aging, exercise affects changes in body weight and body composition in a gender-dependent manner (103). In women, estrogen plays a crucial role in regulating various aspects of metabolism. Estrogens regulate fat development by inhibiting preadipocyte differentiation, reducing lipolysis, favoring

subcutaneous fat storage, and influencing energy expenditure. They boost the basal metabolic rate and can help maintain a healthy weight (104, 105). However, during menopause, declining estrogen levels can lead to increased abdominal fat accumulation. Studies in humans and rodents have shown that reduced estrogen production leads to IR and inflammation, and exercise relieves glucose intolerance and IR (106, 107). Moreover, estrogen deficiency in postmenopausal women and ovariectomized rodents results in increased respiratory exchange rate levels, decreased lipid oxidation, and increased carbohydrate oxidation during rest and exercise, accelerated cell senescence, and impaired bone formation (108, 109). Similarly, changes in male muscle mass, physical activity level, body weight, and fat percentage are closely related to testosterone. A decrease in testosterone levels will lead to an increase in body fat and a decrease in physical activity level (110, 111).

Conversely, a sedentary lifestyle characterized by prolonged sitting or inactivity is associated with an elevated risk of metabolic diseases, including obesity, T2D, and cardiovascular problems (112–114). Sedentary behavior leads to weight gain, reduced muscle mass, and impaired glucose and lipid metabolism (115, 116). It is important to note that even individuals who engage in regular exercise may still be at risk if they spend prolonged periods sitting or being inactive throughout the day (35). To promote metabolic health, it is crucial to incorporate regular physical activity into daily routines. This can include structured exercise sessions, such as workouts or sports, as well as simple lifestyle modifications like choosing to take the stairs instead of the elevator, walking or cycling for transportation, incorporating movement breaks during extended periods of sitting (117, 118). Elderly people are encouraged to walk to shopping when supermarkets are less than a kilometer away, as it is often the preferred mode of transportation over driving a car for their shopping needs (119).

4.3. Smoking and its association with metabolic diseases and aging

Tobacco smoking significantly elevates the risk for metabolic diseases and negatively affects the aging process. Cigarette smoke contains harmful compounds such as nicotine, carbon monoxide, and carcinogens that damage tissues and organs throughout the body. Smoking is linked to metabolic diseases like T2D, IR, obesity, and CVD, primarily due to nicotine's contribution to IR and impaired glucose metabolism (120–123). In addition, smoking induces inflammation, oxidative stress, and endothelial dysfunction, leading to blood vessel damage and an increased risk of CVD (121, 124, 125). It also accelerates aging, causing premature skin aging, impaired wound healing, and elevating the risk of age-related conditions like osteoporosis and cognitive decline (126–128). Quitting smoking is crucial for reducing metabolic disease risk and promoting healthy aging. Immediate benefits post-cessation includes improved lung function, cardiovascular health, and overall well-being (129, 130).

4.4. Alcohol consumption and its impact on metabolic health in aging populations

Alcohol consumption's impact on metabolic health hinges on individual factors and the quantity consumed. While moderate consumption might confer some cardiovascular benefits, excessive and chronic alcohol intake poses severe risks to metabolic health, particularly in aging populations (131). Heavy alcohol use promotes weight gain and obesity due to its caloric density and effects on appetite regulation. It also disrupts glucose metabolism, escalating the risk of IR and T2D (131–133). Toxic byproducts from alcohol metabolism can harm the liver, resulting in fatty liver disease, alcoholic hepatitis, and cirrhosis. Such chronic abuse hampers liver function, negatively impacting nutrient and medication metabolism and clearance, exacerbating metabolic health concerns (134, 135). Furthermore, alcohol can impede the absorption and utilization of essential nutrients, including vitamins and minerals, that are critical for maintaining metabolic health (136). Thus, for maintaining metabolic health in aging populations, it is recommended to moderate alcohol intake (131). Nonetheless, personal health conditions, medications, and other variables may necessitate adjustments to these guidelines, warranting consultation with a healthcare professional.

4.5. Sleep patterns and their relationship with metabolic diseases and aging

Sleep quality and patterns profoundly affect metabolic health and the aging process. Chronic sleep deprivation and disturbances are linked to increased metabolic disease risk and accelerated aging-related complications (137–139). Insufficient sleep and poor sleep quality can lead to obesity, T2D, CVD, and other metabolic disorders, primarily through disturbances in hormonal regulation of appetite and glucose metabolism (140–142). Sleep disruptions can also disrupt the body's circadian rhythm, which regulates metabolic processes. These disturbances, such as shift work or irregular sleep schedules, contribute to metabolic dysregulation, hormonal imbalances, and increased inflammation (143, 144). Moreover, inadequate sleep impairs cognitive function and memory consolidation, which are essential for healthy aging (145, 146). Thus, promoting good sleep hygiene, including maintaining a consistent sleep schedule, creating a comfortable sleep environment, and using relaxation techniques, is crucial. Ensuring sufficient sleep duration, typically 7–9 h for adults, and seeking professional help for sleep disorders can support metabolic health and healthy aging.

4.6. The role of psychological stress and mental health in metabolic diseases and aging

Psychological stress and mental health significantly influence metabolic diseases and aging. Stress, depression, anxiety, and other mental health conditions are linked with metabolic diseases and can hasten the aging process (147–150). Stress and negative emotions can incite unhealthy behaviors such as overeating and inactivity, leading to obesity and related metabolic disorders (151, 152). Moreover, chronic stress disrupts hormonal balance, impairing the body's ability to regulate blood sugar and manage inflammation (153). Recognizing the interplay between mental and physical health, public health initiatives should equally emphasize

mental well-being. Promoting stress management, access to mental health services, and lifestyle changes that foster overall health could enhance interventions targeting healthy aging and metabolic disease prevention.

5. Promoting public health for healthy aging

Healthy aging is the focus of the World Health Organization's aging policy by 2030 (154). The development of clear and targeted public health interventions is essential for mitigating the rising prevalence of metabolic diseases and promoting healthy aging.

These interventions should tackle determinants of metabolic diseases such as unhealthy dietary patterns, sedentary lifestyles, tobacco use, and environmental factors to effectively reduce their incidence and complications (7, 10, 35, 121, 124). Long-term healthy aging approaches require prevention throughout the life course. Specific public health strategies include: building strong social support systems, promoting health literacy promotion and lifestyle awareness and health education for older adult that can empower individuals to prevent metabolic diseases (155). Policies facilitating access to affordable, nutritious food, such as nutrition education, labeling requirements, and restrictions on marketing unhealthy foods have shown effectiveness in preventing metabolic diseases (156, 157).

Promoting physical activity or community volunteer work through community initiatives, workplace wellness programs, and accessible recreational facilities can improve metabolic health by maintaining healthy weight and enhancing insulin sensitivity. Infrastructure that prioritizes active transportation, green spaces, and safe recreational areas can further promote activity and reduce sedentary behavior (158, 159). Additionally, lifelong health promotion and disease prevention activities can help prevent or delay the onset and progression of metabolic diseases. The government should enhance and improve the healthcare system and primary healthcare services. Implementing regular routine screenings for middle-aged and elderly individuals can lead to the early detection and timely intervention of metabolic diseases, thereby minimizing their consequences. Furthermore, providing long-term, effective treatment, nursing care, and psychological support for patients with advanced diseases can enhance their sense of social well-being (160). Health regulations are also critical for promoting healthy aging and metabolic disease prevention. Therefore, a combination of multi-sectoral initiatives can create an environment that supports healthy behavior and promotes public health and healthy aging.

This article has certain limitations. It offers a comprehensive overview of metabolic diseases, but it fails to carry out in-depth analysis of the molecular processes associated with healthy aging and account for individual differences and subtle nuances, such as genetic factors and socio-economic circumstances. These elements play a significant role in the risk and progression of these diseases. Moreover, due to the complexity of the system and confounding variables, determining the causality between environmental/behavioral factors and metabolic diseases presents a challenge. For a complete understanding of metabolic diseases and healthy aging, further research and personalized assessments are critically essential.

6. Conclusion

In summary, this review article emphasizes the important contribution of environmental and behavioral risk factors to the emergence of metabolic diseases and healthy aging. Key risk factors, including diet, physical activity, smoking, alcohol consumption, environmental pollutants, and sleep patterns, have been identified and linked to various metabolic disorders and age-related complications. The findings underscore the importance of public health interventions in addressing metabolic diseases and promoting healthy aging. Further research is needed to understand risk factor interactions, mechanisms, and intervention effects. Addressing metabolic diseases is vital for healthy aging, reducing chronic conditions, and improving quality of life. A holistic approach combining behavior changes, supportive environments, and public health interventions can lead to a healthier future with lower metabolic disease rates and improved well-being in aging populations.

Author contributions

KZ: Conceptualization, Data curation, Methodology, Writing – original draft. YuM: Conceptualization, Data curation, Methodology, Writing – original draft. YL: Conceptualization, Data curation, Investigation, Methodology, Writing – original draft. YS: Conceptualization, Data curation, Investigation, Writing – review & editing. GX: Data curation, Investigation, Writing – review & editing. YaM: Data curation, Investigation, Conceptualization, Writing – review & editing. XS: Conceptualization, Funding acquisition, Supervision, Writing – review & editing. CK: Conceptualization, Data curation, Investigation, Methodology, Supervision, Validation, Writing – review & editing.

Funding

This work was supported by the Taishan Scholars Project of Shandong Province (tsqn202211365) and funding for the Key Disciplines of Medicine and Health in Shandong Province (Endocrinology and Metabolism).

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

References

1. Guo J, Huang X, Dou L, Yan M, Shen T, Tang W, et al. Aging and aging-related diseases: from molecular mechanisms to interventions and treatments. *Signal Transduct Target Ther*. (2022) 7:391. doi: 10.1038/s41392-022-01251-0

2. Paneni F, Diaz Cañestro C, Libby P, Lüscher TF, Camici GG. The aging cardiovascular system: understanding it at the cellular and clinical levels. *J Am Coll Cardiol*. (2017) 69:1952–67. doi: 10.1016/j.jacc.2017.01.064

3. Batsis JA, Villareal DT. Sarcopenic obesity in older adults: aetiology, epidemiology and treatment strategies. *Nat Rev Endocrinol*. (2018) 14:513–37. doi: 10.1038/s41574-018-0062-9

4. Bellary S, Kyrou I, Brown JE, Bailey CJ. Type 2 diabetes mellitus in older adults: clinical considerations and management. *Nat Rev Endocrinol*. (2021) 17:534–48. doi: 10.1038/s41574-021-00512-2

5. Santos AL, Sinha S. Obesity and aging: molecular mechanisms and therapeutic approaches. *Ageing Res Rev*. (2021) 67:101268. doi: 10.1016/j.arr.2021.101268

6. van Dijk SJ, Tellam RL, Morrison JL, Muhlhausler BS, Molloy PL. Recent developments on the role of epigenetics in obesity and metabolic disease. *Clin Epigenetics*. (2015) 7:66. doi: 10.1186/s13148-015-0101-5

7. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev*. (2017) 39:46–58. doi: 10.1016/j.arr.2016.10.005

8. Münzel T, Sørensen M, Gori T, Schmidt FP, Rao X, Brook J, et al. Environmental stressors and cardio-metabolic disease: part I-epidemiologic evidence supporting a role for noise and air pollution and effects of mitigation strategies. *Eur Heart J*. (2017) 38:550–6. doi: 10.1093/eurheartj/ehw269

9. Wei M, Brandhorst S, Shelehchi M, Mirzaei H, Cheng CW, Budniak J, et al. Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. *Sci Transl Med*. (2017):9. doi: 10.1126/scitranslmed.aai8700

10. Howell NA, Booth GL. The weight of place: built environment correlates of obesity and diabetes. *Endocr Rev*. (2022) 43:966–83. doi: 10.1210/endrev/bnac005

11. Park SY, Byun EJ, Lee JD, Kim S, Kim HS. Air pollution, autophagy, and skin aging: impact of particulate matter PM(10) on human dermal fibroblasts. *Int J Mol Sci*. (2018):19. doi: 10.3390/ijms19092727

12. He B, Ni Y, Jin Y, Fu Z. Pesticides-induced energy metabolic disorders. *Sci Total Environ*. (2020) 729:139033. doi: 10.1016/j.scitotenv.2020.139033

13. Yang BY, Fan S, Thiering E, Seissler J, Nowak D, Dong GH, et al. Ambient air pollution and diabetes: a systematic review and meta-analysis. *Environ Res*. (2020) 180:108817. doi: 10.1016/j.envres.2019.108817

14. Zhang Y, Dong T, Hu W, Wang X, Xu B, Lin Z, et al. Association between exposure to a mixture of phenols, pesticides, and phthalates and obesity: comparison of three statistical models. *Environ Int*. (2019) 123:325–36. doi: 10.1016/j.envint.2018.11.076

15. Poggiogalle E, Jamshed H, Peterson CM. Circadian regulation of glucose, lipid, and energy metabolism in humans. *Metabolism*. (2018) 84:11–27. doi: 10.1016/j.metabol.2017.11.017

16. Geidl W, Schlesinger S, Mino E, Miranda L, Pfeifer K. Dose-response relationship between physical activity and mortality in adults with noncommunicable diseases: a systematic review and meta-analysis of prospective observational studies. *Int J Behav Nutr Phys Act*. (2020) 17:109. doi: 10.1186/s12966-020-01007-5

17. Oppert JM, Bellicha A, Ciangura C. Physical activity in management of persons with obesity. *Eur J Intern Med*. (2021) 93:8–12. doi: 10.1016/j.ejim.2021.04.028

18. Manoogian E, Chow LS, Taub PR, Laferrère B, Panda S. Time-restricted eating for the prevention and Management of Metabolic Diseases. *Endocr Rev*. (2022) 43:405–36. doi: 10.1210/endrev/bnab027

19. Anisimova AS, Alexandrov AI, Makarova NE, Gladyshev VN, Dmitriev SE. Protein synthesis and quality control in aging. *Aging (Albany NY)*. (2018) 10:4269–88. doi: 10.18632/aging.101721

20. Fang P, She Y, Yu M, Min W, Shang W, Zhang Z. Adipose-muscle crosstalk in age-related metabolic disorders: the emerging roles of adipo-myokines. *Ageing Res Rev*. (2023) 84:101829. doi: 10.1016/j.arr.2022.101829

21. Arner P, Rydén M. Human white adipose tissue: a highly dynamic metabolic organ. *J Intern Med*. (2022) 291:611–21. doi: 10.1111/joim.13435

22. Petersen MC, Shulman GI. Mechanisms of insulin action and insulin resistance. *Physiol Rev*. (2018) 98:2133–223. doi: 10.1152/physrev.00063.2017

23. Sampath Kumar A, Maiya AG, Shastry BA, Vaishali K, Ravishankar N, Hazari A, et al. Exercise and insulin resistance in type 2 diabetes mellitus: a systematic review and meta-analysis. *Ann Phys Rehabil Med*. (2019) 62:98–103. doi: 10.1016/j.rehab.2018.11.001

24. Li CW, Yu K, Shyh-Chang N, Jiang Z, Liu T, Ma S, et al. Pathogenesis of sarcopenia and the relationship with fat mass: descriptive review. *J Cachexia Sarcopenia Muscle*. (2022) 13:781–94. doi: 10.1002/jcsm.12901

25. Dowling L, Duseja A, Vilaca T, Walsh JS, Goljanek-Whysall K. MicroRNAs in obesity, sarcopenia, and commonalities for sarcopenic obesity: a systematic review. *J Cachexia Sarcopenia Muscle*. (2022) 13:68–85. doi: 10.1002/jcsm.12878

26. Bartke A. Growth hormone and aging. *Rev Endocr Metab Disord*. (2021) 22:71–80. doi: 10.1007/s11154-020-09593-2

27. Frater J, Lie D, Bartlett P, McGrath JJ. Insulin-like growth factor 1 (IGF-1) as a marker of cognitive decline in normal ageing: a review. *Ageing Res Rev*. (2018) 42:14–27. doi: 10.1016/j.arr.2017.12.002

28. Wang W, Tesfay EB, van Klinken JB, Willems van Dijk K, Bartke A, van Heemst D, et al. Clustered Mendelian randomization analyses identify distinct and opposing pathways in the association between genetically influenced insulin-like growth factor-1 and type 2 diabetes mellitus. *Int J Epidemiol*. (2022) 51:1874–85. doi: 10.1093/ije/dyac119

29. Janssen J. Hyperinsulinemia and its pivotal role in aging, obesity, type 2 diabetes, cardiovascular disease and Cancer. *Int J Mol Sci*. (2021) 22:22. doi: 10.3390/ijms22157797

30. De Paoli M, Zakharia A, Werstuck GH. The role of estrogen in insulin resistance: a review of clinical and preclinical data. *Am J Pathol*. (2021) 191:1490–8. doi: 10.1016/j.ajpath.2021.05.011

31. Julien B, Pinteur C, Vega N, Vidal H, Naville D, Le Magueresse-Battistoni B. Estrogen withdrawal and replacement differentially target liver and adipose tissues in female mice fed a high-fat high-sucrose diet: impact of a chronic exposure to a low-dose pollutant mixture(☆). *J Nutr Biochem*. (2019) 72:108211. doi: 10.1016/j.jnutbio.2019.07.002

32. Kelly DM, Jones TH. Testosterone: a metabolic hormone in health and disease. *J Endocrinol*. (2013) 217:R25–45. doi: 10.1530/JOE-12-0455

33. van den Beld AW, Kaufman JM, Zillikens MC, Lamberts S, Egan JM, van der Lely AJ. The physiology of endocrine systems with ageing. *Lancet Diabetes Endocrinol*. (2018) 6:647–58. doi: 10.1016/S2213-8587(18)30026-3

34. Donato J Jr, Wasinski F, Furigo IC, Metzger M, Frazão R. Central regulation of metabolism by growth hormone. *Cells*. (2021):10. doi: 10.3390/cells10010129

35. Lavie CJ, Ozemek C, Carbone S, Katzmarzyk PT, Blair SN. Sedentary behavior, exercise, and cardiovascular health. *Circ Res*. (2019) 124:799–815. doi: 10.1161/CIRCRESAHA.118.312669

36. Palmer AK, Gustafson B, Kirkland JL, Smith U. Cellular senescence: at the nexus between ageing and diabetes. *Diabetologia*. (2019) 62:1835–41. doi: 10.1007/s00125-019-4934-x

37. Laiteerapong N, Ham SA, Gao Y, Moffet HH, Liu JY, Huang ES, et al. The legacy effect in type 2 diabetes: impact of early glycemic control on future complications (the Diabetes & Aging Study). *Diabetes Care*. (2019) 42:416–26. doi: 10.2337/dc17-1144

38. Cicalese SM, da Silva JF, Priviero F, Webb RC, Eguchi S, Tostes RC. Vascular stress signaling in hypertension. *Circ Res*. (2021) 128:969–92. doi: 10.1161/CIRCRESAHA.121.318053

39. Forte M, Stanzione R, Cotugno M, Bianchi F, Marchitti S, Rubattu S. Vascular ageing in hypertension: focus on mitochondria. *Mech Ageing Dev*. (2020) 189:111267. doi: 10.1016/j.mad.2020.111267

40. Glass CK, Olefsky JM. Inflammation and lipid signaling in the etiology of insulin resistance. *Cell Metab*. (2012) 15:635–45. doi: 10.1016/j.cmet.2012.04.001

41. Grandl G, Wolfrum C. Hemostasis, endothelial stress, inflammation, and the metabolic syndrome. *Semin Immunopathol*. (2018) 40:215–24. doi: 10.1007/s00281-017-0666-5

42. Franceschi C, Garagnani P, Parini P, Giuliani C, Santoro A. Inflammaging: a new immune-metabolic viewpoint for age-related diseases. *Nat Rev Endocrinol*. (2018) 14:576–90. doi: 10.1038/s41574-018-0059-4

43. Gonzalez FJ, Xie C, Jiang C. The role of hypoxia-inducible factors in metabolic diseases. *Nat Rev Endocrinol*. (2018) 15:21–32. doi: 10.1038/s41574-018-0096-z

44. Knapp M, Tu X, Wu R. Vascular endothelial dysfunction, a major mediator in diabetic cardiomyopathy. *Acta Pharmacol Sin*. (2019) 40:1–8. doi: 10.1038/s41401-018-0042-6

45. Ali MK, Pearson-Stuttard J, Selvin E, Gregg EW. Interpreting global trends in type 2 diabetes complications and mortality. *Diabetologia*. (2022) 65:3–13. doi: 10.1007/s00125-021-05585-2

46. Zampino M, AlGhatrif M, Kuo PL, Simonsick EM, Ferrucci L. Longitudinal changes in resting metabolic rates with aging are accelerated by diseases. *Nutrients*. (2020):12. doi: 10.3390/nu12103061

47. Silveira Rossi JL, Barbalho SM, Reverete de Araujo R, Bechara MD, Sloan KP, Sloan LA. Metabolic syndrome and cardiovascular diseases: going beyond traditional risk factors. *Diabetes Metab Res Rev*. (2022) 38:e3502. doi: 10.1002/dmrr.3502

48. Sun Z. Aging, arterial stiffness, and hypertension. *Hypertension*. (2015) 65:252–6. doi: 10.1161/HYPERTENSIONAHA.114.03617

49. Wan Z, Song L, Hu L, Lei X, Huang Y, Lv Y, et al. The role of systemic inflammation in the association between serum 25-hydroxyvitamin D and type 2 diabetes mellitus. *Clin Nutr*. (2021) 40:3661–7. doi: 10.1016/j.clnu.2021.04.029

50. Wang X, Mukherjee B, Park SK. Associations of cumulative exposure to heavy metal mixtures with obesity and its comorbidities among U.S. adults in NHANES 2003-2014. *Environ Int*. (2018) 121:683–94. doi: 10.1016/j.envint.2018.09.035

51. Lind PM, Lind L. Endocrine-disrupting chemicals and risk of diabetes: an evidence-based review. *Diabetologia*. (2018) 61:1495–502. doi: 10.1007/s00125-018-4621-3

52. Zhao L, Fang J, Tang S, Deng F, Liu X, Shen Y, et al. PM2.5 and serum metabolome and insulin resistance, potential mediation by the gut microbiome: a population-based panel study of older adults in China. *Environ Health Perspect*. (2022) 130:27007. doi: 10.1289/EHP9688

53. Le Magueresse-Battistoni B, Vidal H, Naville D. Environmental pollutants and metabolic disorders: the multi-exposure scenario of life. *Front Endocrinol*. (2018) 9:582. doi: 10.3389/fendo.2018.00582

54. Lauretta R, Sansone A, Sansone M, Romanelli F, Appetecchia M. Endocrine disrupting chemicals: effects on endocrine glands. *Front Endocrinol*. (2019) 10:178. doi: 10.3389/fendo.2019.00178

55. Le Magueresse-Battistoni B. Endocrine disrupting chemicals and metabolic disorders in the liver: what if we also looked at the female side. *Chemosphere*. (2021) 268:129212. doi: 10.1016/j.chemosphere.2020.129212

56. Le Magueresse-Battistoni B. Adipose tissue and endocrine-disrupting chemicals: does sex matter. *Int J Environ Res Public Health*. (2020) 17:9403. doi: 10.3390/ijerph17249403

57. Beulens J, Pinho M, Abreu TC, den Braver NR, Lam TM, Huss A, et al. Environmental risk factors of type 2 diabetes-an exposome approach. *Diabetologia*. (2022) 65:263–74. doi: 10.1007/s00125-021-05618-w

58. Sun J, Fang R, Wang H, Xu DX, Yang J, Huang X, et al. A review of environmental metabolism disrupting chemicals and effect biomarkers associating disease risks: where exposomics meets metabolomics. *Environ Int*. (2022) 158:106941. doi: 10.1016/j.envint.2021.106941

59. Park SK, Schwartz J, Weisskopf M, Sparrow D, Vokonas PS, Wright RO, et al. Low-level lead exposure, metabolic syndrome, and heart rate variability: the VA normative aging study. *Environ Health Perspect*. (2006) 114:1718–24. doi: 10.1289/ehp.8992

60. Valcke M, Ouellet N, Dubé M, Laouan Sidi EA, LeBlanc A, Normandin L, et al. Biomarkers of cadmium, lead and mercury exposure in relation with early biomarkers of renal dysfunction and diabetes: results from a pilot study among aging Canadians. *Toxicol Lett*. (2019) 312:148–56. doi: 10.1016/j.toxlet.2019.05.014

61. Vasto S, Baldassano D, Sabatino L, Caldarella R, Di Rosa L, Baldassano S. The role of consumption of molybdenum biofortified crops in bone homeostasis and healthy aging. *Nutrients*. (2023):15. doi: 10.3390/nu15041022

62. Li B, Zhang Q, Chang X, Shen Y, Liu T, Liang X, et al. Association of urinary metal levels with metabolic syndrome in coal workers. *Environ Sci Pollut Res Int*. (2023) 30:62892–904. doi: 10.1007/s11356-023-26452-0

63. Liang J, Tian SS, Qiao N, Wang C, Huang JJ, Sun CM, et al. Relationship between physical activity patterns and metabolic syndrome among male coal miners of Shanxi Province in China. *Int J Sport Nutr Exerc Metab*. (2017) 27:50–8. doi: 10.1123/ijsnem.2015-0320

64. Cotrim HP, Carvalho F, Siqueira AC, Lordelo M, Rocha R, De Freitas LA. Nonalcoholic fatty liver and insulin resistance among petrochemical workers. *JAMA*. (2005) 294:1618–20. doi: 10.1001/jama.294.13.1618-b

65. Pearson BL, Ehninger D. Environmental chemicals and aging. *Curr Environ Health Rep*. (2017) 4:38–43. doi: 10.1007/s40572-017-0131-6

66. Ko E, Choi M, Shin S. Bottom-line mechanism of organochlorine pesticides on mitochondria dysfunction linked with type 2 diabetes. *J Hazard Mater*. (2020) 393:122400. doi: 10.1016/j.jhazmat.2020.122400

67. Xu X, Liao W, Lin Y, Dai Y, Shi Z, Huo X. Blood concentrations of lead, cadmium, mercury and their association with biomarkers of DNA oxidative damage in preschool children living in an e-waste recycling area. *Environ Geochem Health*. (2018) 40:1481–94. doi: 10.1007/s10653-017-9997-3

68. Sanmarco LM, Chao CC, Wang YC, Kenison JE, Li Z, Rone JM, et al. Identification of environmental factors that promote intestinal inflammation. *Nature*. (2022) 611:801–9. doi: 10.1038/s41586-022-05308-6

69. Ludwig DS, Ebbeling CB. The carbohydrate-insulin model of obesity: beyond "calories in, calories out". *JAMA Intern Med*. (2018) 178:1098–103. doi: 10.1001/jamainternmed.2018.2933

70. Craig WJ, Mangels AR, Fresán U, Marsh K, Miles FL, Saunders AV, et al. The safe and effective use of plant-based diets with guidelines for health professionals. *Nutrients*. (2021):13. doi: 10.3390/nu13114144

71. Li Y, Schoufour J, Wang DD, Dhana K, Pan A, Liu X, et al. Healthy lifestyle and life expectancy free of cancer, cardiovascular disease, and type 2 diabetes: prospective cohort study. *BMJ*. (2020) 368:l6669. doi: 10.1136/bmj.l6669

72. Heianza Y, Zhou T, Sun D, Hu FB, Qi L. Healthful plant-based dietary patterns, genetic risk of obesity, and cardiovascular risk in the UK biobank study. *Clin Nutr*. (2021) 40:4694–701. doi: 10.1016/j.clnu.2021.06.018

73. Hu Y, Ding M, Sampson L, Willett WC, Manson JE, Wang M, et al. Intake of whole grain foods and risk of type 2 diabetes: results from three prospective cohort studies. *BMJ*. (2020) 370:m2206. doi: 10.1136/bmj.m2206

74. Tardy AL, Pouteau E, Marquez D, Yilmaz C, Scholey A. Vitamins and minerals for energy, fatigue and cognition: a narrative review of the biochemical and clinical evidence. *Nutrients*. (2020):12. doi: 10.3390/nu12010228

75. Longo VD, Antebi A, Bartke A, Barzilai N, Brown-Borg HM, Caruso C, et al. Interventions to slow aging in humans: are we ready. *Aging Cell*. (2015) 14:497–510. doi: 10.1111/acel.12338

76. Dato S, Bellizzi D, Rose G, Passarino G. The impact of nutrients on the aging rate: a complex interaction of demographic, environmental and genetic factors. *Mech Ageing Dev*. (2016) 154:49–61. doi: 10.1016/j.mad.2016.02.005

77. de Lorgeril M, Salen P. The Mediterranean-style diet for the prevention of cardiovascular diseases. *Public Health Nutr*. (2006) 9:118–23. doi: 10.1079/PHN2005933

78. Battino M, Forbes-Hernández TY, Gasparrini M, Afrin S, Cianciosi D, Zhang J, et al. Relevance of functional foods in the Mediterranean diet: the role of olive oil, berries and honey in the prevention of cancer and cardiovascular diseases. *Crit Rev Food Sci Nutr*. (2019) 59:893–920. doi: 10.1080/10408398.2018.1526165

79. Makki K, Deehan EC, Walter J, Bäckhed F. The impact of dietary Fiber on gut microbiota in host health and disease. *Cell Host Microbe*. (2018) 23:705–15. doi: 10.1016/j.chom.2018.05.012

80. Myhrstad M, Tunsjø H, Charnock C, Telle-Hansen VH. Dietary Fiber, gut microbiota, and metabolic regulation-current status in human randomized trials. *Nutrients*. (2020):12. doi: 10.3390/nu12030859

81. Magne F, Gotteland M, Gauthier L, Zazueta A, Pesoa S, Navarrete P, et al. The Firmicutes/Bacteroidetes ratio: a relevant marker of gut Dysbiosis in obese patients. *Nutrients*. (2020):12. doi: 10.3390/nu12051474

82. Shi J, Qiu H, Xu Q, Ma Y, Ye T, Kuang Z, et al. Integrated multi-omics analyses reveal effects of empagliflozin on intestinal homeostasis in high-fat-diet mice. *iScience*. (2023) 26:105816. doi: 10.1016/j.isci.2022.105816

83. Shuwen H, Kefeng D. Intestinal phages interact with bacteria and are involved in human diseases. *Gut Microbes*. (2022) 14:2113717. doi: 10.1080/19490976.2022.2113717

84. Stenman LK, Burcelin R, Lahtinen S. Establishing a causal link between gut microbes, body weight gain and glucose metabolism in humans - towards treatment with probiotics. *Benef Microbes*. (2016) 7:11–22. doi: 10.3920/BM2015.0069

85. Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. *BMJ*. (2018) 361:k2179. doi: 10.1136/bmj.k2179

86. Dalile B, Van Oudenhove L, Vervliet B, Verbeke K. The role of short-chain fatty acids in microbiota-gut-brain communication. *Nat Rev Gastroenterol Hepatol*. (2019) 16:461–78. doi: 10.1038/s41575-019-0157-3

87. Haran JP, McCormick BA. Aging, frailty, and the microbiome-how Dysbiosis influences human aging and disease. *Gastroenterology*. (2021) 160:507–23. doi: 10.1053/j.gastro.2020.09.060

88. Thevaranjan N, Puchta A, Schulz C, Naidoo A, Szamosi JC, Verschoor CP, et al. Age-associated microbial Dysbiosis promotes intestinal permeability, systemic inflammation, and macrophage dysfunction. *Cell Host Microbe*. (2017) 21:455–66.e4. doi: 10.1016/j.chom.2017.03.002

89. Zhou Y, Stubbs RJ, Finlayson G. A neurocognitive perspective on the relationship between exercise and reward: implications for weight management and drug addiction. *Appetite*. (2023) 182:106446. doi: 10.1016/j.appet.2022.106446

90. Guo X, Gong S, Chen Y, Hou X, Sun T, Wen J, et al. Lifestyle behaviors and stress are risk factors for overweight and obesity in healthcare workers: a cross-sectional survey. *BMC Public Health*. (2023) 23:1791. doi: 10.1186/s12889-023-16673-w

91. Amanat S, Ghahri S, Dianatinasab A, Fararouei M, Dianatinasab M. Exercise and type 2 diabetes. *Adv Exp Med Biol*. (2020) 1228:91–105. doi: 10.1007/978-981-15-1792-1_6

92. Savikj M, Stocks B, Sato S, Caidahl K, Krook A, Deshmukh AS, et al. Exercise timing influences multi-tissue metabolome and skeletal muscle proteome profiles in type 2 diabetic patients - a randomized crossover trial. *Metabolism*. (2022) 135:155268. doi: 10.1016/j.metabol.2022.155268

93. Ibeas K, Herrero L, Mera P, Serra D. Hypothalamus-skeletal muscle crosstalk during exercise and its role in metabolism modulation. *Biochem Pharmacol*. (2021) 190:114640. doi: 10.1016/j.bcp.2021.114640

94. Diaz KM, Shimbo D. Physical activity and the prevention of hypertension. *Curr Hypertens Rep*. (2013) 15:659–68. doi: 10.1007/s11906-013-0386-8

95. Palatini P. Blood pressure behaviour during physical activity. *Sports Med*. (1988) 5:353–74. doi: 10.2165/00007256-198805060-00002

96. Lin WY. A large-scale observational study linking various kinds of physical exercise to lipoprotein-lipid profile. *J Int Soc Sports Nutr*. (2021) 18:35. doi: 10.1186/s12970-021-00436-2

97. Nilsson MI, Bourgeois JM, Nederveen JP, Leite MR, Hettinga BP, Bujak AL, et al. Lifelong aerobic exercise protects against inflammaging and cancer. *PLoS One*. (2019) 14:e0210863. doi: 10.1371/journal.pone.0210863

98. Chowdhury KK, Legare DJ, Lautt WW. Insulin sensitization by voluntary exercise in aging rats is mediated through hepatic insulin sensitizing substance (HISS). *Exp Gerontol*. (2011) 46:73–80. doi: 10.1016/j.exger.2010.10.006

99. Pan B, Ge L, Xun YQ, Chen YJ, Gao CY, Han X, et al. Exercise training modalities in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. *Int J Behav Nutr Phys Act*. (2018) 15:72. doi: 10.1186/s12966-018-0703-3

100. Oppert JM, Bellicha A, van Baak MA, Battista F, Beaulieu K, Blundell JE, et al. Exercise training in the management of overweight and obesity in adults: synthesis of the evidence and recommendations from the European Association for the Study of obesity physical activity working group. *Obes Rev*. (2021) 22:e13273. doi: 10.1111/obr.13273

101. Ramos JS, Dalleck LC, Tjonna AE, Beetham KS, Coombes JS. The impact of high-intensity interval training versus moderate-intensity continuous training on vascular function: a systematic review and meta-analysis. *Sports Med*. (2015) 45:679–92. doi: 10.1007/s40279-015-0321-z

102. Haganes KL, Silva CP, Eyjólfsdóttir SK, Steen S, Grindberg M, Lydersen S, et al. Time-restricted eating and exercise training improve HbA1c and body composition in women with overweight/obesity: a randomized controlled trial. *Cell Metab*. (2022) 34:1457–71.e4. doi: 10.1016/j.cmet.2022.09.003

103. McMullan RC, Kelly SA, Hua K, Buckley BK, Faber JE, Pardo-Manuel de Villena F, et al. Long-term exercise in mice has sex-dependent benefits on body composition and metabolism during aging. *Physiol Rep*. (2016) 4:e13011. doi: 10.14814/phy2.13011

104. Zhu J, Zhou Y, Jin B, Shu J. Role of estrogen in the regulation of central and peripheral energy homeostasis: from a menopausal perspective. *Ther Adv Endocrinol Metab*. (2023) 14:20420188231199359. doi: 10.1177/20420188231199359

105. Kuryłowicz A. Estrogens in adipose tissue physiology and obesity-related dysfunction. *Biomedicine*. (2023) 11:690. doi: 10.3390/biomedicines11030690

106. Ko SH, Kim HS. Menopause-associated lipid metabolic disorders and foods beneficial for postmenopausal women. *Nutrients*. (2020) 12:202. doi: 10.3390/nu12010202

107. Ko SH, Jung Y. Energy metabolism changes and dysregulated lipid metabolism in postmenopausal women. *Nutrients*. (2021) 13:4556. doi: 10.3390/nu13124556

108. Ali D, Figeac F, Caci A, Ditzel N, Schmal C, Kerckhofs G, et al. High-fat diet-induced obesity augments the deleterious effects of estrogen deficiency on bone: evidence from ovariectomized mice. *Aging Cell*. (2022) 21:e13726. doi: 10.1111/acel.13726

109. Klinge CM. Estrogenic control of mitochondrial function. *Redox Biol*. (2020) 31:101435. doi: 10.1016/j.redox.2020.101435

110. Bhasin S, Woodhouse L, Casaburi R, Singh AB, Bhasin D, Berman N, et al. Testosterone dose-response relationships in healthy young men. *Am J Physiol Endocrinol Metab*. (2001) 281:E1172–81. doi: 10.1152/ajpendo.2001.281.6.E1172

111. Mudali S, Dobs AS. Effects of testosterone on body composition of the aging male. *Mech Ageing Dev*. (2004) 125:297–304. doi: 10.1016/j.mad.2004.01.004

112. Blümel JE, Fica J, Chedraui P, Mezones-Holguín E, Zuñiga MC, Witis S, et al. Sedentary lifestyle in middle-aged women is associated with severe menopausal symptoms and obesity. *Menopause*. (2016) 23:488–93. doi: 10.1097/GME.0000000000000575

113. Kotseva K, De Backer G, De Bacquer D, Rydén L, Hoes A, Grobbee D, et al. Lifestyle and impact on cardiovascular risk factor control in coronary patients across 27 countries: results from the European Society of Cardiology ESC-EORP EUROASPIRE V registry. *Eur J Prev Cardiol*. (2019) 26:824–35. doi: 10.1177/2047487318825350

114. Carter S, Hartman Y, Holder S, Thijssen DH, Hopkins ND. Sedentary behavior and cardiovascular disease risk: mediating mechanisms. *Exerc Sport Sci Rev*. (2017) 45:80–6. doi: 10.1249/JES.0000000000000106

115. Ekelund U, Brage S, Besson H, Sharp S, Wareham NJ. Time spent being sedentary and weight gain in healthy adults: reverse or bidirectional causality. *Am J Clin Nutr*. (2008) 88:612–7. doi: 10.1093/ajcn/88.3.612

116. Hamburg NM, McMackin CJ, Huang AL, Shenouda SM, Widlansky ME, Schulz E, et al. Physical inactivity rapidly induces insulin resistance and microvascular dysfunction in healthy volunteers. *Arterioscler Thromb Vasc Biol*. (2007) 27:2650–6. doi: 10.1161/ATVBAHA.107.153288

117. Swift DL, McGee JE, Earnest CP, Carlisle E, Nygard M, Johannsen NM. The effects of exercise and physical activity on weight loss and maintenance. *Prog Cardiovasc Dis*. (2018) 61:206–13. doi: 10.1016/j.pcad.2018.07.014

118. Rigamonti AE, De Col A, Tamini S, Cicolini S, Caroli D, De Micheli R, et al. Multidisciplinary integrated metabolic rehabilitation in elderly obese patients: effects on cardiovascular risk factors, fatigue and muscle performance. *Nutrients*. (2019):11. doi: 10.3390/nu11061240

119. Ishikawa M, Yokoyama T, Nakaya T, Fukuda Y, Takemi Y, Kusama K, et al. Food accessibility and perceptions of shopping difficulty among elderly people living alone in Japan. *J Nutr Health Aging*. (2016) 20:904–11. doi: 10.1007/s12603-015-0694-6

120. Durlach V, Vergès B, Al-Salameh A, Bahougne T, Benzerouk F, Berlin I, et al. Smoking and diabetes interplay: a comprehensive review and joint statement. *Diabetes Metab*. (2022) 48:101370. doi: 10.1016/j.diabet.2022.101370

121. Tsai PC, Glastonbury CA, Eliot MN, Bollepalli S, Yet I, Castillo-Fernandez JE, et al. Smoking induces coordinated DNA methylation and gene expression changes in adipose tissue with consequences for metabolic health. *Clin Epigenetics*. (2018) 10:126. doi: 10.1186/s13148-018-0558-0

122. Dikalov S, Itani H, Richmond B, Vergeade A, Rahman S, Boutaud O, et al. Tobacco smoking induces cardiovascular mitochondrial oxidative stress, promotes endothelial dysfunction, and enhances hypertension. *Am J Physiol Heart Circ Physiol*. (2019) 316:H639–639H646. doi: 10.1152/ajpheart.00595.2018

123. Seoane-Collazo P, Diéguez C, Nogueiras R, Rahmouni K, Fernández-Real JM, López M. Nicotine' actions on energy balance: friend or foe. *Pharmacol Ther*. (2021) 219:107693. doi: 10.1016/j.pharmthera.2020.107693

124. Rezk-Hanna M, Benowitz NL. Cardiovascular effects of hookah smoking: potential implications for cardiovascular risk. *Nicotine Tob Res*. (2019) 21:1151–61. doi: 10.1093/ntr/nty065

125. Yang Y, Peng N, Chen G, Wan Q, Yan L, Wang G, et al. Interaction between smoking and diabetes in relation to subsequent risk of cardiovascular events. *Cardiovasc Diabetol*. (2022) 21:14. doi: 10.1186/s12933-022-01447-2

126. Klopack ET, Carroll JE, Cole SW, Seeman TE, Crimmins EM. Lifetime exposure to smoking, epigenetic aging, and morbidity and mortality in older adults. *Clin Epigenetics*. (2022) 14:72. doi: 10.1186/s13148-022-01286-8

127. Tarantino U, Cariati I, Greggi C, Gasbarra E, Belluati A, Ciolli L, et al. Skeletal system biology and smoke damage: from basic science to medical clinic. *Int J Mol Sci*. (2021):22. doi: 10.3390/ijms22126629

128. Ratajczak AE, Szymczak-Tomczak A, Rychter AM, Zawada A, Dobrowolska A, Krela-Kaźmierczak I. Impact of cigarette smoking on the risk of osteoporosis in inflammatory bowel diseases. *J Clin Med*. (2021):10. doi: 10.3390/jcm10071515

129. Russo C, Walicka M, Caponnetto P, Cibella F, Maglia M, Alamo A, et al. Efficacy and safety of Varenicline for smoking cessation in patients with type 2 diabetes: a randomized clinical trial. *JAMA Netw Open*. (2022) 5:e2217709. doi: 10.1001/jamanetworkopen.2022.17709

130. Hu Y, Zong G, Liu G, Wang M, Rosner B, Pan A, et al. Smoking cessation, weight change, type 2 diabetes, and mortality. *N Engl J Med*. (2018) 379:623–32. doi: 10.1056/NEJMoa1803626

131. Hendriks H. Alcohol and human health: what is the evidence. *Annu Rev Food Sci Technol*. (2020) 11:1–21. doi: 10.1146/annurev-food-032519-051827

132. Minzer S, Losno RA, Casas R. The effect of alcohol on cardiovascular risk factors: is there new information. *Nutrients*. (2020):12. doi: 10.3390/nu12040912

133. Millwood IY, Walters RG, Mei XW, Guo Y, Yang L, Bian Z, et al. Conventional and genetic evidence on alcohol and vascular disease aetiology: a prospective study of 500 000 men and women in China. *Lancet*. (2019) 393:1831–42. doi: 10.1016/S0140-6736(18)31772-0

134. Seitz HK, Bataller R, Cortez-Pinto H, Gao B, Gual A, Lackner C, et al. Alcoholic liver disease. *Nat Rev Dis Primers*. (2018) 4:16. doi: 10.1038/s41572-018-0014-7

135. Åberg F, Byrne CD, Pirola CJ, Männistö V, Sookoian S. Alcohol consumption and metabolic syndrome: clinical and epidemiological impact on liver disease. *J Hepatol*. (2023) 78:191–206. doi: 10.1016/j.jhep.2022.08.030

136. Butts M, Sundaram VL, Murughiyan U, Borthakur A, Singh S. The influence of alcohol consumption on intestinal nutrient absorption: a comprehensive review. *Nutrients*. (2023):15. doi: 10.3390/nu15071571

137. Li SB, Damonte VM, Chen C, Wang GX, Kebschull JM, Yamaguchi H, et al. Hyperexcitable arousal circuits drive sleep instability during aging. *Science*. (2022) 375:eabh3021. doi: 10.1126/science.abh3021

138. Marjot T, Ray DW, Williams FR, Tomlinson JW, Armstrong MJ. Sleep and liver disease: a bidirectional relationship. *Lancet Gastroenterol Hepatol*. (2021) 6:850–63. doi: 10.1016/S2468-1253(21)00169-2

139. Adam TC, Drummen M, Macdonald I, Jalo E, Siig-Vestentoft P, Martinez JA, et al. Association of Psychobehavioral Variables with HOMA-IR and BMI differs for men and women with prediabetes in the PREVIEW lifestyle intervention. *Diabetes Care*. (2021) 44:1491–8. doi: 10.2337/dc21-0059

140. Antza C, Kostopoulos G, Mostafa S, Nirantharakumar K, Tahrani A. The links between sleep duration, obesity and type 2 diabetes mellitus. *J Endocrinol*. (2021) 252:125–41. doi: 10.1530/JOE-21-0155

141. Besedovsky L, Lange T, Haack M. The sleep-immune crosstalk in health and disease. *Physiol Rev*. (2019) 99:1325–80. doi: 10.1152/physrev.00010.2018

142. Morrison M, Halson SL, Weakley J, Hawley JA. Sleep, circadian biology and skeletal muscle interactions: implications for metabolic health. *Sleep Med Rev*. (2022) 66:101700. doi: 10.1016/j.smrv.2022.101700

143. Liu H, Chen A. Roles of sleep deprivation in cardiovascular dysfunctions. *Life Sci*. (2019) 219:231–7. doi: 10.1016/j.lfs.2019.01.006

144. Papatriantafyllou E, Efthymiou D, Zoumbaneas E, Popescu CA, Vassilopoulou E. Sleep deprivation: effects on weight loss and weight loss maintenance. *Nutrients*. (2022):14. doi: 10.3390/nu14081549

145. Agorastos A, Olff M. Sleep, circadian system and traumatic stress. *Eur J Psychotraumatol*. (2021) 12:1956746. doi: 10.1080/20008198.2021.1956746

146. Nassan M, Videnovic A. Circadian rhythms in neurodegenerative disorders. *Nat Rev Neurol*. (2022) 18:7–24. doi: 10.1038/s41582-021-00577-7

147. Winkley K, Upsher R, Stahl D, Pollard D, Kasera A, Brennan A, et al. Psychological interventions to improve self-management of type 1 and type 2 diabetes: a systematic review. *Health Technol Assess*. (2020) 24:1–232. doi: 10.3310/hta24280

148. Brugnera A, Compare A, Omboni S, Greco A, Carrara S, Tasca GA, et al. Psychological covariates of blood pressure among patients with hypertension and metabolic syndrome. *Health Psychol*. (2022) 41:946–54. doi: 10.1037/hea0001205

149. Verhoeven JE, Révész D, van Oppen P, Epel ES, Wolkowitz OM, Penninx BW. Anxiety disorders and accelerated cellular ageing. *Br J Psychiatry*. (2015) 206:371–8. doi: 10.1192/bjp.bp.114.151027

150. Verhoeven JE, Révész D, Epel ES, Lin J, Wolkowitz OM, Penninx BW. Major depressive disorder and accelerated cellular aging: results from a large psychiatric cohort study. *Mol Psychiatry*. (2014) 19:895–901. doi: 10.1038/mp.2013.151

151. Konttinen H. Emotional eating and obesity in adults: the role of depression, sleep and genes. *Proc Nutr Soc*. (2020) 79:283–9. doi: 10.1017/S0029665120000166

152. Charansonney OL, Després JP. Disease prevention--should we target obesity or sedentary lifestyle. *Nat Rev Cardiol*. (2010) 7:468–72. doi: 10.1038/nrcardio.2010.68

153. Kymissis P, Shatin L, Brown W. Relationship between high fasting blood sugar and depression in a mental hygiene clinic population. *Can J Psychiatr*. (1979) 24:133–8. doi: 10.1177/070674377902400204

154. Willans B, Desai M, Owen L, Leng G. NICE public health guidance update. *J Public Health (Oxf)*. (2019) 41:642–4. doi: 10.1093/pubmed/fdz087

155. Zhang K, Kan C, Luo Y, Song H, Tian Z, Ding W, et al. The promotion of active aging through older adult education in the context of population aging. *Front Public Health*. (2022) 10:998710. doi: 10.3389/fpubh.2022.998710

156. Reséndiz Lara T, Muñoz Torres AV, Mendoza Salmerón G, Zendejas Vela DD, Medina Bravo P, Roy García I, et al. Education with a multimedia web platform improves knowledge and HbA1c of Mexican patients with type 2 diabetes. Open clinical trial. *Endocrinol Diabetes Nutr*. (2020) 67:530–9. doi: 10.1016/j.endinu.2019.07.011

157. Grummon AH, Reimold AE, Hall MG. Influence of the San Francisco, CA, sugar-sweetened beverage health warning on consumer reactions: implications for equity from a randomized experiment. *J Acad Nutr Diet*. (2022) 122:363–70.e6. doi: 10.1016/j.jand.2021.07.008

158. Pollack Porter KM, Prochnow T, Mahoney P, Delgado H, Bridges Hamilton CN, Wilkins E, et al. Transforming City streets to promote physical activity and health equity. *Health Aff*. (2019) 38:1475–83. doi: 10.1377/hlthaff.2019.00454

159. Juul V, Nordbø E. Examining activity-friendly neighborhoods in the Norwegian context: green space and walkability in relation to physical activity and the moderating role of perceived safety. *BMC Public Health*. (2023) 23:259. doi: 10.1186/s12889-023-15170-4

160. Longevity TLH. Primary care workers vital for healthy longevity. *Lancet Healthy Longev*. (2023) 4:e357. doi: 10.1016/S2666-7568(23)00142-3

161. Blaner WS. Vitamin a signaling and homeostasis in obesity, diabetes, and metabolic disorders. *Pharmacol Ther*. (2019) 197:153–78. doi: 10.1016/j.pharmthera.2019.01.006

162. Révész D, Verhoeven JE, Milaneschi Y, de Geus EJ, Wolkowitz OM, Penninx BW. Dysregulated physiological stress systems and accelerated cellular aging. *Neurobiol Aging*. (2014) 35:1422–30. doi: 10.1016/j.neurobiolaging.2013.12.027

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 17 October 2023
DOI 10.3389/fpubh.2023.1271082

OPEN ACCESS

EDITED BY
Yun Gao,
Sichuan University, China

REVIEWED BY
Jun Liang,
Zhejiang University, China
Petra Poulova,
University of Hradec Králové, Czechia

*CORRESPONDENCE
Hongfang Chen
✉ chf1695@163.com

†These authors have contributed equally to this work and share first authorship

RECEIVED 01 August 2023
ACCEPTED 05 October 2023
PUBLISHED 17 October 2023

CITATION
Wang X, Chen J, Feng M, Zhuang M, Wang J, Zhang L, Liu Y and Chen H (2023) Demand and influencing factors of "Internet + Traditional Chinese Medicine" home nursing service for older adult patients with chronic diseases: a mixed research perspective.
Front. Public Health 11:1271082.
doi: 10.3389/fpubh.2023.1271082

Demand and influencing factors of "Internet + Traditional Chinese Medicine" home nursing service for older adult patients with chronic diseases: a mixed research perspective

Xinghuan Wang[1†], Jinyan Chen[1†], Meiqin Feng[1], Miaoqing Zhuang[1], Jiayi Wang[1], Luyu Zhang[1], Yue Liu[1] and Hongfang Chen[2*]

[1]School of Nursing, Shaanxi University of Traditional Chinese Medicine, Xianyang, China, [2]Personnel Department, Shaanxi Provincial Hospital of Traditional Chinese Medicine, Xi'an, China

Background: In the context of global aging, the characteristics of chronic diseases seriously affect the quality of life of older adults. It is urgent to carry out continuous nursing basis for older adult patients with chronic diseases. In view of the remarkable efficacy of Chinese medicine in the treatment of chronic diseases, this study may help to understand the demand for "Internet + Chinese medicine" home care service and its influencing factors of older adult chronic disease patients, and to provide a reference basis for improving the quality of life of the older adult chronic disease population.

Methods: This is a mixed study. The quantitative study adopted the convenience sampling method, and a total of 308 patients in a third-grade hospital in Shaanxi Province were investigated by general data questionnaire, traditional Chinese medicine service demand questionnaire, traditional Chinese medicine knowledge questionnaire, older adult Chinese medicine attitude questionnaire, and home care demand questionnaire from March to April 2022. In the qualitative study, semi-structured interviews were adopted, and patients were interviewed until the content was saturated. Colaizzi analysis method was used to analyze and summarize the topic of the interview data.

Results: 308 valid questionnaires were collected, and the patients scored (58.42 ± 17.16) on the demand for TCM nursing services, (59.86 ± 11.54) on the knowledge of TCM, (73.03 ± 9.11) on the attitude toward TCM, and (136.84 ± 46.39) on the demand for home care. The results of multiple linear regression showed that learning about the nursing service pathway, knowledge of general knowledge of Chinese medicine, and attitude toward Chinese medicine among the older adult and home care demand were the influencing factors of the demand for Chinese medicine nursing services for older adult patients with chronic diseases ($p < 0.05$). The results of the in-depth interviews were summarized into three themes: facilitating factor, hindering factor, and the "Internet + Chinese medicine" multiple needs of home care.

Conclusion: Older adult patients with chronic diseases have a high intention of home care demand and they are affected by multiple factors. Consequently, the actual demand situation of older adult patients with chronic diseases should

be used as a guide to provide directed and diversified Chinese medicine home care services to meet the individualized needs of the older adult.

KEYWORDS

chronic disease, internet, Chinese medicine, home care, needs

1. Introduction

Population aging has become a global problem and exerted heavy burdens on the health care system and society. By 2030, the world is likely to have 1 billion people aged 65 years or older, accounting for 13% of the total population (1, 2). As the world's most populated country, China is facing a major challenge due to the aging population. China's aging population is estimated to increase at a rate of 5.96 million per year from 2001 to 2020 and then 6.2 million per year from 2021 to 2050, and is expected to exceed 400 million by 2050, accounting for 30% of its total population (3). According to the survey, the death of chronic disease population accounts for 89.82% of total deaths (4). With the increase of average life expectancy, the frequent occurrence of chronic diseases is increasing year by year, such as diabetes, cardiovascular disease, chronic obstructive pulmonary disease, and cancer, which will become an important challenge for the aging society (5, 6).

Older people are vulnerable and have complex health care needs, especially during the transition from hospital to home, which is a vulnerable time for older people. In addition to social reintegration and family reintegration, there is a need to find new care options to maintain the disease (7). Chronic diseases are long-lasting, slow to progress, and often associated with multiple states. Older adults with chronic conditions have ongoing complex care needs that require multiple care settings. Their lifestyle is characterized by frequent changes in health, high rates of rehospitalization, and the long-term involvement of family and health care providers in their care.

With the advancement of wearable health devices, cloud computing, mobile technologies, and Internet of Things, mobile health (m-Health) is rapidly developing and shows a promising future in the management of chronic diseases. Its advantages include its ability to improve the quality of care, reduce the costs of care, and improve treatment outcomes by transferring in-hospital treatment to patient-centered medical treatment at home. M-Health could also enhance the international cooperation of medical providers in different time zones and the sharing of high-quality medical service resources between developed and developing countries (8). Home nursing service is an important part of extended nursing services, which refers to that the community nurses come to the patient's home to provide continuous and systematic basic medical care services under the premise of medical advice. Studies have shown that home care services for older adult patients, taking into account both physical and psychological care, can reduce the burden of disease, solve or improve the health problems of older adult patients, and promote healthy aging. At the same time, it can also make up for the lack of child care and reduce the burden of family life. Therefore, the demand for home care services for older adults gradually increasing, and home care services are imperative.

However, the uneven distribution of caregivers and critical health care workforce shortages are major obstacles to improving disease outcome. Most older adult patients with chronic diseases require long-term out-of-hospital medical care, so there is a greater demand for out-of-hospital care (9, 10). Home care is an extended service after discharge, mainly through the intervention operation of the professional team of home nursing, which can provide highly targeted nursing services for older adult patients with chronic diseases (11). Older adult patients with chronic diseases have low immunity and many underlying diseases, according to the previous health care work more emphasis on care and maintenance during hospitalization, while ignoring the basic health care of patients after discharge. Tele-medicine, e-health, and m-health scenarios can improve health outcomes, quality of life, and well-being and facilitate functional patient empowerment and engagement.

Internationally, the United States, Canada, Australia, and Japan have developed relatively mature home care service models with their own unique characteristics (12). These countries have similar home care service processes, but each has its own characteristics in terms of home care providers and service content. Home health agencies in the United States are the only Medicare-certified providers allowed to provide skilled nursing care for acute, chronic, and rehabilitative conditions in people's homes, with more than 12,300 home-based agencies participating in Medicare in 2015 and approximately 3.5 million Medicare beneficiaries receiving services (13). Most regions of France have begun piloting the inclusion of informal caregivers and social workers from informal healthcare organizations into the assistance system to assist healthcare workers (14). In developed countries abroad, the place of treatment has shifted from hospitals to community-based outpatient clinics and homes, and home care for cancer pain is undertaken by specialized home care teams or agencies (15). Japan promotes a community-based integrated care system, provides financial support through long-term care insurance, and establishes home care visiting stations to provide a variety of home care services to discharged patients (16). In Poland, home pain management nurses, hospital nurses, professional family caregivers, and family members are involved in home care, taking on tasks such as health education, medical counseling, promoting rehabilitation, and rational allocation of medical resources (17). From foreign experience, scientific allocation of home care services and human resources can improve patients' quality of life and satisfaction and promote efficient utilization of limited health resources (18, 19).

A prior literature review also found that the implementation of various home care models in the international arena is a specific model of home care under a unique policy and health insurance system and has its own advantages and disadvantages. Models in which private and social insurance pays and private agencies provide services (United States model). A model in which the government pays and private agencies provide services (the Canadian model). A model in which the government and the individual jointly pay for and diversify the service providers (Australian model). The model of insurance payment and

diversified service providers (Japanese model). However, the health care policy and medical insurance system implemented in China are very different from those of other countries, and the contents of our home care programs are scattered in both theory and practice, without forming a scientific and unified model of home care. Therefore, it is not possible to completely copy the foreign home care model, but to utilize the experience of each country to establish a TCM home care model to meet the specialized care needs of home patients, to reduce the burden on the family and society, and to improve the quality of life of the patients.

The innovation of this study is the effective combination of medical association, "Internet + Chinese medicine" and home care. Older adult patients with chronic diseases, as the disseminator of Chinese medicine culture, utilize the "Internet + " technology, and gradually spread the unique advantages of Chinese medicine among the community patient groups. Utilizing the "Internet Plus" technology, the unique advantages of Chinese medicine are gradually widely disseminated among the community patient groups, thus promoting the sustainable development of the Chinese medicine cause. Adopting a combination of qualitative and quantitative methods, we have gained an in-depth understanding of the needs of older adult patients with chronic diseases for TCM home care services. Through the penetration and integration of TCM technology and home care, we can help patients solve the problems of lack of self-care knowledge and insufficient nursing support after discharge from hospitals in a timely manner, so as to ensure the continuity and timeliness of the service and effectively improve the quality of life of older adult chronic disease patients.

The convenience and effectiveness of "Internet + Traditional Chinese medicine" nursing shows its unique superiority in prevention and treatment, convalescence, rehabilitation, etc. It has outstanding intervention effect on chronic diseases of older adults and can break through the limitations of traditional nursing service mode, and its nursing mode has been recognized and advocated by many scholars (20). However, "Internet + TCM" is currently limited to online appointment registration, patients still need to go to the hospital by themselves, for people still need to improve the convenience, with the concept of continuous nursing in recent years, making "TCM + home service" possible. The unique efficacy of TCM in the chronic disease prevention and treatment system has become a necessary way to consolidate primary health services, and the expansion and extension of the nursing service field has been urgently needed (21). As there are fewer studies on online home care services of TCM, this study integrates quantitative and qualitative findings to explore the current situation of demand for home care services of older adult patients with chronic diseases and the factors influencing it, and to provide reference for the construction of the "Internet + TCM" home care services, with a view to providing reference for the management of chronic diseases and the development of home care services of Chinese medicine.

2. Materials and methods

2.1. Research object

This study selected 308 older adult patients with chronic diseases who met the inclusion and exclusion criteria in seven departments, including geriatrics, cerebral diseases, cardiology, and endocrinology, of Shaanxi Provincial Hospital of Traditional Chinese Medicine from 2022-03-01 to 2022-04-30 as the subjects of the survey. Purposive sampling method was used in the interview part to determine the final inclusion of the interview subjects in this study based on the principle of reaching saturation of information. A total of 25 patients were finally interviewed.

Inclusion criteria: ① Age ≥ 60 years old. ② Medically diagnosed with Chronic diseases such as stroke, coronary heart disease, diabetes, etc. ③ History of the disease is more than 2 years. ④ Score of self-care ability >60 points. ⑤ Ability to read, communicate, and understand, and be able to give informed consent.

Exclusion criteria: ① Combined with malignant tumors or serious organic diseases.② Speech and language disorders and serious audio-visual disorders.

2.1.1. Sample size calculation

Based on the sample size calculation formula of cross-sectional study:

$$n = \left(\frac{u_{\alpha/2}\sigma}{\delta} \right)^2$$

Calculated by "the demand for home care services for older adult patients," (significance level = 0.05, Z = 1.96, refer to the related literature $p = 58.9\%$, $q = 1-p$, and $d = 0.1p$) the minimum calculation value of the sample size is about 268 cases. The minimum calculated value was about 268 cases and considering 15% invalid questionnaires, the study finally selected 308 older adult patients with chronic diseases for the survey. The study was approved by the hospital ethics committee.

2.2. Research methods

2.2.1. Quantitative research

According to the purpose of this study, a general data questionnaire was designed by searching a large number of domestic and foreign literatures on home nursing, combining China's national conditions and the characteristics of chronic diseases in older adults. The content of the questionnaire was verified by six experts, and a preliminary survey was conducted on 50 patients before the formal survey. According to the problems found in the preliminary survey, the questionnaire was further screened and revised, and the following five scales were finalized.

2.2.1.1. General information questionnaire

Sixteen items including age, sex, residence, education level, degree of understanding of the contents of the "Internet + TCM" nursing home service approach, how to learn about the "Internet + nursing home service," and what are the concerns about carrying out the "Internet + TCM" nursing home service etc.

2.2.1.2. Questionnaire on the demand for Chinese medicine services

The scale was compiled by Du (22) to assess the older adult's demand for TCM characteristic services, with a total of 17 items. The degree of demand is mainly defined according to the number of items of TCM characteristic services needed by older adults: no need at all, no need for TCM characteristic services; Not very need, need a traditional Chinese medicine characteristic service; General need,

need 2–3 TCM characteristic services; For those in need, 4–5 TCM characteristic services are needed; Very need, need more than five TCM characteristic services. According to Likert's five-point scale, it is divided into very needed (five points), needed (four points), average (three points), less needed (two points), and not needed (one point). The higher the score, the higher the demand. In this study, the Cronbach's α coefficient was 0.976, half reliability was 0.937, and a KMO value was 0.945, $p < 0.01$.

2.2.1.3. Questionnaire on general knowledge of Chinese medicine

This questionnaire was developed by Ren (23). The objective is to understand the general knowledge of traditional Chinese medicine in older adults and explore the relationship between it and the attitude toward traditional Chinese medicine. The content of the questionnaire includes the knowledge of 10 aspects such as the basic characteristics of traditional Chinese medicine and basic diagnosis and treatment methods. Each item is scored on a Likert four-scale according to the degree of knowledge, where those who choose "fully know" and "basically know" are recorded as knowing, and those who choose not know are not aware. Each item was scored with 2.5–10 points respectively, and the total score of the item was 100 points. The final score was analyzed by SPSS project, and the score was arranged in descending order, with the front and back 27% as high and low level, and the middle 46% as medium level. In this study, the Cronbach's α coefficient was 0.894, with a half reliability of 0.701, and a KMO value of 0.886, $p < 0.01$.

2.2.1.4. Attitude scale of traditional Chinese medicine for older adults

This scale was compiled by Liu (24) to understand the attitude of older adults towards traditional Chinese medicine. The scale was developed by item screening, factor load detection, factor number determination, and SPSS classification processing. It was composed of three dimensions, namely "cognition of current situation of Chinese medicine," "emotional belief of Chinese medicine," and "tendency of seeking medical treatment with Chinese medicine," among which the dimension of "cognition of current situation of Chinese medicine" contained 10 items, and was evaluated from the perspective of older adult people's perception of Chinese medicine service level. The "Emotional Beliefs of Traditional Chinese Medicine" contains 12 items, which are assessed by older adult's trust in the clinical efficacy and price advantages of traditional Chinese medicine. The "Tendency to seek medical Treatment with Traditional Chinese Medicine" consists of three items, which mainly assess the degree of propensity to traditional Chinese medicine when older adults are sick themselves and their family members. There are a total of 25 items, ranging from agree to disagree, with scores ranging from 1 to 4 points. The cognitive dimension of TCM status is negative, and the total score is 100 points. In this study, the Cronbach's α coefficient was 0.827, half reliability was 0.658, and a KMO value was 0.831, $p < 0.01$.

2.2.1.5. Questionnaire on home care needs of patients with chronic diseases

The questionnaire was compiled by Tian (25) to analyze the home nursing needs of discharged patients with chronic diseases, including clinical nursing (12 items), health guidance (13 items), rehabilitation nursing (five items), life nursing (10 items), and psychological nursing (2 items), with a total of 42 items. Likert 3 scoring method was adopted for the questionnaire, which was divided into need (five points), indifferent (three points), and do not need (one point), with a total score of 210 points. The score value obtained by all items in each aspect is summed and the average score is taken as the score value of this aspect (because the number of items contained in each aspect is different, the average value of items is taken to represent the score value of this aspect); The score values obtained by all items are summed and averaged as the score value of total demand. The higher the score, the higher the demand for home care. In this study, the Cronbach's α coefficient was 0.973, half reliability was 0.928, and a KMO value was 0.886, $p < 0.01$.

2.2.2. Qualitative research

Based on the literature review, the interview outline was initially formulated according to the research purpose. Combined with experts' opinions and after pre-interviewing three older adult patients with chronic diseases, the research team repeatedly discussed and revised the final interview outline as follows:

Please tell us about your understanding and willingness to accept the "Internet + Chinese medicine" home care service. (2) What are the benefits to you if the "Internet + Chinese medicine" home care service is carried out? (3) What difficulties or problems will you encounter if the "Internet + Chinese Medicine" home care service is launched? (4) Please tell us what medical and nursing services and TCM nursing techniques you would like to receive in the development of "Internet + TCM" home nursing service for your disease? (5) What needs or suggestions do you have for the development of "Internet + TCM" home care service?

2.2.3. Data collection

2.2.3.1. Quantitative study

The survey was implemented in a one-to-one on-site format. Prior to the survey, a trained investigator explained the purpose and significance of the study to the patient in detail. They sign informed consent questionnaires, which are handed out to patients in person by investigators who can assist patients who cannot fill out the questionnaires themselves. Check immediately after filling, fill and correct in time.

2.2.3.2. Qualitative research

Semi-structured interviews were used, in which the researcher explained the purpose and content of the interview to the interviewer, and audio-recorded the content of the interview with his informed consent. Each interview lasted about 30 min, and non-verbal behaviors such as facial expressions and body movements were recorded in a timely manner. Within 24 h after the interview, the audio recordings were promptly transformed into written texts, and the content of the subsequent interviews was adjusted according to the situation of each interview.

2.2.4. Statistical analysis

2.2.4.1. Quantitative research

Excel was used to input the questionnaire and establish the database. SPSS 26.0 was used for statistical analysis. Describe

categorical variables in terms of frequency and percentage. Normal test was performed on all scale data. If normal distribution was followed, the mean and standard deviation were used to describe continuous variables; otherwise, the median and interquartile distances were used. Independent sample t and one-way ANOVA were used to analyze the demand for traditional Chinese medicine nursing services. Data that met normal distribution and homogeneity of variance were analyzed by using two-independent sample *t* test and ANOVA. Data that did not meet normal and homogeneity of variance were analyzed by non-parametric test. Mann–Whitney U test and Kruskal-Wallis H test were used. Pearson or Spearman correlation was used to analyze the correlation between TCM nursing service demand, TCM knowledge, TCM attitude, and home nursing demand of chronic disease patients. Taking TCM nursing service demand score as dependent variable, the results of univariate analysis and correlation analysis were put into the equation, variables with significant differences were selected as independent variables, and the main influencing factors were determined by multiple linear stepwise regression analysis. All the above tests were conducted by bilateral test, the test level was $a = 0.05$, and $p < 0.05$ was considered to be statistically significant. Cronbach's Alpha and KMO were obtained through the reliability analysis and validity analysis of the four scales.

2.2.4.2. Qualitative research

A semi-structured interview was used, in which the investigator told the interviewer about the purpose and content of the interview and recorded it with their informed consent. Each interview time was approximately 30 min. After the interviews, the interviews were converted into text verbatim and sentence-by-sentence within 24 h by two researchers. The information was organized and analyzed using the colaizzi seven-step analysis method (26). The data were managed and analyzed with the help of Nvivo 12 Plus software.

2.2.5. Ethical approval

All participants were informed of the purpose of the study and obtained written informed consent prior to the survey and interview. The participants voluntarily chose to participate in this study and were free to drop out. The electronic information submitted was anonymous, and only the researchers had access to data. The Ethics Committee of the Shaanxi Provincial Hospital of Traditional Chinese Medicine, Shaanxi Province, China approved this study.

3. Results

3.1. Quantitative findings

3.1.1. General information of respondents and one-way analysis of factors

3.1.1.1. General information of survey respondents

A total of 308 questionnaires were distributed in this study, and 308 valid questionnaires were recovered, with a valid recovery rate of 100%. The age of these 308 older adult patients with chronic diseases was 60–93 (71.06 ± 7.30) years old; the highest concern about the development of Internet + nursing home service was the high cost of the service 144 (46.8%); and the willingness to choose nurses' home service was 227 (72.7%), uncertainty 63 (20.5%), and unwillingness 21 (6.8%). The general information of the survey respondents is shown in Supplementary Table 1.

3.1.2. Older adult patients with chronic diseases need for Chinese medicine nursing service, Chinese medicine awareness, Chinese medicine attitude, and home nursing service demand score

The demand score of TCM nursing service was (58.42 ± 17.16) points. The Chinese medicine knowledge score was (59.86 ± 11.54). The score of TCM attitude was (73.03 ± 9.11), the score of TCM status cognition dimension was (24.18 ± 3.97), the score of TCM emotional belief dimension was (39.86 ± 5.60), and the score of TCM tendency to seek medical treatment dimension was (8.99 ± 2.31). The score of home nursing demand was (136.84 ± 46.39), the score of clinical nursing dimension was (36.62 ± 15.10), the score of health guidance dimension was (50.30 ± 14.93), the score of rehabilitation nursing dimension was (18.08 ± 7.03), and the score of life nursing dimension was (25.60 ± 12.76). The psychological nursing dimension score was (6.23 ± 3.16). Through the items of therapeutic effect, selection tendency, frequency of use, and cognition of Chinese medicine by older adults, we have a good practical use and feeling in the Chinese medicine diagnosis and treatment of older adult patients with chronic diseases.

3.1.3. Multiple regression analysis of the demand for TCM nursing services for older adult patients with chronic diseases

Stepwise multiple linear regression analysis was carried out with the total demand for Chinese medicine nursing service of older adult chronic disease patients as the dependent variable, and the variables with statistically significant differences in the univariate and correlation analyses as the independent variables. The results showed that the facilitating factors were the attitudes of older adults toward Chinese medicine, the obstructing factors were the awareness of the current status of Chinese medicine and digital literacy, and the demand factors were the degree of demand for home care services, which were the influencing factors of the demand for Chinese medicine care services for older adult patients with chronic diseases ($p < 0.05$). The variable assignments are shown in Table 1, and the results of regression analysis are shown in Table 2.

3.2. Qualitative findings

3.2.1. Theme 1: facilitating factors

3.2.1.1. Stronger willingness to participate

Most of the patients expressed their willingness to participate in the "Internet + TCM "home care service model in the interviews. N6: "Now sometimes the bed is not available, you have such good conditions and good services, of course I am willing." N16: "Acceptable, I feel quite good, for those who cannot move freely, cannot take care of themselves, or you are not very convenient, like this situation home care is very good." N1: "Then surely there is a network form of that would be better, there are people who value a little bit, a little bit of economic stability, that's surely a good thing, TCM home care, this trend is good."

TABLE 1 Assigns and variables.

Variables	Assigns
The number of chronic diseases	1 species =1, 2 species =2, 3 species =3, and more than 3 species =4
Whether the caregiver can meet the care needs	Fully satisfy = 1, Can basically satisfy = 2, Cannot satisfy = 3, and Cannot satisfy at all = 4
Knowledge of home care level	Do not understand = 1, Have a certain understanding = 2, and Have experienced the home care service = 3
Know about internet + Nursing home care: newspaper television, mobile computers, and others	Yes = 1, No = 0
There are concerns about nursing door-to-door service, such as low personal safety, high service cost, high risk of nursing operation, large nurse workload, and other	Yes = 1, No = 0
Whether you would like home care services	Willing = 1, uncertain = 2, and unwilling = 3

TABLE 2 Results of multiple linear regression analysis ($n = 308$).

	Regression coefficient	Standard error	Standard coefficient	*T* value	*p* value
(Constant)	−15.646	4.834		−3.237	0.001
Questionnaire on home care needs of patients with chronic diseases	0.254	0.013	0.686	20.085	<0.001
Questionnaire on general knowledge of Chinese medicine	0.262	0.047	0.176	5.558	<0.001
Attitude scale of traditional Chinese medicine	0.304	0.062	0.162	4.928	<0.001
Know about internet + Nursing home care: the mobile phone or computer	3.951	1.337	0.094	2.956	0.003
Know about internet + Nursing home care: the newspaper or television	3.493	1.366	0.079	2.557	0.011

$R = 0.845$, $R^2 = 0.714$, correction $R^2 = 0.709$, $F = 45.159$, $p < 0.001$.

3.2.1.2. Perceived usefulness

Interviewed patients generally agree that "Internet + Chinese medicine" home care has the characteristics of convenience and professional service, in addition, patients believe that Chinese medicine care technology has better advantages and effects on chronic diseases. In addition, "Internet + TCM" home care can provide patients with psychological care. N5: "I think it's good, actually it's very convenient for the patients, it's better for the people." N10: "It is inconvenient to queue up at the hospital. We should develop Chinese medicine home treatment, I think it's good." N19: "Our own massage is definitely not as good as a professional one."

3.2.2. Theme 2: obstacles factors

3.2.2.1. Cognitive limitations

The interviewed patients have only a superficial understanding of the "Internet + Chinese medicine" home care service model, and have no in-depth knowledge of it. N9: "I have only seen it in the media, on TV, on the bulletin boards, but I have not knew anything else about it, so my knowledge of it is quite shallow." N11: "If you look at people like us who can move on our own, we do not usually need home care. Those who generally need home care are those who lie in bed and are basically immobile." N22: "I've heard of it by chance, but I think it's quite far away from me, and I have not taken it into consideration. Whether it can be involved depends on the financial situation of the family."

3.2.2.2. Low level of digital literacy

Introducing the "Internet + TCM" home care model to patients before the interview. Older adult patients with chronic diseases have relatively less access to cell phones and the Internet, and their ability to use cell phones is limited, resulting in a lower level of digital literacy, which hinders the willingness of some patients to participate in the "Internet + Chinese medicine" home care service. N4: "I cannot go on the Internet, but I usually come to the hospital when it's time. It's hard for me to understand some of the online operations, no way." N5: "The hospital sometimes has some medical information on the public number, but I do not have to add these public numbers, I do not know how to do this."

3.2.2.3. Cost of services and geographical factors

The cost of diagnosis and treatment, geographical and transportation barriers, and the lack of institutions and equipment make it difficult and challenging to carry out "Internet + TCM" home care services at this stage. N8: "This is because the older adult people have to consider the issue of cost, and participation in health insurance must be considered." N21: "This and some of the country's policies are related to various aspects, for example, now like family wards or community hospitals, the government has to do that." The community does not have these facilities yet, this service model, first of all this institution has to be available. N12: "It would be better for urban or urban–rural areas. Because people live more sparsely, the population is not so full, and in addition people are more dispersed, and the medical conditions are limited in rural areas."

3.2.3. Theme 3: multiple needs of "Internet + TCM" home care

3.2.3.1. Demand for the provision of diversified care programs

"Internet + Chinese medicine" home care needs to provide Chinese medicine nursing appropriate technology, basic care, Chinese and

Western medicine combined care, health guidance, and other comprehensive and systematic care programs. N21: "For example, some simple physical therapy, infusion, these are all possible." N8: "The best is more complete, incorporating both conventional Western therapy and Chinese medicine." N12: "Look at the treatment of disease, it is comprehensive treatment, you cannot say that Western medicine is good and take away Chinese medicine, Chairman Mao has said that we should combine Chinese and Western medicine." N9: "I think if I can really do it, in fact, according to my current situation, my problem is not very serious, if I really encounter some problems, I can consult you."

3.2.3.2. Dialectical care and the need for quality care

Some patients expect "Internet + Chinese medicine" home care in the implementation of the process of nursing staff can be based on the actual situation of the patient's condition dialectical care, and enjoy quality care services. N14: "If traditional Chinese medicine home care can really care for the actual situation of the patient's condition, the effect must be obvious." N22: "Home care needs a good attitude and service, and the technology is slightly excellent. Because Chinese medicine itself is the treatment of chronic diseases and health care, the effect is slightly slower, if the technology is not good, you cannot see the effect."

3.2.3.3. The need to improve the health insurance and service system

The health insurance reimbursement system in the "Internet + nursing" field is still in the exploration stage, only some developed regions to carry out pilot projects, has not yet been fully promoted and implemented, the patient hopes that the health insurance will included the "Internet + Chinese medicine" home care field while constructing the formation of the "Internet + Chinese medicine" home care management network demand. N8: "I think it's still medical insurance, and it would be nice if it could participate, but I think it would be a bigger percentage." N17: "Because most of the older adult now have health insurance, home care and health insurance are linked, and home care can be reimbursed as part of the reimbursement." N15: "I suggest that this must not be copied, but must be based on the needs, according to the characteristics of the local community, that is, it is necessary to establish a targeted, distinctive model in line with the national conditions, local characteristics of the model." N16: "To form a management network, a service network, for ex ample, in this region you include all the outlets that can be involved, then the service is a little bit easier."

4. Discussion

4.1. Strengthening the demand for care and enhancing facilitating factors

The results of the quantitative study showed that 72.7% of the respondents were willing to receive home care services from nurses, and it was also understood through interviews that patients had a positive attitude towards it, similar to the results of previous studies (27, 28). This indicates that patients have a high demand for "Internet + TCM" home care. The reason for this may be related to the fact that "Internet + TCM" nursing can enable patients to enjoy high-quality medical services conveniently and optimize the allocation of medical resources.

Perceived usefulness refers to the extent to which users believe that the application system can improve their work efficiency, and the perceived usefulness of the application system (29), which can motivate patients to be more willing to participate in the home-based model. Some studies show that perceived usefulness has a positive impact on patients' attitudes toward participating in "Internet + Nursing," and the more patients pay attention to the actual effects of "Internet + Nursing," the stronger their willingness to use it (30, 31). In addition, due to the diseases of older adult patients with chronic diseases, the use of Internet + Nursing has a positive impact on their attitude toward the use of Internet + Nursing. In addition, due to the characteristics of the diseases of older adult chronic disease patients, if they do not have effective management, the disease will worsen and deteriorate (32). Therefore, the penetration and integration of Chinese medicine technology and home care ensures the continuity and timeliness of services, and the home can enjoy professional nursing services, which significantly improves the quality of life of such patients. Along with the progress of Internet technology, home care will gradually become the development trend of medical service industry (33, 34). The home care service model of TCM can effectively meet the nursing needs of older adult patients with chronic diseases, and further research should focus on the home care model to solve the needs of older adult patients (35).

Therefore, it is suggested that the medical staff should continuously improve the knowledge quality and cognitive level of patients. From the perspective of cultural literacy of Chinese medicine, help the patients to form a correct understanding of the concepts and ideas of Chinese medicine, which in turn promotes the promotion and application of traditional Chinese medicine technology and the development of the Chinese medicine healthcare industry.

4.2. Improve the service system and overcome obstacles factors

The results of the quantitative multifactorial analysis study indicate that the cognitive level of TCM knowledge of the older adult chronic disease population will affect the nursing needs of traditional Chinese medicine. From the scores of the knowing items, it can be understood that the older adult chronic disease has a low knowledge of TCM and stays at the level of the therapeutic tools (36). In the qualitative study, it was also shown that the interviewed patients had only a superficial understanding of the "Internet + Chinese medicine" home care service model, but did not have an in-depth understanding of it, and some of the patients said that they had not understood this model. The reason for this may be related to the short period of time since the introduction of the "Internet + Nursing" policy, and the fact that medical institutions in the region have not yet launched the corresponding service system, which is similar to the results of study of Thomas (37). The results of the quantitative multifactorial analysis of this study showed that cell phones and television in the "Internet + Nursing" service pathway affect the demand for Chinese medicine care for older adult patients with chronic diseases, which is consistent with the qualitative results.

Digital literacy refers to patients' access to and ability to use computers and the Internet (38). This indicates that patients have little access to the Internet and have limited ability to use mobile phones, computers, and other electronic devices, resulting in a low level of

digital literacy of patients, which hinders the willingness of some patients to participate in "Internet + traditional Chinese medicine" home care services. It may also be related to physiological decline, cognitive and learning decline and economic factors in older adult patients with chronic diseases, which is consistent with the findings of the study of Ha (39). In addition, the quantitative study showed that the highest concern of older adult patients with chronic diseases about "Internet + Nursing" home care service was the high cost of the service (46.8%), which was consistent with the results of the qualitative study. The interviewed patients indicated that they needed to consider the cost of the service, and that there was a demand for the inclusion of health insurance in this model. The reason may be that the willingness to use is related to the value and price of this model, and patients' willingness to use is affected by online diagnosis and treatment costs, medical insurance reimbursement, etc. Patients will consider the comparison of online and offline medical treatment costs, and the category and proportion of medical insurance reimbursement (40). The United States, Japan, and European countries and other countries have formed a more mature and distinctive home care service model (41, 42). While China's Internet + home care service is still in its infancy, there are limitations in the content and scope of services.

It is necessary to strengthen the publicity of "Internet + Chinese medicine" home care services, carry out diversified, multi-channel, online and offline publicity methods, improve patients' awareness of "Internet + Chinese medicine" home care, enhance social influence, and change patients' inherent medical habits. And the creation and improvement of the "Internet + traditional Chinese medicine" home care service model has a practical role. It is suggested that medical institutions should, according to the national situation, start from the policy of home service, service cost, reimbursement system, and other aspects, in order to provide guarantee for the development of "Internet + Chinese medicine" home care service model suitable for older adult patients with chronic diseases.

4.3. Improve service quality and provide precise TCM care

The results of this study show that older adult patients with chronic diseases hope that "Internet + Chinese medicine" home care can enjoy targeted, high-quality, integrated Chinese and Western medicine nursing services. Nurses in the home care service need to have the ability to provide high-quality "Internet + Chinese medicine nursing service" (43). Research has confirmed that the dialectical and holistic concepts of TCM nursing techniques have the advantage of improving the health status of older adult patients with chronic diseases from a holistic perspective, promoting recovery and alleviating pain, and facilitating dialectical nursing care from a wide range of diseases (44). At the same time, quality care emphasizes people-oriented, providing patients with a full range of nursing services, in line with the holistic concept of Chinese medicine nursing and people-oriented ideology, the integration of appropriate technology of Chinese medicine nursing into quality nursing services can not only improve the quality of nursing services, but also accelerate the promotion of the culture of traditional Chinese medicine (45). In addition, studies have shown that Chinese and Western medicine culture can be promoted faster. Studies have shown that integrated Chinese and Western medicine care can provide patients with multifaceted care, regulate their physical and psychological conditions, improve their health awareness and clinical symptoms (46, 47).

It can be seen that we should strengthen the training of nursing staff, invite Chinese medicine nursing experts to organize overall training, teachers and students, carry out special lectures, Chinese medicine nursing knowledge and technology competitions. Encourage nurses to invest in research of TCM nursing and actively learn the characteristic nursing techniques of TCM. Through training, the ability to communicate and the ability to deal with emergencies will be enhanced, the dialectical thinking of nursing staff is cultivated, and the knowledge and skills of TCM nursing staff are improved, so as to provide patients with accurate, high-quality and diversified TCM nursing services.

4.4. Potential shortcomings and limitations

4.4.1. Potential shortcomings

Both the medical association service model and home care services are in their infancy, and there are service team members with low professional quality, low motivation, and unclear division of labor. The service content is relatively single, not strong in specialty, unable to meet the needs of patients. Relevant supporting policies are not perfect, and there is a lack of unified and standardized service processes and standards.

4.4.2. Limitations

First of all, this study only selected patients from one hospital in Xi'an due to manpower and time constraints, and the results of the study may have some regional limitations. In future studies, researchers can select several different regions to increase the sample size of the study and further explore the current situation and influencing factors of the demand for TCM home care for older adult patients with chronic diseases.

Second, this study used purposive sampling method for qualitative research, and its findings can only represent the experience of some patients and cannot be inferred to the whole. Random stratified sampling in different regions makes the study more rigorous.

Finally, this study used a combination of quantitative and qualitative research methods, and the two research methods complemented each other, while the qualitative research obtained new relevant factors not reflected in the quantitative part of this study through the deeply excavated information. Further relevant factors need to be added in future investigations.

5. Conclusion

In summary, although "Internet + Chinese medicine" home care service is in the exploratory stage, older adult patients with chronic diseases have higher demand for it and stronger willingness to participate in it, and it has a broad development prospect, but there are still many concerns. Medical institutions should strengthen publicity and promotion efforts to increase the social influence and participation of "Internet + Chinese medicine" home care services. Also, strengthen the training of nursing staff, comprehensively improve their comprehensive quality, provide patients with high-quality and diversified care programs. The government should strengthen support, improve the medical insurance system, increase capital investment, and build a more scientific, feasible and reasonable

"Internet + traditional Chinese medicine" home care service model for older adult patients with chronic diseases. The survey respondents of this study are mainly gathered in a tertiary hospital, which may have a certain bias. The next step is to examine patients' needs for home care services from all angles and in all aspects in different regions, so that the results of the study can be more representative.

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

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

Author contributions

XW: Data curation, Formal analysis, Investigation, Validation, Writing – original draft, Writing – review & editing. JC: Data curation, Formal analysis, Writing – review & editing. MF: Writing – original draft. MZ: Software, Supervision, Writing – review & editing. JW: Data curation, Investigation, Writing – original draft. LZ: Formal analysis, Methodology, Writing – original draft. YL: Data curation, Investigation, Writing – original draft. HC: Methodology, Project administration, Resources, Supervision, Visualization, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. The study was carried out with financial support from the Shaanxi Provincial Key Scientific Research Program (2022SF-176).

Acknowledgments

Writing so far, thousands of thoughts. A teacher is easy to find, but a 'good' teacher is hard to find. First of all, I would like to express my sincere thanks to my graduate tutor, HC. From the topic selection, development to writing of the paper cannot be separated from your patient guidance. Your fine and rigorous work style, rigorous and realistic scientific research attitude, calm and sharp way of thinking have all influenced me and guided me to keep moving forward. Secondly, I would like to express my sincere thanks to the leaders and teachers of the school and hospital for their training and guidance, and for providing us with high-quality learning resources. I would like to thank my classmates for the excitement and excitement of discussing scientific research problems and finding new ideas and solving doubts together and the provincial fund for its financial support. Finally, I would like to express my sincere thanks to all the teachers of the magazine for taking time out of their busy schedules to review my articles. I wish you good health and success in your work!

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.2023.1271082/full#supplementary-material

References

1. Cheng XJ, Hu GQ. Progress in research of burden of disease attributed to population ageing. *Zhonghua Liu Xing Bing Xue Za Zhi*. (2020) 41:1915–20. doi: 10.3760/cma.j.cn112338-20191220-00905

2. Volkert J, Schulz H, Härter M, Wlodarczyk O, Andreas S. The prevalence of mental disorders in older people in Western countries—a meta-analysis. *Ageing Res Rev*. (2013) 12:339–53. doi: 10.1016/j.arr.2012.09.004

3. Chen Z, Yu J, Song Y, Chui D. Aging Beijing: challenges and strategies of health care for the elderly. *Ageing Res Rev*. (2010) 9:S2–5. doi: 10.1016/j.arr.2010.07.001

4. Xia Z, Jiang YY, Dong WL, Mao F, Zhang S, Dong JQ. Chronic and non-communicable disease mortality and trends in Chinese elderly, 2004-2018. *Zhonghua Liu Xing Bing Xue Za Zhi*. (2021) 42:499–507. doi: 10.3760/cma.j.cn112338-20200208-00079

5. Cavatorti S, Pezzoli G, Righetti P, Chiappa C, Levati S, D'Angelo V, et al. What are the needs of caregivers caring for people living in chronic conditions? *Qualt Res Prof Inferm*. (2021) 74:81–8. doi: 10.7429/pi.2021.742081

6. Giampaoli S, Viscogliosi G, Vannuzzo D. We all want to live longer, but not grow old. *Monaldi Arch Chest Dis*. (2017) 87:843. doi: 10.4081/monaldi.2017.843

7. Murray J, Hardicre N, Birks Y, O'Hara J, Lawton R. How older people enact care involvement during transition from hospital to home: a systematic review and model. *Health Expect*. (2019) 22:883–93. doi: 10.1111/hex.12930

8. Sun J, Guo Y, Wang X, Zeng Q. mHealth for aging China: opportunities and challenges. *Aging Dis*. (2016) 7:53–67. doi: 10.14336/AD.2015.1011

9. Wang Z, Fan Y, Lv H, Deng S, Xie H, Zhang L, et al. The gap between self-rated health information literacy and internet health information-seeking ability for patients with chronic diseases in rural communities: cross-sectional study. *J Med Internet Res*. (2022) 24:e26308. doi: 10.2196/26308

10. Yuan Y, Xu H-W, Zhang S, Wang Y, Kitayama A, Takashi E, et al. The mediating effect of self-efficacy on the relationship between family functioning and quality of life among elders with chronic diseases. *Nurs Open*. (2021) 8:3566–74. doi: 10.1002/nop2.906

11. Deek H, Hamilton S, Brown N, Inglis SC, Digiacomo M, Newton PJ, et al. Family-centred approaches to healthcare interventions in chronic diseases in adults: a quantitative systematic review. *J Adv Nurs*. (2016) 72:968–79. doi: 10.1111/jan.12885

12. Morris JN, Berg K, Howard EP, Jonsson PV, Craig M. Functional recovery within a formal home care program. *J Am Med Dir Assoc*. (2019) 20:1001–6. doi: 10.1016/j.jamda.2018.12.014

13. Squires A, Miner S, Liang E, Lor M, Stimpfel AW. How language barriers influence provider workload for home health care professionals: a secondary analysis of interview data. *Int J Nurs Stud*. (2019) 99:103394. doi: 10.1016/j.ijnurstu.2019.103394

14. Bousquet J, Meissonnier M, Michalet V, Toupnot A, Paccard D, Noguès M, et al. A novel approach to integrated care using mobile technology within home services. The ADMR pilot study. *Maturitas*. (2019) 129:1–5. doi: 10.1016/j.maturitas.2019.07.023

15. Ferrell BR. Family caregiving and Cancer pain management. *Anesth Analg*. (2019) 129:1408–13. doi: 10.1213/ANE.0000000000003937

16. Yu S-J. Role of visiting nursing Care in Japanese Home Healthcare. *Hu Li Za Zhi*. (2018) 65:11–6. doi: 10.6224/JN.201802_65(1).03

17. Marcinowicz L, Chlabicz S. Functioning of family nursing in transition: an example of a small town in Poland. Are there any benefits for patients? *Health Expect*. (2004) 7:203–8. doi: 10.1111/j.1369-7625.2004.00279.x

18. Pisano González MM, González Pisano AC, Abad BA. Community and family nurse: present keys, future challenges. *Enferm Clin*. (2019) 29:365–9. doi: 10.1016/j.enfcli.2019.10.005

19. Zimansky M, Franke I, Heller A-C, Remmers H. Evaluation of the implementation process of family nursing in oncology. *Pflege*. (2018) 31:331–7. doi: 10.1024/1012-5302/a000640

20. Lhotska L, Doležal J, Adolf J, Potůček J, Křížek M, Chbani B. Personalized monitoring and assistive systems: case study of efficient home solutions. *Stud Health Technol Inform*. (2018) 249:19–28. doi: 10.3233/978-1-61499-868-6-19

21. Fan X, Meng F, Wang D, Guo Q, Ji Z, Yang L, et al. Correction to: perceptions of traditional Chinese medicine for chronic disease care and prevention: a cross-sectional study of Chinese hospital-based health care professionals. *BMC Complement Altern Med*. (2019) 19:26. doi: 10.1186/s12906-019-2434-7

22. Du Y, Li P, Wu H, Feng T. Analysis of the cognition, demand and satisfaction of the elderly in elderly care institutions on Chinese medicine specialty services. *Chin J Gen Pract*. (2021) 20:568–74. doi: 10.3760/cma.j.cn114798-20201120-01177

23. Ren L. (2016). The study of the attitudes and needstowards tradional Chinese medcine among the elderly in Chongqi main urban area. Chongqing Medical University. CNKI.

24. Ren L, She J. Elderly's attitude and demands of traditional Chinese medicine in Chongqing Main urban areas. *Military Nurs*. (2015) 32:11–4. doi: 10.3969/j.issn.1008-9993.2015.17.003

25. Tian Y. (2015). A 3 armour hospital patients with chronic diseases hospital home care demand survey and influence factors analysis. Shanxi Medical University. CNKI.

26. Vignato J, Inman M, Patsais M, Conley V. Computer-assisted qualitative data analysis software, phenomenology, and Colaizzi's method. *West J Nurs Res*. (2022) 44:1117–23. doi: 10.1177/01939459211030335

27. Masumeh A, Mahnaz S. Interpreting the lived experiences of home caregivers in the families of patients with Covid-19 in Iran: a phenomenological study. *Int J Qual Health Care*. (2022) 34. doi: 10.1093/intqhc/mzab144

28. Thomas K, Dettwiller P, GonzalezChica D. Who cares about aboriginal aged care? Evidence of home care support needs and use in rural South Australia. *Aust J Rural Health*. (2023) 31:704–13. doi: 10.1111/ajr.12992

29. Marini SD, Hasman A, Huijer HA-S. Information technology for medication administration: assessing bedside readiness among nurses in Lebanon. *Int J Evid Based Healthcare*. (2009) 7:49–58. doi: 10.1111/j.1744-1609.2008.00119.x

30. Xie C, Jia S, He C. An empirical study on the factors affecting elderly Users' continuance intention of shared nurses. *Risk Manag Healthcare Policy*. (2020) 13:1849–60. doi: 10.2147/RMHP.S261827

31. Tennant R, Allana S, Mercer K, Burns CM. Caregiver expectations of interfacing with voice assistants to support complex home care: mixed methods study. *JMIR Hum Factors*. (2022) 9:e37688. doi: 10.2196/37688

32. Fabian F, Frederike B, Jürgen B, Maria BE, Bernhard H, Klaus K, et al. Local, collaborative, stepped and personalised care management for older people with chronic diseases (LoChro): study protocol of a randomised comparative effectiveness trial. *BMC Geriatr*. (2019) 19. doi: 10.1186/s12877-019-1088-0

33. Read Paul L, Salmon C, Sinnarajah A, Spice R. Web-based videoconferencing for rural palliative care consultation with elderly patients at home. *Support Care Cancer*. (2019) 27:3321–30. doi: 10.1007/s00520-018-4580-8

34. Greenup EP, McCusker M, Potts BA, Bryett A. The efficacy of telemedicine-supported discharge within an in home model of care. *Telemed J E Health*. (2017) 23:763–5. doi: 10.1089/tmj.2016.0216

35. Olsen CF, Bergland A, Debesay J, Bye A, Langaas AG. Striking a balance: health care providers' experiences with home-based, patient-centered care for older people-a meta-synthesis of qualitative studies. *Patient Educ Couns*. (2019) 102:1991–2000. doi: 10.1016/j.pec.2019.05.017

36. Michael E, Luise B, Sebastian L, Eric DT, Julian M, Fabian D, et al. Cross-sectional survey and Bayesian network model analysis of traditional Chinese medicine in Austria: investigating public awareness, usage determinants and perception of scientific support. *BMJ Open*. (2023) 13. doi: 10.1136/bmjopen-2021-060644

37. Thomas F. Home care in Germany during the COVID-19 pandemic: a neglected population? *J Nurs Scholarsh*. (2022) 55:215–25. doi: 10.1111/jnu.12851

38. Klecun E, Lichtner V, Cornford T. E-literacy in health care. *Stud Health Technol Inform*. (2014) 205:843–7. doi: 10.3233/978-1-61499-432-9-843

39. Ha J, Park HK. Factors affecting the acceptability of Technology in Health Care among Older Korean Adults with multiple chronic conditions: a cross-sectional study adopting the senior technology acceptance model. *Clin Interv Aging*. (2020) 15:1873–81. doi: 10.2147/CIA.S268606

40. Clare CPHJ, George H, Jeff P. Predictors of home care costs among persons with dementia, amyotrophic lateral sclerosis, and multiple sclerosis in Ontario. *Health Serv Insights*. (2020) 13. doi: 10.1177/1178632920903731

41. Liu X, Li X. Inspiration of American long-term care service system to China. *J Chang Univ*. (2017) 27:6–10.

42. Zhang J, Lei L. The composition, characteristics and issues of Japan's long-term care insurance system. *Jpn Stud*. (2017) 1:59–66. doi: 10.16496/j.cnki.rbyj.2017.01.007

43. Andrade AM, Silva KL, Seixas CT, Braga PP. Nursing practice in home care: an integrative literature review. *Rev Bras Enferm*. (2017) 70:210–9. doi: 10.1590/0034-7167-2016-0214

44. Cao Y, Li T, Xu Y, Zhang Y, Nian J, Li Q, et al. Observation on the clinical effect of thunder-fire moxibustion combined with acupressure on ocular muscle spasm: a clinical randomized controlled trial. *Medicine (Baltimore)*. (2020) 99:e21586. doi: 10.1097/MD.0000000000021586

45. Su H, Wen Y, Kang D. Application of refined nursing combined with comprehensive treatment of traditional Chinese and Western medicine in gastrointestinal dysfunction after tumor operation. *Evid Based Complement Alternat Med*. (2022) 2022:4957061–7. doi: 10.1155/2022/4957061

46. Zhang J, Ma T, Liu S, Zhao Y, Tang L. Nursing perspective of the expert consensus on diagnosis and treatment of integrated Chinese and Western medicine in lung cancer. *J Integr Nurs*. (2022) 4:1–7. doi: 10.4103/JIN.JIN_61_21

47. Chu L, Zhang Y. A study on nursing effect of integrated traditional Chinese and Western medicine management mode on COVID-19. *Jpn J Nurs Sci*. (2021) 18. doi: 10.1111/jjns.12411

frontiers | Frontiers in Endocrinology

TYPE Original Research
PUBLISHED 20 October 2023
DOI 10.3389/fendo.2023.1266207

OPEN ACCESS

EDITED BY
Yun Gao,
Sichuan University, China

REVIEWED BY
Vida Demarin,
International Institute for Brain Health, Croatia
Yalin Guan,
Tianjin Huanhu Hospital, China

*CORRESPONDENCE
Yongchun Chen
841874197@qq.com

RECEIVED 24 July 2023
ACCEPTED 06 October 2023
PUBLISHED 20 October 2023

CITATION
Yang T, Wang Y, Zhang X, Xiang S, Wen J, Wang W, Guan K, Wang W, Yang Y, Hao L and Chen Y (2023) Prevalence and influencing factors of abnormal carotid artery intima-media thickness in Henan Province in China.
Front. Endocrinol. 14:1266207.
doi: 10.3389/fendo.2023.1266207

Prevalence and influencing factors of abnormal carotid artery intima-media thickness in Henan Province in China

Tingting Yang[1], Yating Wang[2], Xiaoke Zhang[3], Siyun Xiang[1], Jing Wen[1], Wen Wang[1], Ke Guan[1], Weixiang Wang[1], Yang Yang[1], Liuwei Hao[4] and Yongchun Chen[1]*

[1]Department of Nutrition, Henan Provincial People's Hospital and Zhengzhou University People's Hospital, Zhengzhou, China, [2]Department of Ultrasound, Henan Provincial People's Hospital and Zhengzhou University People's Hospital, Zhengzhou, China, [3]Department of Reproductive Medicine, The Third Affiliated Hospital of Zhengzhou University, Zhengzhou, China, [4]Department of Health Management, Henan Provincial People's Hospital and Zhengzhou University People's Hospital, Zhengzhou, China

Background: Carotid intima-media thickness (CIMT) has been shown to be a valuable predictor of cardiovascular diseases (CVDs). The aim of this study was to investigate the influencing factors of CIMT among adults in Central China.

Methods: A total of 2,578 participants who underwent physical examination in Henan Provincial People's Hospital between January 2018 and July 2018 were enrolled. The respondents were divided into two subgroups according to their CIMT value (CIMT ≥1.0 mm group and CIMT <1.0 mm group). Variables considered were age, gender, total cholesterol, triglycerides, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) triglycerides, fasting blood glucose, and uric acid levels, as well as hypertension, diabetes, body mass index (BMI), waist-to-hip ratio, body fat percentage, and visceral fat area (VFA). Logistic regression analysis was performed to explore the potential factors influencing CIMT.

Results: The proportion of CIMT ≥1.0 mm among the physical examination population was 27.42% (707/2 578). The analysis of the two groups revealed significant differences in age, sex, hypertension, diabetes, total cholesterol, and HDL cholesterol. In the logistic regression analysis, age (*OR*=1.071, 95%*CI*=1.062–1.080), male sex (*OR*=2.012, 95%*CI*=1.251–2.238), hypertension (*OR*=1.337, 95%*CI*=1.031–1.735), diabetes (*OR*=1.535, 95%*CI*=1.045–2.255), HDL cholesterol (*OR*=0.540, 95%*CI*=0.366–0.796), and LDL cholesterol (*OR*=1.336, 95%*CI*=1.154–1.544) were significantly associated with abnormal CIMT.

Conclusion: Early screening should be carried out among men, the older adults, and those with hypertension, diabetes, and dyslipidemia.

KEYWORDS

cardiovascular risk, influencing factors, prevalence, China, CIMT

1 Introduction

Cardiovascular diseases (CVDs) have become a leading cause of morbidity, mortality, and disability in most countries globally (1). According to the data of the 2019 global disease burden report, from 1990 to 2019, the number of patients with CVDs increased from 271 million to 523 million, and the number of deaths increased from 12.1 million to 18.6 million (2). The prevalence of CVDs in China is on the rise. According to the data of China cardiovascular health and disease report 2020, the current number of patients with CVDs is estimated to be 330 million, and there is one patient with CVDs for every five people (3). Therefore, it is essential to reduce the risk of CVDs by exploring preventive methods.

Carotid intima-media thickness (CIMT), measured using noninvasive high-resolution ultrasound techniques, has been shown as a predictor of CVDs that is independent of the routine vascular risk factors (4). In a Japanese cohort study of 4,724 participants aged 59.7 ± 11.9 years, those with Max CIMT ≥1.7 mm had a 1.95-fold higher risk of CVDs than those with Max CIMT <1.7 mm (5). Willeit (6) carried out a meta-analysis on the relationship between CIMT and the risk of CVDs, and systematically reviewed the results of 119 randomized controlled trials, which showed that each 10 μm/year reduction of CIMT progression resulted in a relative risk of CVDs of 0.91. Previous studies have supported the use of CIMT as an alternative marker of CVDs risk, and intervention on the progress of CIMT could effectively reduce the risk of CVDs.

In China, most previous studies on CIMT have focused on its relationship with CVDs (7, 8), few studies have focused on the influencing factors of CIMT, and most of them have studied specific diseases (9). There is no research on the influencing factors of CIMT in Chinese adults who undergo physical examination. Therefore, the aim of this study was to investigate the prevalence of CIMT and explore the potential risk factors for increased CIMT in a physical examination population in central China.

2 Materials and methods

2.1 Study population

Participants who underwent medical examination in the physical examination center of a tertiary hospital in Henan Province, China, from January 2018 to July 2018 were retrospectively included. If The participants meet the following criteria were included: (1) age ≥18 years old; (2) availability of ultrasound examination of the internal carotid artery; and (3) availability of body fat composition examination results using bioimpedance analysis (BIA). The following participants were excluded: (1) those who had undergone internal carotid plaque surgery; (2) those with a history of administration of lipid-lowering drugs. All the information was obtained from health examination records and inquiries before health examination. Finally, 2,578 participants were included in the study. The study design was approved by the ethics committee of participating institutes. All methods were performed in accordance with the relevant guidelines and regulations by including a statement in the methods section to this effect. All participants had provided written informed consent and their personal information was kept confidential.

2.2 Measurements of CIMT

The CIMT was measured using high-resolution B-mode ultrasonography with a 7.5-MHz linear array scan (EPIQ7 ultrasound system, Philips Healthcare, Bothell, WA, USA) by professional radiologists. The bilateral carotid arteries of each participant were examined by longitudinal and transverse scanning with the participant in the supine position during the diastolic phase of the cardiac cycle. CIMT was defined as the distance between the leading edge of the lumen interface and the media-adventitial interface of the far wall. Measurements were obtained on each side at 1–2 cm proximal to the bifurcation of the posterior carotid wall. Each artery was measured three times, and the CIMT value represented the average value of six measurements. An increased CIMT was defined as a value of ≥1.0 mm (10). Thus, participants were divided into two groups: normal CIMT (CIMT<1.0 mm) and abnormal CIMT (CIMT ≥1.0 mm).

2.3 Clinical data and biochemical analysis

Venous blood was collected in the morning after 12-h overnight fasting. Measurements were performed using routine laboratory methods for serum parameters such as total cholesterol, triglyceride, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) triglyceride, fasting blood glucose, and uric acid. Diabetes was diagnosed if a participant had a fasting blood glucose level of ≥7.0 mmol/L, a 2-h postprandial blood glucose level of >11.1 mmol/L, or diabetes had been diagnosed before the investigation. Hypertension was diagnosed if systolic blood pressure (SBP) was ≥140 mmHg, if diastolic blood pressure (DBP) was ≥90 mmHg, or if the patient had self-reported hypertension.

2.4 Body composition measurement

Body composition was measured by BIA using the InBody 770 (InBody Co., Ltd., Seoul, Korea), which could estimate body mass index (BMI), waist-to-hip ratio, body fat percentage, and visceral fat area (VFA). Waist-to-hip ratio was classified as normal or over-standard with cut off levels for normal classification of 0.9 for males and 0.8 for females.

2.5 Statistical analysis

All statistical analyses were performed using IBM statistics (SPSS) V.22. The continuous variables are expressed as means ± standard deviation, and categorical variables are expressed as counts and percentages. Comparisons between the two groups were performed using the Student's t-test and the Chi-square test.

Multivariable logistic regression analysis was used to assess independent relationships for several explanatory variables determined abnormal on CIMT. The odds ratios (OR) and their 95% confidence intervals (95% *CI*) were used to present correlations. $P<0.05$ was considered statistically significant.

3 Results

Overall, 2,578 participants were included in this study, including 1,803 (69.94%) males and 775 (30.06%) females. The average age of the participants was 55.36 ± 14.17 years. A total of 404 participants (15.73%) were deemed obese (BMI >27.9 kg/m^2), and 1,866 (72.38%) participants were in the over-standard group on the basis of waist-to-hip ratio. The average body fat percentage and VFA of the participants was 28.26% ± 7.13% and 94.76 ± 34.01 cm^2, respectively. Among the participants, 144 (12.53%) had type 2 diabetes mellitus and 422 (16.37%) had hypertension. There were 707 (27.42%) participants with a CIMT greater than or equal to 1.0 mm. Table 1 shows the basic characteristics of the study population.

The proportion of CIMT ≥1.0 mm in males was 32.29%, which was significantly higher than that in females (15.87%), $P<0.001$. The incidence of diabetes and hypertension was higher in the CIMT ≥1.0 mm group than in the CIMT <1.0 mm group ($P<0.001$).

TABLE 1 Characteristics of the study population.

Characteristics		Number(%)/Mean(SD)
Gender	Male	1803(69.94)
	Female	775(30.06)
Age(years)		55.36(14.17)
BMI (kg/m^2)	<24.0	1033(40.23)
	24.0~27.9	1131(44.04)
	>27.9	404(15.73)
Waist-to-hip ratio	Normal	712(27.62)
	Over-standard	1866(72.38)
Type 2 diabetes	Yes	144(5.59)
	No	2434(94.41)
Hypertension	Yes	422(16.37)
	No	2156(83.63)
CIMT (mm)	<1.0	1871(72.58)
	≥1.0	707(27.42)
Total cholesterol (mg/dL)		4.86(0.94)
Triglycerides (mg/dL)		1.85(1.32)
HDL cholesterol (mg/dL)		1.29(0.29)
LDL cholesterol (mg/dL)		2.59(0.70)
Uric acid (μmol/L)		356.36(92.15)
Body fat percentage (%)		28.26(7.13)
VFA(cm^2)		94.76(33.24)

Participants tended to be older in the CIMT ≥1.0 mm group compared to the CIMT <1.0 mm group (63.89 ± 13.07 years vs. 50.89 ± 13.09 years, respectively, $P<0.001$). Total cholesterol and HDL cholesterol were also found to be significantly different in the CIMT ≥1.0 mm group than in the control subjects. There were no significant differences in BMI, waist-to-hip ratio, triglycerides, LDL cholesterol, uric acid, body fat percentage, and VFA between the two groups (Table 2).

In the multivariable logistical regression analysis, independent abnormal CIMT determinants for the entire group were age (*OR*=1.071, 95%*CI*=1.062–1.080, $P<0.001$), sex (*OR*=1.673, 95% *CI*= 1.251–2.238, $P=0.001$) (ref. female), hypertension (*OR*=1.337, 95%*CI*=1.031–1.735, $P=0.029$), diabetes (*OR*=1.535, 95%*CI*=1.045–2.255, $P=0.029$), HDL cholesterol (*OR*=0.540, 95%*CI*=0.366–0.796, $P=0.002$), and LDL cholesterol (*OR*=1.336, 95%*CI*=1.156–1.544, $P<0.001$). Multivariable regression analysis results are shown in Table 3.

4 Discussion

CVDs have become a worldwide public health problem and a serious threat to human health. Atherosclerosis is the leading cause of CVDs resulting in high rates of mortality and morbidity in the population. Atherosclerosis begins early in life, and it can be latent for a long time before the formation of atherosclerotic plaque (11). Thus, identification of individuals with subclinical atherosclerosis is necessary for early active prevention of CVDs. Previous studies have confirmed that CIMT can be recognized early and should be considered as an important marker of severe atherosclerosis in the future (5, 9). In this study, we found that the prevalence of abnormal CIMT in central China was 27.42%, which was closer to the prevalence reported by Peige et al. in 2018, i.e., 27.22% (12), but significantly higher than the prevalence reported by Yu et al. in 2019, i.e., 3.2% (13). The differences might be partly attributable to the participants' personal factors (age, sex) and investigation methods (sample selection method, sample size). Thus, it is of great significance to study the CIMT of physical examination population, which can identify the risk factors of CIMT in a time and effectively, and help to prevent the occurrence of CVDs in the early stage.

Logistic regression analysis showed that older age, male sex, hypertension, diabetes, and low HDL cholesterol and high LDL cholesterol levels were independent risk factors for abnormal CIMT. The risk of abnormal CIMT increased 1.071 times for each year of age, which was consistent with the results of Medhioub et al. (14). With increasing age, the metabolic function of the body decreases, the arterial intimal load increases, and the risk of arterial intimal thickening also increases. The risk of abnormal CIMT was 1.673 times higher in males than in females, which may be due to the differences in lifestyle and work stress between males and females. Hypertension and diabetes have been proved to be linked with abnormal CIMT (15–17). Additionally, dyslipidemia was an independent influencing factor for CIMT thickening. Sustained abnormal lipid metabolism would lead to the lipid depositing under the intima, resulting in CIMT thickening, atherosclerosis, and decrease vascular wall compliance (18).

TABLE 2 Comparison of basic information of the two groups.

Characteristics		CIMT(mm)		t/χ^2	*P*
		<1.0	≥1.0		
Gender	Male	1219(67.61)	584(32.29)	74.314	<0.001
	Female	652(84.13)	123(15.87)		
Type 2 diabetes	Yes	1806(74.20)	628(25.80)	57.685	<0.001
	No	65(45.14)	79(54.86)		
Hypertension	Yes	1651(76.58)	505(23.42)	105.951	<0.001
	No	220(52.13)	202(47.87)		
BMI (kg/m^2)	<24.0	743(71.93)	290(28.07)	1.475	0.478
	24.0~27.9	817(72.24)	314(27.76)		
	>27.9	303(75.00)	101(25.00)		
Waist-to-hip ratio	Normal	509(71.49)	203(28.51)	0.584	0.445
	Over-standard	1362(72.99)	504(27.01)		
Age(years)		50.89±13.09	63.89±13.07	22.53	<0.001
Triglycerides (mg/dL)		1.87±1.41	1.79±1.06	1.605	0.109
Total cholesterol (mg/dL)		4.89±0.92	4.79±0.98	2.364	0.018
HDL cholesterol (mg/dL)		1.31±0.29	1.25±0.29	4.236	<0.001
LDL cholesterol (mg/dL)		2.59±0.68	2.58±0.74	0.319	0.750
Uric acid (μmol/L)		354.54±94.17	361.12±86.49	1.613	0.107
VFA(cm^2)		94.73±33.56	94.85±32.41	0.083	0.934
Body fat percentage (%)		28.26±7.34	28.26±6.53	0.003	0.998

Our study indicated that LDL was positively associated with CIMT, which was consistent with previous studies (19–21). However, these studies did not found a relationship between HDL and CIMT. Guo et al. (22) conducted a study on the influencing factors for CIMT in the population of diabetes, and found that LDL was positive related to CIMT, while HDL was negatively corrected with CIMT, which was consistent with the results of our study. Early intervention for high-risk individuals with abnormal CIMT is needed for reducing incidence of CVDs.

It was worth noting that our study did not find a correlation between obesity-related indicators and CIMT, which was inconsistent with previous studies. In 2014, a study on 3,381 healthy people over 40 years of age showed that waist-to-hip ratio and VFA were independently related to increased CIMT; however, no significant correlation was found between BMI and CIMT (23). In addition, a Brazilian survey of 8,449 participants aged between 35 and 74 years of age explored the relationship between CIMT and abdominal obesity, and showed that waist circumference, waist-to-hip ratio and abdominal fat area were significantly correlated with CIMT (24). Yu et al. (13) also analyzed the relationship between abdominal obesity and CIMT and found that there was a correlation between the VFA and increased CIMT. Therefore, more research that explores the relationship between abdominal obesity and CIMT in larger study populations is needed.

TABLE 3 Multiple logistical regression analysis results for variables characterizing the 2,578 subjects and abnormal CIMT.

variables	β	S.E.	Wald	*OR* (95%*CI*)	*P*
Age (years)	0.068	0.004	264.097	1.071(1.062-1.080)	<0.001
Gender (ref. female)	0.515	0.149	2.012	1.673(1.251-2.238)	0.001
Hypertension (ref. No)	0.291	0.133	4.790	1.337(1.031-1.735)	0.029
Type 2 diabetes (ref. No)	0.429	0.196	4.768	1.535(1.045-2.255)	0.029
HDL cholesterol (mg/dL)	-0.616	0.198	9.675	0.540(0.366-0.796)	0.002
LDL cholesterol (mg/dL)	0.290	0.074	15.391	1.336(1.156-1.544)	<0.001
Constant	-4.474	0.522	73.563	0.011	<0.001

Our study had several limitations. First, this study followed a cross-sectional study design, which restricted the predictive effect of the temporality and causality of the observed relationships. Second, the data were collected from participants who voluntarily underwent internal carotid artery ultrasound testing in the health examination center, thus, response bias was unavoidable. Third, other potential risk factors for abnormal CIMT (such as residence, eating habits, daily exercise, smoking, drinking, and other occupational health factors) were not investigated. In the future, community-based multicenter large-sample studies, covering populations from different regions and including more influencing factors, should be conducted to verify the results of this study.

5 Conclusion

In conclusion, the results of this study showed that the prevalence of abnormal CIMT was high in a physical examination population in central China. For the older adults people, men, and people with hypertension, diabetes, and dyslipidemia, it is of great importance to carry out early internal carotid artery ultrasound examination. It is also crucial to implement county-level prevention measures to reduce the incidence of CVDs.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Henan Provincial People's Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

TY: Conceptualization, Project administration, Validation, Writing – original draft. YW: Formal Analysis, Investigation, Writing – review & editing. XZ: Data curation, Writing – original draft. SX: Investigation, Writing – original draft. JW: Investigation, Writing – original draft. WW: Investigation, Writing – original draft. KG: Investigation, Writing – original draft. WXW: Investigation, Writing – original draft. YY: Investigation, Writing – original draft. LH: Investigation, Writing – original draft. YC: Project administration, Resources, Supervision, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This study was supported by the Henan Medical Education Research Project (Wjlx2022015). The funder had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Acknowledgments

All of the authors are grateful to the participants and the staff members involved in this research.

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

References

1. GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* (2018) 392:1736–88. doi: 10.1016/S0140-6736(18)32203-7

2. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990-2019: update from the GBD 2019 study. *J Am Coll Cardiol* (2020) 76:2982–3021. doi: 10.1016/j.jacc.2020.11.010

3. Tsukinoki R, Murakami Y, Huxley R, Ohkubo T, Fang X, Suh I, et al. Does body mass index impact on the relationship between systolic blood pressure and cardiovascular disease?: meta-analysis of 419 488 individuals from the Asia pacific cohort studies collaboration. *Stroke* (2012) 43:1478–83. doi: 10.1161/STROKEAHA.112.650317

4. Zaidi NR, Gilani SA, Mehboob R, Waseem H, Hassan A. Diagnostic accuracy of carotid intima media thickness by B-mode ultrasonography in coronary artery disease patients. *Arch Med Sci Atheroscler Dis* (2020) 5:e79–84. doi: 10.5114/amsad.2020.95651

5. Kokubo Y, Watanabe M, Higashiyama A, Nakao YM, Nakamura F, Miyamoto Y. Impact of intima-media thickness progression in the common carotid arteries on the risk of incident cardiovascular disease in the suita study. *J Am Heart Assoc* (2018) 7:e007720. doi: 10.1161/JAHA.117.007720

6. Willeit P, Tschiderer L, Allara E, Reuber K, Seekircher L, Gao L, et al. Carotid intima-media thickness progression as surrogate marker for cardiovascular risk: meta-

analysis of 119 clinical trials involving 100 667 patients. *Circulation* (2020) 142:621–42. doi: 10.1161/CIRCULATIONAHA.120.046361

7. Fernández-Alvarez V, Linares Sánchez M, López Alvarez F, Suárez Nieto C, Mäkitie AA, Olsen KD, et al. Evaluation of intima-media thickness and arterial stiffness as early ultrasound biomarkers of carotid artery atherosclerosis. *Cardiol Ther* (2022) 11:231–47. doi: 10.1007/s40119-022-00261-x

8. Miao M, Zhou G, Bao A, Sun Y, Du H, Song L, et al. Triglyceride-glucose index and common carotid artery intima-media thickness in patients with ischemic stroke. *Cardiovasc Diabetol* (2022) 21:43. doi: 10.1186/s12933-022-01472-1

9. Kuang D, You H, Ding F, Xue J, Chen J, Ronco C, et al. Intima-media thickness of the carotid artery and its correlation factors in maintenance hemodialysis patients: a cross-sectional study. *Blood Purif* (2009) 28:181–6. doi: 10.1159/000227787

10. Watanabe I, Shintani Y, Terada S, Fujii T, Kiuchi S, Nakanishi R, et al. A clinical association between an increasing renal resistive index and the atherosclerotic burden in patients with a preserved renal function. *Intern Med* (2020) 59:909–16. doi: 10.2169/internalmedicine.3232-19

11. Song P, Fang Z, Wang H, Cai Y, Rahimi K, Zhu Y, et al. Global and regional prevalence, burden, and risk factors for carotid atherosclerosis: a systematic review, meta-analysis, and modelling study. *Lancet Glob Health* (2020) 8:e721–9. doi: 10.1016/S2214-109X(20)30117-0

12. Song P, Xia W, Zhu Y, Wang M, Chang X, Jin S, et al. Prevalence of carotid atherosclerosis and carotid plaque in Chinese adults: A systematic review and meta-regression analysis. *Atherosclerosis* (2018) 276:67–73. doi: 10.1016/j.atherosclerosis.2018.07.020

13. Yu Y, Zhang FL, Yan XL, Zhang P, Guo ZN, Yang Y. Visceral adiposity index and cervical arterial atherosclerosis in northeast China: a population based cross-sectional survey. *Eur J Neurol* (2021) 28:161–71. doi: 10.1111/ene.14513

14. Medhioub M, Bouzaidi K, Bachali A, Khsiba A, Hamzaoui L, Azouz MM. The risk of subclinical carotid atherosclerosis in patients with chronic hepatitis C. *Tunis Med* (2021) 99:449–55.

15. Zhang L, Fan F, Qi L, Jia J, Yang Y, Li J, et al. The association between carotid intima-media thickness and new-onset hypertension in a Chinese community-based population. *BMC Cardiovasc Disord* (2019) 19:269. doi: 10.1186/s12872-019-1266-1

16. Tebar WR, Santos IS, Meneghini V, Bittencourt MS, Lotufo PA, Bensenor IM. Eight-year change in carotid intima-media thickness and associated risk factors in adults with and without psoriasis - the ELSA-Brasil cohort study. *Braz J Med Biol Res* (2023) 56:e12609. doi: 10.1590/1414-431X2023e12609

17. Santos EHS, Santos Neto PJD, Santos IS. Carotid intima-media thickness in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil): a narrative review. *Sao Paulo Med J* (2018) 136:64–72. doi: 10.1590/1516-3180.2017.0272141017

18. Bouillet B, Gautier T, Terriat B, Lagrost L, Verges B, Petit JM. CETP activity is not associated with carotid intima-media thickness in patients with poorly controlled type two diabetes. *Acta Diabetol* (2019) 56:749–54. doi: 10.1007/s00592-019-01340-7

19. Jia X, Qi Y, Zheng R, Lin L, Hu C, Zhu Y, et al. Non-HDL-cholesterol, and LDL-cholesterol predicts risk of increased arterial stiffness and elevated carotid intima-media thickness in middle-aged and elderly chinese adults. *Front Cardiovasc Med* (2022) 9:906396. doi: 10.3389/fcvm.2022.906396

20. Staudt A, Stock K, Gande N, Bernar B, Hochmayr C, Pechlaner R, et al. Early Vascular Ageing (EVA) Study Group. Impact of lifestyle and cardiovascular risk factors on early atherosclerosis in a large cohort of healthy adolescents: The Early Vascular Ageing (EVA)-Tyrol Study. *Atherosclerosis* (2020) 305:26–33. doi: 10.1016/j.atherosclerosis.2020.05.011

21. Dawson JD, Sonka M, Blecha MB, Lin W, Davis PH. Risk factors associated with aortic and carotid intima-media thickness in adolescents and young adults: the Muscatine Offspring Study. *J Am Coll Cardiol* (2009) 53(24):2273–9. doi: 10.1016/j.jacc.2009.03.026

22. Guo HJ, Li CC, Bian XY, Hao Q. Correlation study on the relationship between dyslipidemia and carotid intima-media thickness in patients with diabetes mellitus. *Pak J Med Sci* (2023) 39:875–9. doi: 10.12669/pjms.39.3.6866

23. Ren C, Zhang J, Xu Y, Xu B, Sun W, Sun J, et al. Association between carotid intima-media thickness and index of central fat distribution in middle-aged and older adults Chinese. *Cardiovasc Diabetol* (2014) 13:139. doi: 10.1186/s12933-014-0139-2

24. Eickemberg M, Amorim LDAF, Almeida MDCC, Aquino EML, Fonseca MJMD, Santos IS, et al. Indicators of abdominal adiposity and carotid intima-media thickness: results from the longitudinal study of adult health (ELSA-Brazil). *Arq Bras Cardiol* (2019) 112:220–7. doi: 10.5935/abc.20180273

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 22 May 2024
DOI 10.3389/fpubh.2024.1375227

OPEN ACCESS

EDITED BY
Yun Gao,
Sichuan University, China

REVIEWED BY
Joao Soares Martins,
National University of East Timor, Timor-Leste
Daniel Edem Kpewou,
University for Development Studies, Ghana

*CORRESPONDENCE
Panniyammakal Jeemon
✉ jeemon@sctimst.ac.in

RECEIVED 23 January 2024
ACCEPTED 06 May 2024
PUBLISHED 22 May 2024

CITATION
Ravindranath R, Sarma PS, Sivasankaran S, Thankappan KR and Jeemon P (2024) Voices of care: unveiling patient journeys in primary care for hypertension and diabetes management in Kerala, India.
Front. Public Health 12:1375227.
doi: 10.3389/fpubh.2024.1375227

Voices of care: unveiling patient journeys in primary care for hypertension and diabetes management in Kerala, India

Ranjana Ravindranath[1], P. Sankara Sarma[1], Sivasubramonian Sivasankaran[2], Kavumpurathu Raman Thankappan[3] and Panniyammakal Jeemon[1]*

[1]Achutha Menon Centre for Health Science Studies, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India, [2]Manipal Academy of Higher Education, Manipal, Karnataka, India, [3]Amrita Institute of Medical Sciences, Kochi, Kerala, India

Background: Diabetes and hypertension are leading public health problems, particularly affecting low- and middle-income countries, with considerable variations in the care continuum between different age, socio-economic, and rural and urban groups. In this qualitative study, examining the factors affecting access to healthcare in Kerala, we aim to explore the healthcare-seeking pathways of people living with diabetes and hypertension.

Methods: We conducted 20 semi-structured interviews and one focus group discussion (FGD) on a purposive sample of people living with diabetes and hypertension. Participants were recruited at four primary care facilities in Malappuram district of Kerala. Interviews were transcribed and analyzed deductively and inductively using thematic analysis underpinned by Levesque et al.'s framework.

Results: The patient journey in managing diabetes and hypertension is complex, involving multiple entry and exit points within the healthcare system. Patients did not perceive Primary Health Centres (PHCs) as their initial points of access to healthcare, despite recognizing their value for specific services. Numerous social, cultural, economic, and health system determinants underpinned access to healthcare. These included limited patient knowledge of their condition, self-medication practices, lack of trust/support, high out-of-pocket expenditure, unavailability of medicines, physical distance to health facilities, and attitude of healthcare providers.

Conclusion: The study underscores the need to improve access to timely diagnosis, treatment, and ongoing care for diabetes and hypertension at the lower level of the healthcare system. Currently, primary healthcare services do not align with the "felt needs" of the community. Practical recommendations to address the social, cultural, economic, and health system determinants include enabling and empowering people with diabetes and hypertension and their families to engage in self-management, improving existing health information systems, ensuring the availability of diagnostics and first-line drug therapy for diabetes and hypertension, and encouraging the use of single-pill combination (SPC) medications to reduce pill burden. Ensuring equitable access to drugs may improve hypertension and diabetes control in most disadvantaged groups. Furthermore, a more comprehensive approach to healthcare policy that

recognizes the interconnectedness of non-communicable diseases (NCDs) and their social determinants is essential.

KEYWORDS

access, primary health, health needs, community, NCD, qualitative research, health care pathway

1 Introduction

Noncommunicable diseases (NCDs), also known as chronic diseases, are a major global health challenge responsible for more than two-thirds (73%) of all-cause mortality (1). Furthermore, the majority of NCD deaths occur in low- and middle-income countries (LMICs) (2). Importantly, many NCD-related deaths are premature and preventable (2, 3). Even after a decade since the launch of the National Programme for Prevention & Control of Non-Communicable Diseases (NP-NCD) by the government of India, the prevalence, awareness, treatment, and control rates of diabetes and hypertension remain abysmally poor in primary care settings with notable variations across districts, age, and socio-economic groups (4–6).

Globally, primary health care is recognized as the cornerstone of developing a resilient health system approach to preventing and controlling NCDs (7, 8). Previous evidence suggests that an effective primary health care system contributes to NCD control by encouraging a healthy lifestyle, preventing the onset of NCDs, decreasing premature NCD-related deaths, improving the quality of care, and reducing hospital admissions related to NCDs (9–11). Additionally, Primary Health Centers (PHC) fosters community involvement in NCD prevention and control, ensuring equitable NCD care access (12). However, in India, health systems were initially designed to address acute communicable diseases and maternal and child health (13) but now grapple with the challenge of delivering care for chronic conditions (14, 15). The primary care system for NCDs remains weak with underfunding, fragmented service delivery, and poorly functioning referral systems and faces significant resource constraints, including limited health workforce, medicine, supplies, and infrastructure (16–19). Further, this situation is worsened by disparities of socio-economic class, caste, and gender, which manifest as health inequalities (20). Recently, the Government of India launched the National Health Protection Mission known as the *Ayushman Bharat* to bring a comprehensive range of services closer to communities by transforming PHCs and sub-centers into Health and wellness centers (HWCs) and achieve universal health coverage in India (21–24).

In parallel, the Government of Kerala initiated the "*Aardram Mission*" in 2017 to revitalize the PHCs, recognizing the importance of strengthening universal primary care (25). This transformation involved upgrading PHCs to Family Health Centers (FHCs), which aligned with the national model of HWCs, with additional healthcare providers, and a comprehensive package of primary care services (25). Furthermore, the services at PHCs were strategically restructured to address the current epidemiological situation, with a particular focus on NCDs (26, 27). The increasing prevalence of diabetes and hypertension is considered a primary driver of this epidemiological transition.

Despite the discourse in policies regarding the importance of comprehensive care for managing diabetes and hypertension, research on patient experience remains under-investigated. Evidence highlights the central role of patient experience in healthcare quality (28). Therefore, mapping the entire patient journey and understanding various factors that influence how people with diabetes and hypertension access the healthcare system when needed is the key to understanding the patient experience and identifying any existing gaps. Against this background, our study aimed to explore the experiences of persons living with diabetes and hypertension (PLWDH) regarding their access to primary health care services to manage these conditions and to examine if the community expectations from FHCs resonate with the above-proposed policy direction.

2 Methods

2.1 Study design

This study is an exploratory (29) descriptive (30) qualitative research involving data collection through semi-structured interviews and focus-group discussions conducted among persons with diabetes, hypertension, or both in outpatient settings in Malappuram, Kerala.

2.2 Study setting

We conducted this study in purposively selected four FHCs of Malappuram, Kerala, from September 2022 to March 2023. Notably, all these health centers underwent a transformation in the initial phase of the *Aardram* mission in 2017. Malappuram, a northern district in Kerala, has a population of 4,112,920 (31). Malappuram was among the first districts in Kerala where the National Program for NCDs was implemented, and the community-based palliative care model for NCD was piloted in 1996 (32). A recent study in the district reported an NCD-multimorbidity prevalence of 39.8% among people seeking care from FHCs. Notably, the prevalence was higher in men (42.6%) than in women (38.1%). Hypertension and diabetes were the predominant coexisting chronic conditions (33). Malappuram is divided into 15 health blocks, with 59 fully functional FHCs implementing the national program for preventing and controlling non-communicable diseases (NP-NCD) across these blocks (33).

FHCs provide a range of services--- including health promotion activities, screening, laboratory services, and outpatient management for patients with diabetes and hypertension under the NCD program. The state has recently initiated the population-based screening of

NCDs and risk factors (26), facilitated by Accredited Social Health Activists (ASHAs) and (JPHN), and suspected cases are referred to medical officers at FHCs. Patients requiring specialized care are referred to NCD clinics in community health centers or district hospitals. Additionally, the program offers free medicines for diabetes and hypertension at these facilities, with patients receiving their prescribed medications every month following consultation at the FHCs. Electronic health records and information systems at the patient level are being introduced in these centers (34).

2.3 Study participants, sampling strategy

The study population included adult individuals living with confirmed diabetes/hypertension or both, regardless of the disease stage or control status, in four FHCs in the Malappuram district. Purposive sampling (35) was used to identify eligible participants, following inclusion criteria: adults (18 years of age and older) seeking healthcare from public facilities or both public and private healthcare facilities for a minimum of six months. The assistance of local community health workers facilitated the identification of participants.

2.4 Data collection

In the first phase, semi-structured interviews were conducted face-to-face (36) with twenty adult participants. RR conducted all interviews in Malayalam using topic guides (Supplementary material S1). Pre-testing of the topic guides was undertaken before data collection. Each selected respondent was interviewed in a calm setting within health facility premises. All interviews were audio-recorded, and their duration ranged from 20 to 60 minutes.

We conducted one focus group discussion (FGD) (37) with six adults in the study area during the second phase. A heterogeneous group was selected for the FGD with different control statuses – achieved, not achieved, and taking insulin/oral hypoglycaemics or both, diagnosed but did not initiate the treatment. An experienced social worker and a junior public health nurse identified and recruited eligible participants for FGD. A topic guide was used to introduce different themes during the discussion. Basic demographic details like age, gender, marital status, education, and occupation were collected from each participant. Topics encompassed patients' experiences of living with a chronic illness, health care utilization, and challenges in accessing health care. The FGD was audio-recorded and lasted for 60 minutes.

RR translated and transcribed all the interviews. Transcripts were checked multiple times to minimize mistakes made during transcription. Participant recruitment concluded following thematic saturation (meaning the researchers collectively determined that additional interviews were unlikely to yield new insights or information on the subject) (38). In total, 26 people participated in the study.

2.5 Data analysis

The analysis of interview transcripts and fieldwork notes employed a thematic analysis approach (39). A coding framework was developed after multiple readings of the transcripts and notes (40). This framework was systematically applied to the dataset with attention to recurring codes and their clustering around specific contexts. The coded data were organized to facilitate thematic interpretation. Ongoing discussions among all authors informed this analytical process, with consensus achieved through iterative reviews of codes and themes. Emphasis was placed on discerning similarities and differences across participants' data, aiming to construct an explanation of the findings. Notably, any deviant cases were scrutinized to enhance the trustworthiness and rigor of the qualitative analysis (41).

The thematic framework derived from this analytical process closely aligns with the conceptual framework proposed, which focuses on the patient's ability to access healthcare services (42). However, it is important to note that this framework was not applied as an *a priori* model for the research; instead, it was introduced in a subsequent stage to inform further analysis of patients' health-seeking pathways and to explore perceived barriers to care among these healthcare users. The Levesque framework encompasses different stages of healthcare-seeking pathways, providing a valuable lens for examining the narratives of the study participants.

The patient journey for NCDs can be structured into five stages: awareness, screening, diagnosis, treatment, and adherence (Figure 1) incorporating rehabilitation (43). The accessibility of services shapes the patient's journey. Levesque et al.'s access-to-care model served as our conceptual framework to examine the factors influencing access to care at both the health system and population levels. The model examined healthcare access across five dimensions: approachability, acceptability, availability and accommodation, affordability, and appropriateness. The above-mentioned access dimensions are influenced by the patient's ability to perceive, seek, reach, pay, and engage. Access results from the interplay between supply and demand dimensions within the continuum of care, spanning from individuals' recognition of health needs to healthcare outcomes (42).

3 Results

A total of 26 people living with diabetes/hypertension or both participated in the study. These participants varied in age, chronic conditions, control status, and background. The patients were aged between 43 and 67 years, with seven participants diagnosed only with diabetes, five with hypertension, and three with both diabetes and hypertension, while the remaining four participants suffered from other comorbidities associated with these conditions (Table 1). Most of them were unemployed ($n = 14$), and identified themselves as poor.

Our analysis demonstrated factors contributing to a complex health-seeking pathway for individuals with diabetes and hypertension. These factors align with the five domains outlined in the Levesque framework (42). The five identified themes correspond to the key access dimensions and associated abilities from the patient's viewpoint, as depicted in Figure 2. The themes and the illustrative quotes are presented in Table 2. Additional quotes can be found in Supplementary Table S2.

3.1 Approachability and ability to perceive

Approachability refers to the "ability of individuals with healthcare needs to identify, to seek information on the existing

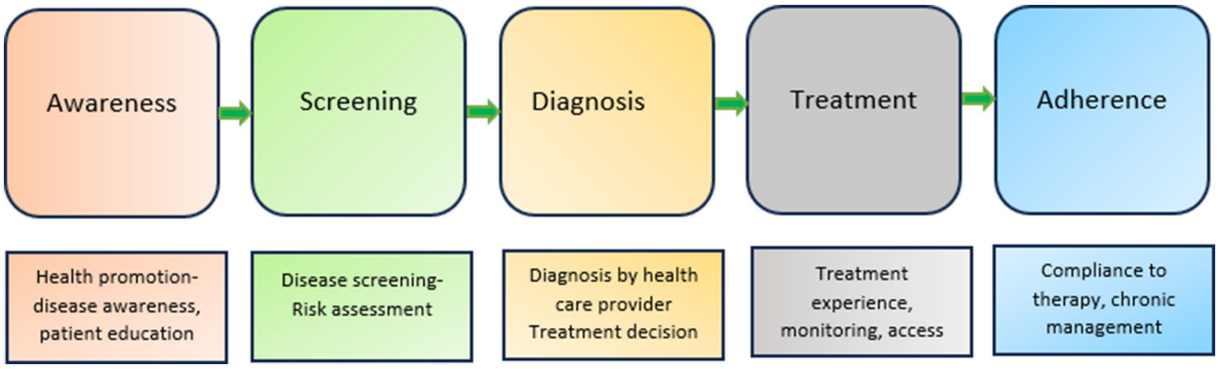


FIGURE 1
Patient journey for NCDs [Reprinted from Devi et al. (43)].

forms of services and perceive their potential impact on their health" (42). Some participants said they were provided sufficient information on the services available in health facilities through community health staff like ASHAs and JPHNs. Few participants recalled outreach screening activities for diabetes and hypertension conducted in public spaces like Anganwadi's in their area. However, many patients also reported several other sources of information available to them besides those provided by community health workers and doctors. For instance, patients gained prior knowledge through personal experience from family members, friends, and media. Patients reported these sources provided information on lifestyle changes, medication adherence, etc.

Participants' ability to perceive the need for care was determined by factors such as patients' knowledge about health conditions (perception of risk), age, education, and beliefs related to health and illness. Ensuring timely access to healthcare services and optimal adherence to long-term treatments relied on patients' understanding of their chronic condition when symptoms arise. Most of the patients reported being aware of hypertension and diabetes before diagnosis. However, participants reported sub-optimal knowledge of preventive measures and treatment needs. Older women interviewed in the study were unaware that hypertension is usually asymptomatic, and there was limited knowledge of potential outcomes. When asked what causes hypertension, one patient interviewed reported that stress causes hypertension. Some of the participants failed to understand their symptoms were indicative of diabetes and hypertension and that addressing their condition might entail more than just making lifestyle changes; instead, it may require long-term treatment as well. Some participants also believed that chronic diseases like diabetes and hypertension only impact older adults.

Instances were reported when patients did not receive sufficient information and support from the healthcare field staff to develop an adequate understanding of their condition, even after being suspected of diabetes or hypertension, in screening camps. Inadequate knowledge about their conditions led these participants to wait until their conditions were no longer manageable, leading to delays in seeking care.

In general, when assessing the patients' views in our study on diabetes and hypertension, the younger individuals minimized its importance. In contrast, mostly the older group of patients acknowledged the severity of the condition and sought treatment.

3.2 Acceptability and ability to seek

This theme addresses "the social and cultural factors that affect patient's ability to receive and accept healthcare services" (42). Our conversations showed that study participants desired FHCs to function as health facilities catering to minor health concerns. There was a general acknowledgment among people that FHCs were not equipped to handle complex medical conditions. As a result, people did not anticipate that FHC staff would address all health issues. Moreover, patients did not expect to get integrated care for managing multiple chronic conditions from FHCs.

Despite the nature of the visit being routine follow-ups, some patients preferred specialist services if their budget allowed. However, the availability of free medications and services and proximity to the residence enticed them to seek care from the FHCs.

We found that private care with specialists was predominantly reserved for managing immediate medical issues or complications arising from their conditions. The participants also commonly believed that higher-level hospitals would offer superior healthcare due to enhanced diagnostic capabilities and skilled medical professionals. Most of the patients had consulted multiple providers since their initial diagnosis.

The participants' social background and trust in the healthcare system affected their ability to access healthcare services. The degree of trust was influenced by their personal (or social network's) prior encounters with services, the reputation of selected health facilities, and the belief that higher-level health facilities offered better service quality. Prescribers' attitudes influenced trust in treatment. People had preconceived notions about the doctors and other staff. People often complained that doctors in FHCs failed to give them sufficient attention and respect. The perception of the government doctors' indifferent attitude stemmed from the belief that they were not incentivized or paid extra at government facilities. Patients also believed that in private practice, doctors spent time and prescribed medications that were more effective in improving blood sugar levels and controlling blood pressure, enhancing the perception of better healthcare outcomes under private care. Thus, in addition to expertise in clinical skills, patients valued the doctor's communication style. On the other hand, we observed a decline in trust in a physician due to an unfavorable experience, leading a participant to abstain from using health services provided by that doctor.

10.3389/fpubh.2024.1375227

TABLE 1 Characteristics of study participants.

Participant ID	Age (in years)	Gender	Marital status	Level of Education	Occupation	Chronic NCD (self-reported diagnosis)
1	67	Female	Married	Lower Primary	Housewife	Diabetes hypertension
2	55	Male	Married	High school	Skilled worker	Hypertension
3	48	Male	Married	Completed high school	Technical worker	Diabetes, hypertension
4	52	Female	Married	Completed high school	Housewife	Diabetes
5	57	Female	Married	High school	Skilled worker	Diabetes
6	64	Female	Married	Lower Primary	Housewife	Diabetes
7	59	Female	Married	Secondary	Housewife	Diabetes, Hypertension, and Cardiovascular diseases (CVD)
8	45	Female	Married	Completed Secondary	Skilled worker	Diabetes
9	51	Female	Married	High school	Skilled laborer	Hypertension, asthma
10	63	Male	Married	Upper Primary	Manual laborer	Hypertension
11	44	Female	Widowed	Degree	Skilled worker	Hypertension
12	53	Female	Married	Completed high school	Skilled worker	Diabetes, hypertension
13	59	Female	Married	Completed secondary	Housewife	Hypertension
14	45	Female	Married	Completed Secondary	Technical worker	Diabetes
15	62	Male	Married	Lower Primary	Manual laborer	Diabetes, hypertension
16	56	Female	Married	Lower Primary	Unable to work	Diabetes, Hypertension, and CVD
17	66	Female	Married	Lower Primary	Housewife	Hypertension
18	56	Female	Married	Upper Primary	Housewife	Diabetes
19	48	Female	Unmarried	Secondary	Manual laborer	Diabetes
20	55	Male	Married	Lower Primary	Manual laborer	Diabetes
21	60	Female	Married	Upper Primary	Housewife	Diabetes and early-stage renal disease
22	66	Female	Married	Lower Primary	Unable to work	Diabetes
23	57	Female	Married	Complete Secondary	Housewife	Hypertension
24	43	Male	Married	Degree	Skilled worker	Diabetes and hypertension
25	51	Female	Widowed	Secondary	Housewife	Diabetes
26	48	Female	Married	Completed Secondary	Housewife	Hypertension

Many participants were accustomed to pursuing alternative therapies, such as traditional medicines, rooted in their cultural practices. Our interviews with some patients revealed that they discontinued the prescribed allopathic medications and adopted traditional medicines without any formal advice after achieving the control status. Some patients considered medicines as chemicals with potential side effects and resorted to alternate systems of medicines. While others developed a fear of becoming dependent on medications lifelong, leading them to explore alternative treatments to reduce reliance on medicines provided by the facility. Previous lack of improvement with allopathic treatment and success stories from people who have experienced positive results with alternate treatment prompted a few to consider these options.

3.3 Availability and ability to reach

This theme concerns "the extent to which people can avail healthcare services" (42). Few participants highlighted that the remote geographic location of the health center hindered their access to healthcare services. Private transportation to healthcare facilities was expensive and challenging for older patients, restricted by the distance they could travel.

The capability of the older participants to reach the facility was influenced by the presence of a family member or neighbor who could accompany them to the healthcare facilities.

Most respondents emphasized that in the past few years (due to the restructuring of primary care services under the *Aardram* mission), they have experienced improved healthcare services through

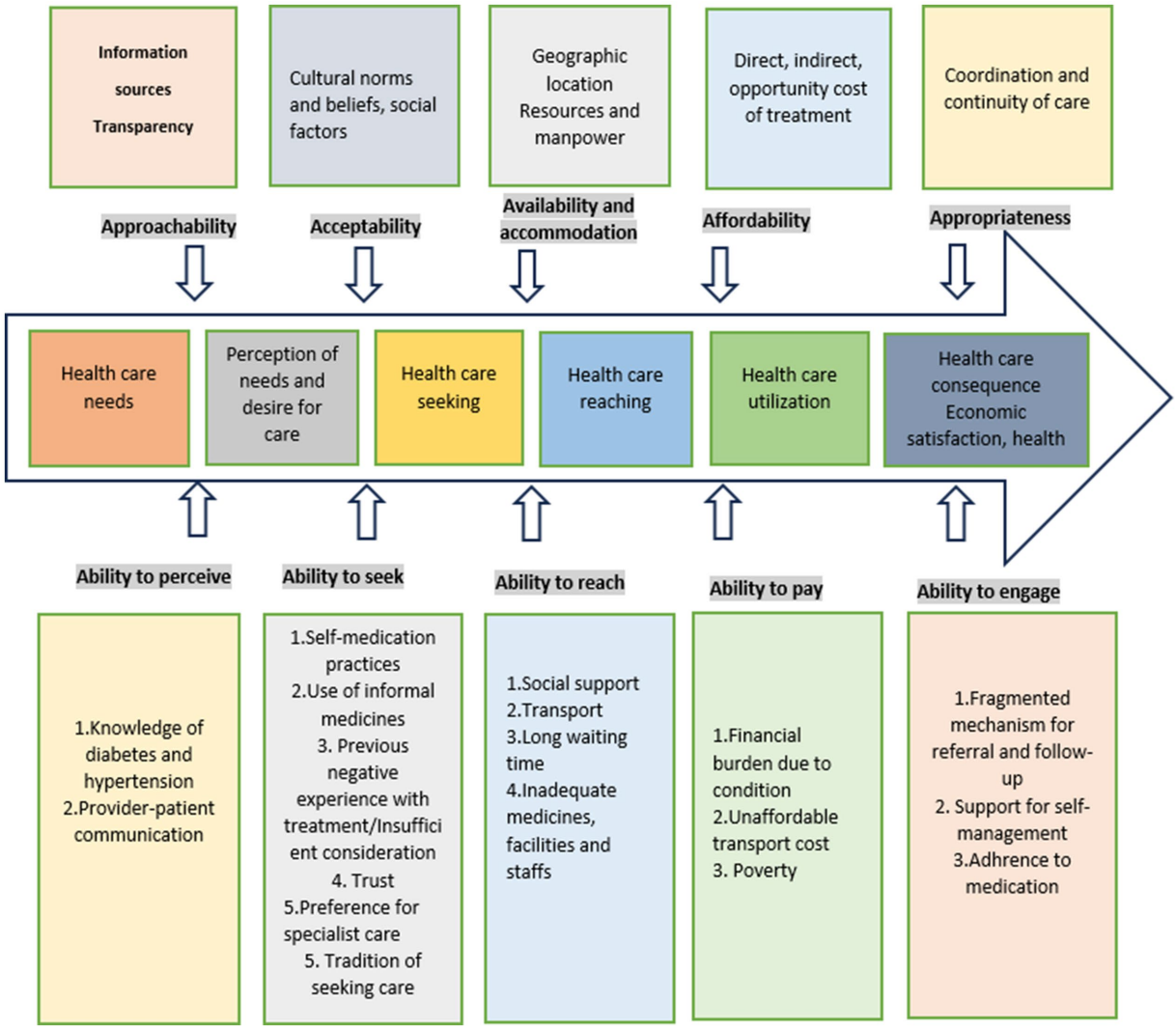


FIGURE 2
Conceptualization of access to care through patient perspectives from Kerala, India.

upgrades in infrastructure, greater availability of doctors and laboratory facilities, and the introduction of evening out patients' departments (OPDs). While expanded provision of the services was positively viewed to enhance accessibility, respondents noted the major deficiencies in service adequacy. A prevailing concern among most patients was the irregular availability of free medicines, leading to challenges in adhering to their prescribed treatment. Several patients reported that the shortage of drugs compelled them to personally bear the cost of purchasing them from local pharmacies. Furthermore, few patients expressed dissatisfaction with the facility's restricted range of treatment options, often limited to just two or three medications for addressing their medical conditions.

Patients who had multiple NCDs described intensified symptoms associated with a lack of access to medicines. One patient talked about the challenges she faced in accessing a reliable supply of insulin.

In some cases, health services were available to patients, but this did not translate to services being accessible to patients. For instance, in health centers, laboratories and pharmacies were available at the same location. Still, these services were often unavailable due to a lack of supplies, medicines, or human resources. Most participants said the public health facility was usually crowded, with substantial waiting times and an inconvenience in managing fasting tests due to the overcrowding and the timing of lab procedures. Consequently, many patients resorted to visiting private clinics or laboratories to monitor their glucose levels, incurring additional time and expenses. Almost all the patients voiced their dissatisfaction with being asked to return to FHC every month to obtain medicines, finding it inconvenient and burdensome.

3.4 Affordability and ability to pay

This theme encompasses the economic capacity of people to afford healthcare expenses. Despite medications being free at public health facilities, the recurring scarcity of medicines and the need for frequent doctor visits were deemed financially challenging for many. This financial barrier had two aspects: the expense of regular medications and the cost of immediate prescriptions during symptom

TABLE 2 Themes and illustrative quotes.

Themes	Illustrative quotes
Approachability and ability to perceive	*"Any health issue we have, I always call the JPHN* sister; I have called her even at 10 PM, and she answers all my queries very politely. She always explains in detail, and I can understand her. When she comes to Anganwadi, she always informs us about all activities and services in the health center. I shifted my treatment to a primary health center from a private one because she asked me. She knows my situation. In primary health centers, medicines, and services are free of cost, but in private, we should wait hours for tokens and pay big money."* **(44-year-old woman with diabetes)** *"I waited a year and a half to start medication after being diagnosed because I did not experience any issues related to this condition. There were no headaches, tiredness, or shivering. Shouldn't we be concerned when these symptoms appear?."* **(59-year-old woman with hypertension)** *"Following Ramadan, I experienced weight loss, increased water intake, and frequent urination. Unaware of these as diabetes symptoms, I was pleased with my weight loss and attributed frequent urination to staying well-hydrated. Nevertheless, friends and relatives noticed the weight loss, questioning its cause, and a relative suggested a blood test. The private lab reported a fasting sugar level above 230, indicating a high likelihood of diabetes, and advised an immediate doctor's visit."* **(55-year-old woman with diabetes)** *"Occasionally, I checked my blood pressure and blood sugar during the monthly NCD screening camp in Anganwadi. Both readings were slightly elevated, around 10–20 points higher than normal. The JPHN sister recommended diet restrictions in one visit for a potential cure and never asked me to consult a doctor or start medication. I tried to follow a restricted diet for 1.5 years and assumed I was all right. However, I faced severe pneumonia six months ago, impacting my lungs. I was hospitalized for over ten days at a private hospital. Tests revealed a blood sugar level above 350, affecting my kidneys and eyes. Since then, I've consistently taken medications for blood pressure, diabetes, and kidney concerns. The doctor stressed the lifelong need for medication."* **(60-year-old woman with diabetes and early renal disease)**
Acceptability and ability to seek.	*"I believe a comprehensive full body checkup and review are necessary due to my use of insulin, aspirin, and various medications for conditions like high blood pressure, high cholesterol, and diabetes. This is especially important after my heart surgery three years ago. Unfortunately, the primary health center lacks the required specialists and facilities for this evaluation."* **(56-year-old woman with diabetes, hypertension, and CVD).** *"The hospital staff has designated treating people with diabetes or hypertension to Mondays and Wednesdays from the FHC. If we cannot make it on those days, the pharmacist reluctantly provides medicines, with grumbling. I once asked him why he was here if he could not accommodate other days. Our schedules do not always align with these days, as we have other commitments. When I raised this with a doctor, no action was taken. Respect for older adults should be a mutual value from childhood. I'm unhappy with staff behavior, but due to financial constraints, we have no choice but to return for medicines."* **(66-year-old woman with hypertension)** *"In public healthcare facilities, the doctors often rush through appointments, barely allowing patients a moment to sit. They promptly reach for our notebooks and jot down medicines without inquiring about our concerns. Even when we try to communicate, they aren't truly listening. There seems to be no need for them to refer to previous prescriptions nowadays. If we present our notebooks, they repeat the same medications. When consulted privately, the same doctor took the time to explain everything in detail to me."* **(44-year-old woman with hypertension)** *"I heard from fellow visitors of this facility that the medicines offered here are of low dose and quality. I sought care from Dr. X at XX Hospital, a private establishment. Over time, I have consistently consulted him for various health concerns due to my trust in his expertise and prescribed medications. Upon reviewing all my medical reports, Dr. X assured me everything was normal. He said I was fit and healthy for my age, offering a reassuring pat on my shoulder. This brought about a sense of relief in me."* **(66-year-old woman with diabetes)** *"I was taking allopathic medicines, and my sugar was in control, but then you see, people started telling me, that continuously taking allopathic medicines is dangerous, damaging my kidneys, so I was worried and thought of trying Ayurveda. I experimented with 'kanthari Mallika kashayam,' a herbal decoction, for a period. A traditional healer from Attapadi supplied the medicines monthly to my maternal home. In March, I consumed two bottles. After breakfast, the healer advised a daily intake of 200 milliliters in a glass of hot water. My relatives, including my uncle and brother, also used it and suggested it to me. Given our family's strong history of diabetes—most family members over 45 years old have it—I decided to try it for a few months. I reduced my intake of other medicines and insulin, only taking half a tablet. However, I did not experience any benefits; I felt worse. Consequently, I resumed my allopathic tablets."* **(56-year-old woman with diabetes, hypertension, and CVD)**
Availability and ability to reach	*"Getting to XXX health center poses a significant challenge due to the absence of a suitable bus route. The limited daily bus schedule of 3–4 trips does not extend to the facility. Moreover, there is an uphill walk from the bus stop to the hospital premises. I feel tired to walk. I cannot cover the expense of taking an auto-rickshaw."* **(62-year-old man with diabetes and hypertension)** *"Initially, I used to accompany two others (neighbors) on our visits, but since their blood sugar levels did not improve and they discontinued their visits, I found it difficult to continue going alone. Consequently, I have stopped visiting the facility temporarily."* **(66-year-old woman with diabetes)** *"While improvements like infrastructure such as airport chairs and water facilities have been made, our most critical needs are still unaddressed. The efforts are commendable, but it would be highly beneficial if we could receive all necessary medications free of charge. We are willing to patiently wait in line if it means accessing medicines without cost."* **(FGD)** *"From my experience, I have noticed that when I consume tablets available at health centers, there is no improvement in sugar levels; they remain persistently high and result in increased fatigue. However, it is only when I use insulin I observe a reduction. But I do not receive a consistent supply of three insulin bottles monthly."* **(60-year-old woman with diabetes and early renal disease)** *"Doctor opts for fasting sugar tests, which lead me to private laboratories. The public health facility is often crowded, and enduring lengthy waits without eating becomes challenging. Typically, the lab procedures commence around 9 AM in this health center, which further adds to the difficulty of waiting without food."* **(45-year-old woman with diabetes).**

(Continued)

TABLE 2 (Continued)

Themes	Illustrative quotes
Affordability and ability to pay	*"Formerly, we received four bottles of insulin from this facility. However, this supply has ceased and we receive only two. Upon my inquiry to doctors, we were informed that medication is now prioritized for emergency and new diabetic cases. All of us are above 60 years old and unemployed, so purchasing medicines from private pharmacies is challenging. We are buying from Jan Aushadhi stores and spending 300 rupees per month to cover our medication expenses."***(62-year-man with diabetes and hypertension)*** *"Everything's expensive now. Sadly, I am also not receiving the old age pension, leaving me without financial support. I rely on the ration shop's yellow card for free rice. Due to excruciating leg pain, I cannot work and even struggle to walk to the restroom. Seeking private medical consultation requires around 300–400 rupees, which I cannot afford. In government healthcare, I do not receive all the necessary medications."***(62-year-old woman with diabetes and peripheral artery disease, for 12 years)*** *"I sought medical advice from Dr S a few years back, but I had to discontinue due to financial issues. Instead of visiting the doctor when I feel unwell, I occasionally purchase medicines using my previous prescription. However, my irregularity in seeking medical care has made me hesitant to return to the same doctor. The lack of money has caused me to lapse in my treatment. I am aware that diabetes is a chronic condition that requires consistent medication (pauses and tears up)."***(51-year-old woman with diabetes)***
Appropriateness and ability to engage	*"Occasionally, I experience headaches and a general feeling of unease, and I'm uncertain how to handle these situations. I usually opt to wait and observe if the symptoms alleviate naturally. If they persist, I may need to consider visiting the doctor at the FHC once more. Managing these health concerns comes with associated costs, such as transportation and medication expenses. So, I tolerate."***(49-year-old woman with diabetes)*** *"In my perspective, when a patient visits a doctor or nurse, their soothing and comforting words alone can alleviate a significant portion of our distress. For instance, addressing us affectionately and engaging in casual conversation while administering medication can help dull the pain. When my husband was hospitalized at MMM (a private hospital), I vividly remember the kidney specialist who attended to him. This doctor would call and inquire, "How's Appu Etta doing? What did you have for breakfast?" Those simple inquiries brought about a sense of ease and positivity. However, the doctor at the health center has a very quick temper and frequently raises his voice, making it difficult for us to approach them with any questions or concerns. He maintains a strict demeanor, and I fear him. Our interactions usually conclude with him prescribing medications, which we then purchase before returning home. I distinctly recall an incident where he scolded a diabetic person who wished to collect medications for his wife as well."***(60-year-old woman with diabetes on insulin)*** *"When my leg pain worsens, I visit a private healthcare facility. However, during my visits, doctors scolded me for using medications for diabetes from public healthcare providers. There is the Jan Aushadhi store pharmacy, where medicines are cheaper. Private doctors allege that the public health centers and Jan Aushadi store distribute outdated medications, advising us to dispose of these tablets. They even warn that using such medicines might lead to other health issues. Some professionals go so far as to claim that any medication obtained for free is of subpar quality. As a result, I find myself uncertain where to place my trust."***(62-year-old woman with diabetes and peripheral artery disease, for 12 years, on a woman with oral hypoglycemic)*** *"Many of us, particularly those dealing with diabetes and hypertension, share this general sentiment that the medicines provided at this facility are outdated and seem ineffective, which is the cause behind our uncontrolled blood sugar levels. During our wait to see the doctor, I've heard numerous individuals express similar concerns about the medications."***(FGD)*** *"When I feel excessively tired, I may take a whole pill instead of the usual half. Generally, there is not much else that needs to be done. Doctors typically continue prescribing the same medications. As a result, I do not find it necessary to make monthly visits to the clinic."***(55-year-old man with diabetes)*** *"I try to include salads or opt for wheat-based foods during dinner. I have learned about dietary limitations and the significance of physical activities such as walking and sit-ups through sessions and gatherings held at the government hospital in Perinthalmanna. In the past, I used to engage in walks lasting 1 to 1.5 h, often with the company of my friends. Unfortunately, following my heart surgery, I've had to discontinue all forms of physical activity due to my limitations. Despite this, I still manage to carry out routine tasks at a more leisurely pace."***(56-year-old woman with diabetes, hypertension, and CVD, underwent surgery three years ago)*** *"I am consuming a considerable number of tablets each day, three before meals, four after meals. Additionally, I administer insulin right after eating. Following this medication routine and accompanying it with water, my stomach feels quite full, making me lose my appetite for dinner?! This poses a significant concern for me, as extensive use of medicines leaves me wondering whether my body can tolerate too many medicines. If possible, I wish to curtail few medicines."***(56-year-old woman with diabetes, hypertension, and CVD, underwent surgery three years ago)***

exacerbations, requiring hospitalizations, antibiotics, etc. Participants perceived that private health facilities offer superior service quality, leading many participants to choose out-of-pocket expenses for these hospitals despite the financial strain. Most respondents reported they lacked any form of health insurance.

The burden of out-of-pocket spending was highlighted as a core issue for older adults with chronic illnesses. Out-of-pocket expenses and financial constraints resulted in treatment gaps and often resulted in making choices about which medications to buy following a doctor's prescription.

Participants emphasized that time spent on all-day travel hindered patients from working, earning an income, or attending to family responsibilities. Young male patients reported discontinuing monthly visits to public facility doctors due to the substantial time investment.

3.5 Appropriateness and ability to engage

Appropriateness refers to "how well services align with client requirements, including timely delivery, a thorough evaluation of health issues for accurate treatment determination, and the technical and interpersonal excellence of services" (42).

The long-term management of diabetes and hypertension demands consistent adherence to a treatment plan. Various factors

affected the participants' ability to follow their extended management plan. Long-term care involved regular hospital visits for obtaining medications and during worsening of symptoms. However, not all patients in our study could manage regular visits due to affordability issues, which interfered with adherence. The patient-provider relationship was an important factor related to adherence and patient satisfaction. Our interviews with patients revealed trust was is fostered when providers see patients as individuals, not merely cases. Additionally, displaying acceptance and respect contributed to nurturing this sense of confidence. Patients also expressed their frustration while reporting that they often left OPDs without getting the information they wanted, feeling overwhelmed and unable to understand the information provided. It was evident from patients' accounts that they lacked preparedness to manage their health conditions when experiencing symptoms like pain and fatigue. These factors contributed to feelings of uncertainty about their future health. However, a few patients felt capable and confident in managing their conditions. They acquired skills through diverse experiences—some from their encounters and others from both within and outside the healthcare system. Patients with positive experiences in managing their conditions exhibited greater motivation to remain committed to long-term care.

People with multiple chronic conditions often required multiple healthcare providers, which were rarely coordinated with one another. Most of the interviewed patients with multimorbidity reported visiting different doctors and usually received conflicting advice. A patient in our study felt conflicted because private doctors criticized her for using medications from government healthcare providers. Private doctors claimed these medicines might be outdated or of poor quality. This created confusion and uncertainty for her when deciding whom to trust for her healthcare. Furthermore, some patients during discussions shared their belief that any medicines received for free could be of lower quality.

Most patients believed that their medical conditions were both progressive and permanent, with little influence from either themselves or their doctors on their future prognosis. This perspective made it difficult for them to grasp the concept of preventive care and how it could benefit them. Patients adhered to the advice they perceived as beneficial, pragmatic, and able to sustain them. Some patients mentioned that they were more inclined to follow medication prescriptions at the time of diagnosis. However, as they gained more experience and knowledge, they became discerning about the advice they followed and adjusted it to fit their situations. Interestingly, patients had received dietary advice from various sources outside the health center, with the most common sources being private doctors, community members, and social media.

Patients dealing with multiple health conditions in our study emphasized the influence of pill burden on their adherence to therapy. They found it challenging to cope with a substantial number of daily tablets. Moreover, the quantity of tablets also appeared to affect how patients subjectively viewed their health status.

4 Discussion

This study provides valuable insights into the healthcare processes of people living with diabetes and hypertension in public health facilities in Kerala, India. The access to Healthcare conceptual framework (42) enabled us to analyze the intricate process of access within the health systems and the context of the population. Our analysis identified various factors that influence the access to primary health services for the management of diabetes and hypertension, including participants' limited knowledge of their condition, self-medication practices, physical distance to health facilities, availability of social support, high out-of-pocket expenditure, lack of trust, attitude of healthcare providers, medicine availability, and pill burden. Currently, primary healthcare services often do not sufficiently address the community's needs. Provision of care to individuals with diabetes and hypertension was often fragmented, leading to multiple visits to advanced healthcare facilities (hospitals), consultations with specialists, and the simultaneous use of various medications. These findings are similar to a study in the Kolar district of Karnataka, which found that the fragmented "treatment-in-silos" hindered patients' long-term adherence to treatment, especially as they age or face disabilities (19).

In our study, participant's understanding of diabetes and hypertension varied and was often linked to their symptoms, presence of comorbidities, age, and education. The practice of self-medication emerged as a prevalent health behavior, where people sought advice from relatives or friends and obtained traditional remedies. Formal allopathic healthcare was mostly sought when self-medication did not improve their condition, potentially delaying timely treatment and sometimes even worsening the condition. Diagnosed patients also practiced self-medication when their symptoms were controlled. Previous studies reported using self-medication, including traditional herbal remedies, in Indian healthcare (44, 45). During the interviews, participants also spoke about the restricted variety of drugs at PHCs and frequently expressed doubts about the effectiveness of these drugs for their conditions.

Participants in our study who were predominantly from a low economic status reported limited access to hypertension and diabetes services. Previous evidence suggests clustering of NCDs in disadvantaged groups who have low education status and live in poor communities. These, together with inadequate access to health care, further exacerbate health inequalities in NCD (46). The *Makkale Thedi Maruthuvam*" scheme is an initiative by the Government of Tamil Nadu to enhance equitable access by screening people aged 30 years and above for diabetes and hypertension, delivering essential medicines, and reviewing treatment compliance at the doorsteps of eligible patients (47). Such initiatives may reduce the frequency of monthly visits for medication refills and improve follow-up care. Practical actions to reduce NCD inequities should encompass prioritizing the service delivery and follow-up for the most susceptible people with diabetes and hypertension based on risk assessment and disparities in access to care.

Access to care was facilitated through support from family and other social networks. This finding is consistent with earlier research, as systematic reviews have established that social support enhances treatment adherence among individuals with NCDs by offering consistent reminders for timely medication consumption (48–50). In high-income countries, well-designed randomized control trials have demonstrated that diabetic populations benefit from peer/CHWs support, improving clinical and behavioral outcomes, including better glycaemic control (51–53). Programs like the UK's Expert Patient

Program provide a cost-effective approach combining peer support and structured education to enhance chronic health support (54, 55). Similarly, the Kerala Diabetes Prevention Program (K-DPP) (56) is a community-based peer-support lifestyle intervention program adapted from evidence-based interventions developed initially in high-income countries and has successfully reduced cardiometabolic risk in high-risk adults over two years. Furthermore, K-DPP encouraged healthier behaviors in peer leaders, like increased physical activity, improved dietary habits, and reduced alcohol consumption (57).

Participants recognized hypertension and diabetes as a lifelong disease, but older individuals were more committed to medication adherence. However, their understanding of long-term prevention steps and self-management was limited due to inadequate communication and support from healthcare workers at all healthcare system levels. Many patients felt overwhelmed by the complexity of managing chronic disease, struggling to initiate and sustain health-promoting behaviors due to uncertainty about where to start. In previous studies most patients seeking care from public healthcare facilities reported minimal or no assistance for self-management (19, 58). This highlights the need to enable and empower patients to participate in managing their care along the continuum spanning from prevention to end of life. Self-care or self-management is one form of intervention that has been of particular interest to manage chronic conditions better and address the socioeconomic challenges LMICs face (59). Many experts have asserted that effective management of chronic diseases occurs when patients are empowered to participate in their care actively. Most chronic care models, including the chronic care model, support self-management skills as an essential component of chronic care (60). Self-management interventions, including SMS-based education, guideline-based teaching sessions, and telephonic counseling, have demonstrated the potential to improve patient health outcomes (61–63). Our findings indicate the need for further research on self-management strategies for CVD, focusing on long-term sustainability, to suit the Kerala context.

Participants' access to healthcare services was strongly shaped by their trust in the health system and social environment. Trust was influenced by previous personal or network experiences, the reputation of healthcare facilities, and the belief that higher-level facilities offer better service quality and prescribers' attitudes. While FHC doctors reported to address patients hastily, people expected extensive conversations and meticulous examinations. This finding aligns with previous research, emphasizing the significance of positive patient-health professional relationships on patients' adherence to treatment (64), particularly when patients perceive healthcare providers as compassionate and caring.

Among our study participants, medication non-adherence stemmed from multifaceted factors, encompassing psychosocial elements (perceived lack of social support), structural challenges (clinic distance and medication expenses), therapy-related issues (multiple visits, polypharmacy, pill burden), and barriers within the healthcare system (e.g., insufficient counseling, erratic medicine supply from public health facilities, and patient-provider relationship). Additionally, patients trust in healthcare systems and beliefs regarding medications and their perceptions of their illness contribute to non-adherence. Evidence suggests that the use of single-pill combination (SPC) is safe and has the potential to improve patient adherence and blood pressure control, particularly in LMICs (65). In 2019, the World Health Organization (WHO) incorporated SPC into the Essential medicines list (66). We encourage the uptake and use of SPCs in primary care settings to improve blood pressure control and simplify treatment regimens.

Previous studies have proposed that an integrated approach to NCD care can streamline and save patient time and costs. For example, Peck et al. (67) have shown that integrating NCD and human immunodeficiency virus (HIV) treatment services reduces patient travel burden, allows personalized treatment approaches, and addresses the lack of support for patient follow-up and self-management in the current healthcare system. Frenk discusses integrating interventions and adopting a diagonal approach to health system improvements across multiple conditions while emphasizing the need for tangible improvements in health outcomes (68).

Our further observation pertains to the linear nature of Levesque et al.'s framework (42). While this framework has recognized factors influencing the healthcare-seeking pathways of individuals with NCDs, it does not fully explain why patients progress through these multidirectional pathways. Consistent with Nguyen et al.'s findings (69), we observed that patients frequently navigate the care pathway in a non-linear manner due to the challenges of diagnosis and the long-term management of chronic conditions. This process involves loops and cycles, with patients moving forward and backward in pursuit of healthcare across various facilities. Consequently, an alternative non-linear representation, incorporating broader healthcare system factors, would better depict the interconnected elements influencing access to healthcare services.

Consistent with prior research, our study reveals that individual "abilities" are primarily influenced by the "system" and its deficiencies, rather than solely being the responsibility of individuals. Thus, the central aspect of any intervention may involve a substantial investment in enhancing the accessibility of the system to empower an individual's "ability" to interact with it effectively.

4.1 Strengths and limitations of the study

The study has several limitations. Firstly, in its emphasis on capturing patients' viewpoints, the study did not incorporate the healthcare workers (supply side), which could have provided valuable insights. Secondly, although efforts were made to include equal representation of male and female participants, most respondents were women, reflecting the predominant population seeking healthcare in the state. Thirdly, the quality of care provided to the patients and the resulting health outcomes were beyond the scope of the study.

A key strength of our study is that we have considered the most prevalent NCDs, like diabetes and hypertension, to explore how patients seek care for chronic conditions in Malappuram. Although variations may exist among different illnesses, experiences are likely similar due to the current state of the healthcare system in Kerala and India. Primary care services are weak, and health systems lack capacity to address chronic illnesses. Secondly, our prolonged engagement within the study sites, as we regularly visited the facilities and stayed in the local community, enabled us to obtain data with rich insights into how people experience care. Thirdly, using Levesque's access

framework in the analysis enhances the potential for replication of this study in other contextually similar settings.

4.2 Implication for practice and research

Preventing the rising burden of NCDs is challenging as it necessitates addressing the underlying social determinants of health (70). Moreover, the organization of care for individuals with NCDs is intricate and resource-intensive, and multiple concurrent chronic conditions, known as multimorbidity, further complicate matters (71–74). It is important to recognize that the roots of NCDs are deeply entrenched in society's social, political, and economic structures.

Unfortunately, it appears that those shaping current policies and resource allocation are either unaware of or choose to overlook the realities on the frontlines of healthcare. Physicians often find themselves bridging the gap between treating individual illnesses and meeting the needs of patients grappling with multimorbid NCDs. Reachable and reliable care and support must be ensured at the initial point of contact. Healthcare professionals must deliver attentive support tailored to individuals' perceived needs, incorporate self-management support to influence patients' behavior, and maximize the use and effectiveness of community service. Furthermore, we need a more comprehensive approach to healthcare policy that recognizes the interconnectedness of NCDs and the social determinants that affect their occurrence and management. Such a shift in policy and resource allocation is essential to effectively address our society's growing burden of NCDs.

5 Conclusion

The patient journey in managing diabetes and hypertension is multifaceted, involving multiple entry and exit points within the healthcare system. This study underscores the complexity of healthcare access and how access was affected by various factors. Unfortunately, there is a lack of a patient-centred care process that delves into the self-management efforts required by patients and explores how healthcare providers can offer adequate support. Consequently, it is crucial to rethink the design and organization of care for individuals with chronic diseases. This involves reframing the patient journey, acknowledging it as one characterized by multiple touchpoints where patients may initiate their healthcare pathway at different stages but consistently require good quality, affordable care and support at various junctures.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Institutional Ethics Committee of Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCT/IEC/ 1908). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

RR: Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Writing – original draft, Writing – review & editing. PS: Conceptualization, Methodology, Supervision, Writing – review & editing. SS: Conceptualization, Methodology, Supervision, Writing – review & editing. KT: Conceptualization, Methodology, Supervision, Writing – review & editing. PJ: Conceptualization, Formal analysis, Funding acquisition, Methodology, Supervision, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This study is partially funded through the Health Policy Analysis Fellowship program, supported by the Alliance for Health Policy and Systems Research, Switzerland, and managed through the University of Cape Town, South Africa. RR was awarded this fellowship.

Acknowledgments

The authors express their appreciation to the Alliance for Health Policy and Systems Research, Switzerland, for supporting this study. Gratitude is extended to individuals with diabetes and hypertension who generously shared their valuable insights during the study. Special acknowledgment is given to Linju Maria Joseph, Tijo George, Krishnendu C, and Arun Jose for their significant contributions to interpreting the study's results.

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.2024.1375227/full#supplementary-material

References

1. Lancet T. GBD 2017: a fragile world. *Lancet*. (2018) 392:1683. doi: 10.1016/S0140-6736(18)32858-7

2. Niessen LW, Mohan D, Akuoku JK, Mirelman AJ, Ahmed S, Koehlmoos TP, et al. Tackling socioeconomic inequalities and non-communicable diseases in low-income and middle-income countries under the sustainable development agenda. *Lancet Lond Engl.* (2018) 391:2036–46. doi: 10.1016/S0140-6736(18)30482-3

3. WHO. (2023) Non communicable diseases. Available at: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases

4. Amarchand R, Kulothungan V, Krishnan A, Mathur P. Hypertension treatment cascade in India: results from National Noncommunicable Disease Monitoring Survey. *J Hum Hypertens*. (2023) 37:394–404. doi: 10.1038/s41371-022-00692-y

5. Prenissl J, Jaacks LM, Mohan V, Manne-Goehler J, Davies JI, Awasthi A, et al. Variation in health system performance for managing diabetes among states in India: a cross-sectional study of individuals aged 15 to 49 years. *BMC Med.* (2019) 17:92. doi: 10.1186/s12916-019-1325-6

6. Sarma PS, Sadanandan R, Thulaseedharan JV, Soman B, Srinivasan K, Varma RP, et al. Prevalence of risk factors of non-communicable diseases in Kerala, India: results of a cross-sectional study. *BMJ Open*. (2019) 9:e027880. doi: 10.1136/bmjopen-2018-027880

7. WHO. (2023) WHO package of essential noncommunicable (PEN) disease interventions for primary health care. Available at: https://www.who.int/publications-detail-redirect/9789240009226

8. Demaio AR, Nielsen KK, Tersbøl BP, Kallestrup P, Meyrowitsch DW. Primary health care: a strategic framework for the prevention and control of chronic non-communicable disease. *Glob Health Action*. (2014) 7:24504. doi: 10.3402/gha.v7.24504

9. Haque M, Islam T, Rahman NAA, McKimm J, Abdullah A, Dhingra S. Strengthening primary health-care services to help prevent and control long-term (chronic) non-communicable diseases in low- and middle-income countries. *Risk Manag Healthc Policy*. (2020) 13:409–26. doi: 10.2147/RMHP.S239074

10. Hansen J, Groenewegen PP, Boerma WGW, Kringos DS. Living in A country with A strong primary care system is beneficial to people with chronic conditions. *Health Aff (Millwood)*. (2015) 34:1531–7. doi: 10.1377/hlthaff.2015.0582

11. Bitton A, Fifield J, Ratcliffe H, Karlage A, Wang H, Veillard JH, et al. Primary healthcare system performance in low-income and middle-income countries: a scoping review of the evidence from 2010 to 2017. *BMJ Glob Health*. (2019) 4:e001551. doi: 10.1136/bmjgh-2019-001551

12. Varghese C, Nongkynrih B, Onakpoya I, McCall M, Barkley S, Collins TE. Better health and wellbeing for billion more people: integrating non-communicable diseases in primary care. *BMJ*. (2019) 364:l327. doi: 10.1136/bmj.l327

13. Vlassoff C, Tanner M, Weiss M, Rao S. Putting people first: A primary health care success in rural India. *Indian J Community Med*. (2010) 35:326–30. doi: 10.4103/0970-0218.66896

14. Samb B, Desai N, Nishtar S, Mendis S, Bekedam H, Wright A, et al. Prevention and management of chronic disease: a litmus test for health-systems strengthening in low-income and middle-income countries. *Lancet*. (2010) 376:1785–97. doi: 10.1016/S0140-6736(10)61353-0

15. Gabert R, Ng M, Sogarwal R, Bryant M, Deepu RV, McNellan CR, et al. Identifying gaps in the continuum of care for hypertension and diabetes in two Indian communities. *BMC Health Serv Res*. (2017) 17:846. doi: 10.1186/s12913-017-2796-9

16. Ramani S, Sivakami M. Community perspectives on primary health centers in rural Maharashtra: what can we learn for policy? *J Fam Med Prim Care*. (2019) 8:2837–44. doi: 10.4103/jfmpc.jfmpc_650_19

17. Sodani P, Sharma K. Strengthening primary level health service delivery: lessons from a state in India. *J Fam Med Prim Care*. (2012) 1:127–31. doi: 10.4103/2249-4863.104983

18. Bhaumik S. Health and beyond. Strategies for a better India: concept paper on primary health Care in India. *J Fam Med Prim Care*. (2014) 3:94–7. doi: 10.4103/2249-4863.137608

19. Lall D, Engel N, Devadasan N, Horstman K, Criel B. Challenges in primary care for diabetes and hypertension: an observational study of the Kolar district in rural India. *BMC Health Serv Res*. (2019) 19:44. doi: 10.1186/s12913-019-3876-9

20. Patel V, Mazumdar-Shaw K, Kang G, Das P, Khanna T. Reimagining India's health system: a Lancet citizens' commission. *Lancet Lond Engl*. (2021) 397:1427–30. doi: 10.1016/S0140-6736(20)32174-7

21. Angell BJ, Prinja S, Gupt A, Jha V, Jan S. The Ayushman Bharat Pradhan Mantri Jan Arogya Yojana and the path to universal health coverage in India: overcoming the challenges of stewardship and governance. *PLoS Med*. (2019) 16:e1002759. doi: 10.1371/journal.pmed.1002759

22. Ministry of Health and Family Welfare, Governmnet of India. (2023) Operational guidelines on wellness interventions for Ayushman Bharat health and wellness Centres | National Health Systems Resource Centre. Available at: https://nhsrcindia.org/operational-guidelines-wellness-interventions-ayushman-bharat-health-and-wellness-centres

23. Government Of India. (2022) Ayushman Bharat – national health protection mission. Available at: https://www.india.gov.in/spotlight/ayushman-bharat-national-health-protection-mission. (Accessed on September, 2022).

24. Government Of India. (2022) Official website Ayushman Bharat. Available at: https://ab-hwc.nhp.gov.in/. (Accessed on January, 2022).

25. Arogyakeralam. (2022) National Health Mission Kerala-Aardram. Available at: https://arogyakeralam.gov.in/2020/04/01/aardram/. (Accessed on October, 2022).

26. Sadanandan R, Sivaprasad S. Adding screening for "end organ damage" to the noncommunicable disease package in primary care. *Indian J Ophthalmol*. (2021) 69:3064–7. doi: 10.4103/ijo.IJO_1496_21

27. Sivaprasad S, Netuveli G, Wittenberg R, Khobragade R, Sadanandan R, Gopal B, et al. Complex interventions to implement a diabetic retinopathy care pathway in the public health system in Kerala: the Nayanamritham study protocol. *BMJ Open*. (2021) 11:e040577. doi: 10.1136/bmjopen-2020-040577

28. Oben P. Understanding the patient experience: A conceptual framework. *J Patient Exp*. (2020) 7:906–10. doi: 10.1177/2374373520951672

29. Stebbins RA. *Exploratory research in the social sciences [internet]*. Thousand Oaks, CA: SAGE Publications, Inc (2001).

30. Sandelowski M. What's in a name? Qualitative description revisited. *Res Nurs Health*. (2010) 33:77–84. doi: 10.1002/nur.20362

31. Population Census. (2022) Malappuram Municipality City population census 2011-2023 | Kerala. Available at: https://www.census2011.co.in/data/town/803269-malappuram-kerala.html. (Accessed on September, 2022).

32. Philip RR, Philip S, Tripathy JP, Manima A, Venables E. Twenty years of home-based palliative care in Malappuram, Kerala, India: a descriptive study of patients and their care-givers. *BMC Palliat Care*. (2018) 17:26. doi: 10.1186/s12904-018-0278-4

33. Ismail S, Stanley A, Jeemon P. Prevalence of multimorbidity and associated treatment burden in primary care settings in Kerala: a cross-sectional study in Malappuram District, Kerala, India. *Wellcome Open Res*. (2022) 7:67. doi: 10.12688/wellcomeopenres.17674.2

34. Joseph L, Greenfield S, Manaseki-Holland S, Lekha TR, Sujakumari S, Panniyammakal J, et al. Patients', carers' and healthcare providers' views of patient-held health records in Kerala, India: A qualitative exploratory study. *Health Expect*. (2023) 26:1081–95. doi: 10.1111/hex.13721

35. Given LM. *The SAGE encyclopedia of qualitative research methods*. Thousand Oaks, CA: SAGE Publications (2008). 1073 p.

36. Britten N. Qualitative interviews in medical research. *BMJ*. (1995) 311:251–3. doi: 10.1136/bmj.311.6999.251

37. Caillaud S, Flick U. Focus groups in triangulation contexts In: RS Barbour and DL Morgan, editors. *A new era in focus group research: Challenges, innovation and practice*. London: Palgrave Macmillan UK (2017). 155–77.

38. Hennink MM, Kaiser BN, Marconi VC. Code saturation versus meaning saturation: how many interviews are enough? *Qual Health Res*. (2017) 27:591–608. doi: 10.1177/1049732316665344

39. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol*. (2006) 3:77–101. doi: 10.1191/1478088706qp063oa

40. Kiger ME, Varpio L. Thematic analysis of qualitative data: AMEE guide no. 131. *Med Teach*. (2020) 42:846–54. doi: 10.1080/0142159X.2020.1755030

41. Pope C, Ziebland S, Mays N. Analysing qualitative data. *BMJ*. (2000) 320:114–6. doi: 10.1136/bmj.320.7227.114

42. Levesque JF, Harris MF, Russell G. Patient-centred access to health care: conceptualising access at the interface of health systems and populations. *Int J Equity Health*. (2013) 12:18. doi: 10.1186/1475-9276-12-18

43. Devi R, Kanitkar K, Narendhar R, Sehmi K, Subramaniam K. A narrative review of the patient journey through the Lens of non-communicable diseases in low- and middle-income countries. *Adv Ther*. (2020) 37:4808–30. doi: 10.1007/s12325-020-01519-3

44. Vishnu N, Mini GK, Thankappan KR. Complementary and alternative medicine use by diabetes patients in Kerala, India. *Glob Health Epidemiol Genomics*. (2017) 2:e6. doi: 10.1017/gheg.2017.6

45. Greenhalgh T. Drug prescription and self-medication in India: An exploratory survey. *Soc Sci Med*. (1987) 25:307–18. doi: 10.1016/0277-9536(87)90233-4

46. Cesare MD, Khang YH, Asaria P, Blakely T, Cowan MJ, Farzadfar F, et al. Inequalities in non-communicable diseases and effective responses. *Lancet*. (2013) 381:585–97. doi: 10.1016/S0140-6736(12)61851-0

47. Thiagesan R, Soundari H, Kalpana B, Gopichandran V. "Makkalai Thedi Maruthuvam" scheme in Tamil Nadu: an intersectionality-based analysis of access to NCD care. Indian. *J Med Ethics*. (2023) VIII:203–9. doi: 10.20529/IJME.2023.015

48. Miller TA, DiMatteo MR. Importance of family/social support and impact on adherence to diabetic therapy. *Diabetes Metab Syndr Obes*. (2013) 6:421–6. doi: 10.2147/DMSO.S36368

49. Walsh JME, McDonald KM, Shojania KG, Sundaram V, Nayak S, Lewis R, et al. Quality improvement strategies for hypertension management: a systematic review. *Med Care*. (2006) 44:646–57. doi: 10.1097/01.mlr.0000220260.30768.32

50. Glynn LG, Murphy AW, Smith SM, Schroeder K, Fahey T. Self-monitoring and other non-pharmacological interventions to improve the management of hypertension in primary care: a systematic review. *Br J Gen Pract J R Coll Gen Pract*. (2010) 60:e476–88. doi: 10.3399/bjgp10X544113

51. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. (2002) 346:393–403. doi: 10.1056/NEJMoa012512

52. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and diabetes study. *Diabetes Care*. (1997) 20:537–44. doi: 10.2337/diacare.20.4.537

53. Tuomilehto J, Lindström J, Eriksson JG, Valle TT, Hämäläinen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. (2001) 344:1343–50. doi: 10.1056/NEJM200105033441801

54. Donaldson L. Expert patients usher in a new era of opportunity for the NHS: the expert patient programme will improve the length and quality of lives. *BMJ*. (2003) 326:1279–80. doi: 10.1136/bmj.326.7402.1279

55. Tattersall R. The expert patient: a new approach to chronic disease management for the twenty-first century. *Clin Med*. (2002) 2:227–9. doi: 10.7861/clinmedicine.2-3-227

56. Thankappan KR, Sathish T, Tapp RJ, Shaw JE, Lotfaliany M, Wolfe R, et al. A peer-support lifestyle intervention for preventing type 2 diabetes in India: A cluster-randomized controlled trial of the Kerala diabetes prevention program. *PLoS Med*. (2018) 15:e1002575. doi: 10.1371/journal.pmed.1002575

57. Haregu T, Aziz Z, Cao Y, Sathish T, Thankappan KR, Panniyammakal J, et al. A peer support program results in greater health benefits for peer leaders than other participants: evidence from the Kerala diabetes prevention program. *BMC Public Health*. (2023) 23:1175. doi: 10.1186/s12889-023-16049-0

58. Humphries C, Jaganathan S, Panniyammakal J, Singh S, Goenka S, Dorairaj P, et al. Investigating clinical handover and healthcare communication for outpatients with chronic disease in India: A mixed-methods study. *PLoS One*. (2018) 13:e0207511. doi: 10.1371/journal.pone.0207511

59. Hearn J, Ssinabulya I, Schwartz JI, Akiteng AR, Ross HJ, Cafazzo JA. Self-management of non-communicable diseases in low- and middle-income countries: A scoping review. *PLoS One*. (2019) 14:e0219141. doi: 10.1371/journal.pone.0219141

60. Bodenheimer T, Wagner EH, Grumbach K. Improving primary Care for Patients with Chronic IllnessThe chronic care model, part 2. *JAMA*. (2002) 288:1909–14. doi: 10.1001/jama.288.15.1909

61. Sherifali D, Berard LD, Gucciardi E, MacDonald B, MacNeill G. Self-management education and support. *Can J Diabetes*. (2018) 42:S36–41. doi: 10.1016/j.jcjd.2017.10.006

62. McManus RJ, Mant J, Bray EP, Holder R, Jones MI, Greenfield S, et al. Telemonitoring and self-management in the control of hypertension (TASMINH2): a randomised controlled trial. *Lancet*. (2010) 376:163–72. doi: 10.1016/S0140-6736(10)60964-6

63. McLean G, Band R, Saunderson K, Hanlon P, Murray E, Little P, et al. Digital interventions to promote self-management in adults with hypertension systematic review and meta-analysis. *J Hypertens*. (2016) 34:600–12. doi: 10.1097/HJH.0000000000000859

64. Mechanic D. Changing medical organization and the Erosion of trust. *Milbank Q*. (1996) 74:171–89. doi: 10.2307/3350245

65. Bruyn E, Nguyen L, Schutte AE, Murphy A, Perel P, Webster R. Implementing single-pill combination therapy for hypertension: A scoping review of key health system requirements in 30 low- and middle-income countries. *Glob Heart*. (2022) 17:6. doi: 10.5334/gh.1087

66. WHO. (2023) WHO model lists of essential medicines. Available at: https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/essential-medicines-lists

67. Peck R, Mghamba J, Vanobberghen F, Kavishe B, Rugarabamu V, Smeeth L, et al. Preparedness of Tanzanian health facilities for outpatient primary care of hypertension and diabetes: a cross-sectional survey. *Lancet Glob Health*. (2014) 2:e285–92. doi: 10.1016/S2214-109X(14)70033-6

68. Frenk J. Reinventing primary health care: the need for systems integration. *Lancet*. (2009) 374:170–3. doi: 10.1016/S0140-6736(09)60693-0

69. Nguyen TA, Pham YN, Doan NP, Nguyen TH, Do TT, Van Vu G, et al. Factors affecting healthcare pathways for chronic lung disease management in Vietnam: a qualitative study on patients' perspectives. *BMC Public Health*. (2021) 21:1145. doi: 10.1186/s12889-021-11219-4

70. Sreekumar S, Ravindran TKS. A critique of the policy discourse on primary health care under the Aardram mission of Kerala. *Health Policy Plan*. (2023) 38:949–59. doi: 10.1093/heapol/czad041

71. Pefoyo AJK, Bronskill SE, Gruneir A, Calzavara A, Thavorn K, Petrosyan Y, et al. The increasing burden and complexity of multimorbidity. *BMC Public Health*. (2015) 15:415. doi: 10.1186/s12889-015-1733-2

72. Mini GK, Thankappan KR. Pattern, correlates and implications of non-communicable disease multimorbidity among older adults in selected Indian states: a cross-sectional study. *BMJ Open*. (2017) 7:e013529. doi: 10.1136/bmjopen-2016-013529

73. Oni T, McGrath N, BeLue R, Roderick P, Colagiuri S, May CR, et al. Chronic diseases and multi-morbidity--a conceptual modification to the WHO ICCC model for countries in health transition. *BMC Public Health*. (2014) 14:575. doi: 10.1186/1471-2458-14-575

74. Arokiasamy P, Uttamacharya JK. Multi-morbidity, functional limitations, and self-rated health among older adults in India: cross-sectional analysis of LASI pilot survey, 2010. *SAGE Open*. (2015) 5:215824401557164. doi: 10.1177/2158244015571640

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 30 May 2024
DOI 10.3389/fpubh.2024.1364735

OPEN ACCESS

EDITED BY
Yun Gao,
Sichuan University, China

REVIEWED BY
Karolina Kopacz,
Medical University of Lodz, Poland
Spyridon Kanellakis,
Harokopio University, Greece

*CORRESPONDENCE
Liheng Chen,
✉ chenliheng0786@163.com

RECEIVED 03 January 2024
ACCEPTED 06 May 2024
PUBLISHED 30 May 2024

CITATION
Zhou C, Yang L, Liu C, Ma H, Yang F and Chen L (2024) Associations between special diet and incidence risk of osteoporosis: a Mendelian randomization study.
Front. Public Health 12:1364735.
doi: 10.3389/fpubh.2024.1364735

Associations between special diet and incidence risk of osteoporosis: a Mendelian randomization study

Changwen Zhou[1], Lixue Yang[1,2], Ce Liu[1], Hongzhong Ma[1], Feng Yang[1,2] and Liheng Chen[2]*

[1]The First Clinical Medical Research Institute, Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, China, [2]Affiliation Hospital of Shaanxi University of Chinese Medicine, Xianyang, Shaanxi, China

Introduction: Osteoporosis is a prevalent challenge in clinical orthopedics, affecting a significant percentage of individuals aged 50 and above. The goal of this study was to comprehensively understand the relationships between a specialized dietary regimen and the risk of developing osteoporosis.

Methods: This study employed extensive genome-wide association study (GWAS) summary statistics derived from the UK Biobank. It encompassed 8 kinds of special diets and 7 datasets pertaining to osteoporosis and associated symptoms. The principal analytical approach employed was the inverse-variance weighted method. Additionally, sensitivity analysis was employed to elucidate the diverse multiplicity patterns observed in the final model.

Results: Our results showed that there is significant evidence that a gluten-free diet is associated with osteoporosis [odds ratio (OR): 1.080, 95% confidence interval (CI): 1.048–1.112, $p = 4.23E-07$)]. Furthermore, there exists a suggestive link between the three distinct dietary approaches and osteoporosis [(OR: 0.949, 95%CI: 0.929–0.970, $p = 3.00E-06$) for comprehensive consumption; (OR: 1.053, 95%CI: 1.018–1.089, $p = 2.23E-03$) for abstaining from wheat consumption; (OR: 1.036, 95%CI: 1.005–1.068, $p = 1.97E-02$) for abstaining from sugar consumption]. No additional correlation between the special dietary regimens and osteoporosis has been observed.

Conclusion: Our research has uncovered a notable correlation between a gluten-free diet and the occurrence of osteoporosis. Furthermore, it exerts a promoting influence on the onset of osteoporosis, which stands in direct contradiction to the therapeutic principles for Celiac Disease's complications. As such, a novel association among these three elements is postulated.

KEYWORDS

osteoporosis, dietary habits, gluten-free diet, Mendelian randomization, celiac disease

1 Introduction

Osteoporosis, a challenge frequently encountered in the realm of clinical orthopedics, exerts a substantial influence on the decision-making process pertaining to numerous treatment alternatives. According to the most recent research, osteoporosis affects a noteworthy 10.2% of individuals aged 50 years and above, with an anticipated rise to 13.6% by the year 2030 (1).

Nevertheless, despite the exorbitant annual expenditures reaching billions of dollars for the treatment of osteoporosis in the United States, with projected costs expected to persistently escalate (2), the problem persists. It is imperative to ascertain modifiable protective or risk factors in order to avert the onset and progression of osteoporosis.

Diet has gained significant attention among researchers as an easily obtainable and modifiable factor. Several systematic studies have demonstrated the presence of the influence of diet and nutrition on osteoporosis, although conclusive findings are hindered by factors such as heterogeneity and small sample sizes (3, 4). Current research indicates that dairy products, protein, vitamin D, vitamin K, fruits and vegetables, and adherence to a Mediterranean diet all contribute to the promotion of bone health (4, 5). However, it is important to note that eating habits encompass not only the act of food consumption but also the deliberate exclusion of specific food items. This study defines the latter as "special diets" and explores these novel avenues to comprehensively elucidate the influence of diet on osteoporosis.

In this instance, Mendelian randomization (MR) presents itself as a viable approach for deducing the interconnections amidst distinctive dietary patterns and osteoporosis. MR employs genetic variants as instrumental variables (IVs) for the exposure (such as specialized diets) to facilitate inferential associations (6). This method significantly mitigates the influence of confounding factors commonly encountered in observational studies. By virtue of the random allocation of alleles during conception, the relationship between genetic variations and disease outcomes remains less susceptible to environmental and confounding factors (7, 8).

In this investigation, summary statistics derived from genome-wide association studies (GWAS) were employed to perform a two-sample MR analysis, aiming to comprehensively delineate the relationships between a specialized dietary regimen and the risk of developing osteoporosis.

2 Materials and methods

2.1 Study design

Our MR study was built upon three underlying hypotheses: Firstly, genetic variations are intimately connected with the particular exposure in question. Secondly, genetic variations are not associated with any confounding variables. Lastly, genetic variations are unable to have a direct effect on the outcome, but only through the specific exposure being examined (8). The data employed in this study were sourced from previously published summary statistics of GWAS, thus obtaining ethical approval and informed consent was not required. In this study, we designated the special diet as the exposure variable and executed a series of matching analyses with osteoporosis-related indicators as individual outcomes. The specific matching process is elucidated in Figure 1.

2.2 Selection of instrumental variables and data source

The genetic variants pertaining to special diets were obtained from two UK Biobank cohorts consisting of approximately 461,046 and 64,949 individuals (9). The initial list comprised 8 special diets: "Never eat sugar: Sugar or foods/drinks containing sugar"(NOSUGAR), "Never eat wheat: Wheat or products containing wheat"(NOWHEAT), "Never eat dairy: Dairy or products containing dairy"(NODAIRY), "Never eat eggs: Eggs or foods containing eggs"(NOEGG), "Eggs, dairy, wheat, sugar: I eat all of the above"(ALL), "Type of special diet followed: Gluten-free"(GLUTEN), "Type of special diet followed: Vegetarian"(VEGE) and "Type of special diet followed: Low calorie"(CALO). To select valid IVs, we included single nucleotide polymorphisms (SNPs) at the genome-wide significant level ($p < 5 \times 10^{-8}$) (10) and applied strict cutoff values ($R^2 < 0.001$; region size = 10,000 kb) to exclude SNPs that are in linkage disequilibrium. As NODAIRY, NOEGG, NOWHEAT, GLUTEN, VEGE and CALO have less than 5 SNPs that meet the strict threshold ($p < 5 \times 10^{-8}$), we used a relaxed threshold ($p < 5 \times 10^{-5}$; $R^2 < 0.001$; region size = 10,000 kb) to select SNPs for these diets. Moreover, SNPs with a minimum allele frequency (MAF) of less than 0.05 were excluded as the association between these SNPs and special diets was deemed to be unstable (11). To satisfy the second and third critical hypotheses, all selected SNPs were evaluated using the PhenoScanner database (12), and none of them needed to be excluded. Additionally, we ruled out SNPs associated with multiple special diets to reduce potential pleiotropy across the SNPs (Supplementary Table S1). Lastly, *F*-statistics were employed to evaluate SNPs with weak IVs bias (13). The *F*-statistics formula is $F = R^2 \times (N\text{-}2)/(1\text{-}R^2)$, where N represents the sample size, and R^2 refers to the variance of exposure explained by IVs. Only the SNP with *F*-statistics >10 were considered for inclusion in the MR analysis (11).

To evaluate the association between special diets and the incidence risk of osteoporosis in a more comprehensive manner, we aimed to include all eligible GWAS of osteoporosis by conducting an extensive search of the public Integrative Epidemiology Unit (IEU) GWAS database[1] (14). We selected two GWAS data sets from UK Biobank. In addition to osteoporosis patients diagnosed based on hospitalization records and using diagnosis codes; we also considered the low willingness of older adult/adults patients to medical treatment, patients with suspected osteoporosis classified by the interviewer based on the description of the participants were deliberately included. On this basis, we believe that it is necessary to include bone density, a diagnostic indicator of osteoporosis, in the study to improve the reliability of the study. The specific information of the summary-level data included in this study is shown in Supplementary Table S2.

2.3 Statistical analysis

MR analysis utilized SNPs as proxies for predicting the impact of special diets on osteoporosis risk. The study employed the fixed-effects inverse-variance weighted (IVW) method as the primary technique to estimate the association between the genetic prediction level of special diets and osteoporosis risk (15). The IVW method combines Wald estimates for each SNP using a meta-analysis approach to derive an overall estimate of the effect of special diets on osteoporosis. The IVW method is capable of providing unbiased estimates if horizontal or vertical pleiotropy is balanced. Sensitivity analysis was conducted using the weighted median approach, which allowed for the inclusion

1 https://gwas.mrcieu.ac.uk/

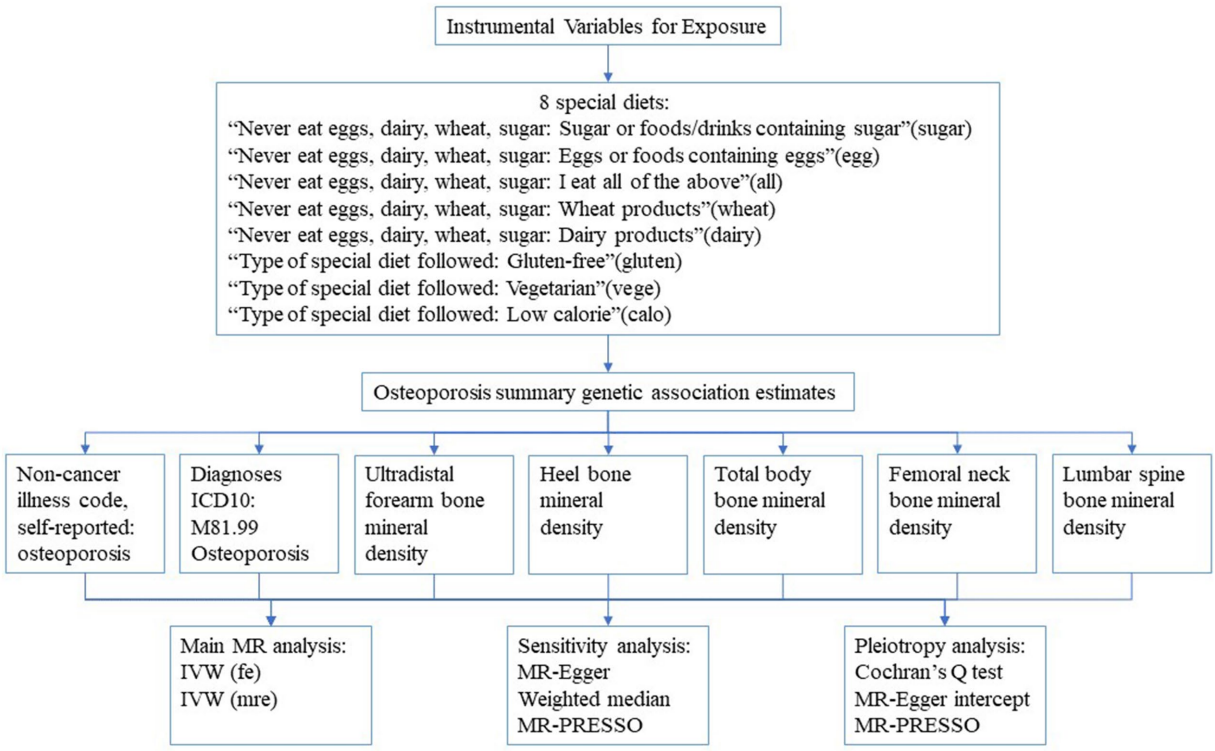


FIGURE 1
The flow chart of study design. IVW, Inverse variance weighted; fe, fixed-effects; mre, multiplicative random-effects.

of invalid genetic variants while still producing a consistent point estimate (16). The InSIDE hypothesis formed the basis for the MR-Egger method, which provides a valid test of the null associational hypothesis and a consistent estimate of the associational effect, even if all genetic variants are invalid IVs. However, the MR-Egger method may produce inaccurate estimates and may be significantly influenced by external genetic variants (17). Lastly, the MR-PRESSO method used a global test to assess horizontal pleiotropy and outliers, as well as to compare results before and after outliers was removed (18).

In each analysis of special diets and osteoporosis, Cochran's Q statistics were employed to quantify the heterogeneity between IVs (19). In the event that heterogeneity is detected ($P_{\text{Cochran's Q}} < 0.05$), the multiplicative random-effects IVW model is implemented to circumvent the bias toward weaker instrument exposure associations (20). The MR-Egger intercept test utilized the intercept term to assess pleiotropy (21). If a significant difference between the intercept term and zero exists, it is plausible that there is horizontal pleiotropy between IVs. Additionally, forest plots, scatter plots, funnel plots, and leave-one-out analysis plots were generated to depict the results with high-confidence. Specifically, the forest plot intuitively presents the impact of each SNP on the outcome, while the leave-one-out analysis determines the visual robustness of the results. The scatter plot illustrates the fitting results of various MR analyses, and the funnel plot visually evaluates the heterogeneity of IVs.

The 95% confidence interval (CI) of the odds ratio (OR) was utilized to estimate the association between special diets and osteoporosis. A suggestive correlation was established if $p < 0.05$, whereas high-confidence associations survived multiple tests with a threshold of 0.006 (= 0.05/8) by Bonferroni correction.

All data analysis in this study was executed using R software (version 4.1.3). The R packages utilized for MR analyses included TwoSampleMR (22) and MR-PRESSO (18) packages.

3 Results

3.1 Special diet and osteoporosis

Supplementary Table S3 presents the distinct characteristics of 346 IVs across 8 special diets. With all IVs exhibiting F statistics exceeding 10 (minimum = 16, maximum = 672), the risk of weak instrument bias is effectively mitigated. By referencing Supplementary Table S4 and Figure 2, the fixed-effects IVW method indicated that osteoporosis (self-reported) was significantly associated with ALL (OR: 0.949, 95%CI: 0.929–0.970, $p = 3.00\text{E-}06$), GLUTEN (OR: 1.080, 95%CI: 1.048–1.112, $p = 4.23\text{E-}07$) and NOWHEAT (OR: 1.053, 95%CI: 1.018–1.089, $p = 2.23\text{E-}03$), while NOSUGAR (OR: 1.036, 95%CI: 1.005–1.068, $p = 1.97\text{E-}02$) was suggestively associated. Notably, evidence of heterogeneity was found in NOWHEAT ($P_{\text{Cochran's Q}} < 0.05$), suggesting the possibility of fixed-effects IVW estimation bias (refer to Supplementary Table S5). However, the random-effects IVW method proposed a suggestive association between NOWHEAT and osteoporosis (self-reported). Results of sensitivity analyses, except for MR-Egger, were directionally consistent with the IVW method. The MR-Egger analysis revealed a conflicting point estimate for the association between SUGAR and osteoporosis (self-reported) in comparison to the main analysis (IVW method). No horizontal pleiotropy was observed in the MR-Egger intercept test (shown in

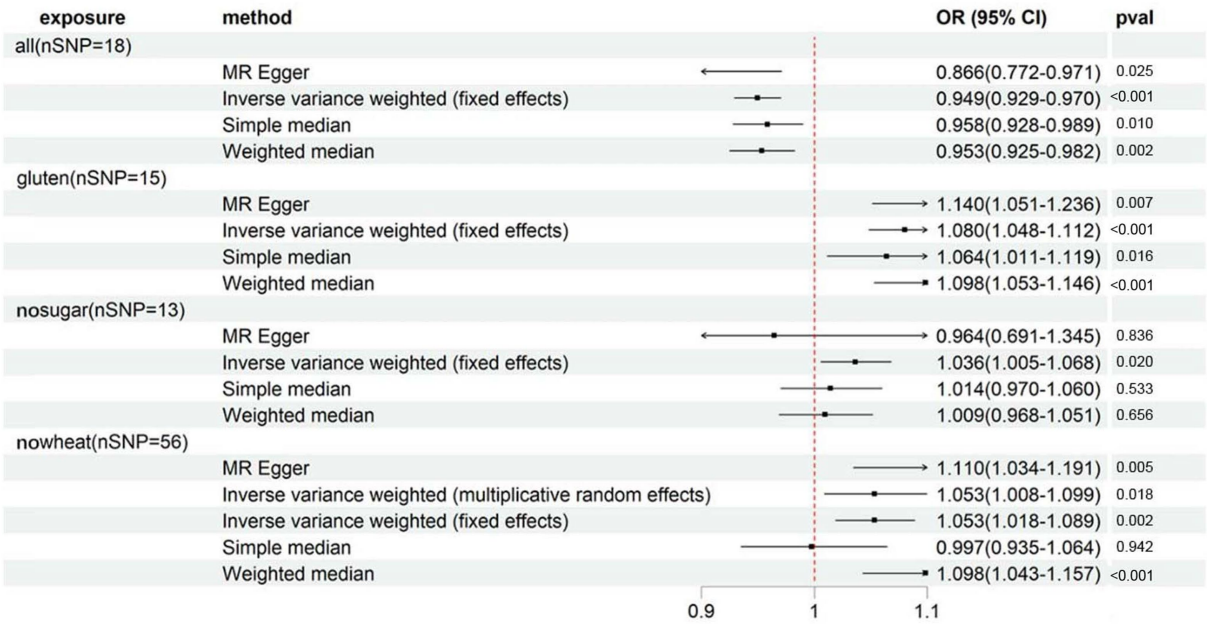


FIGURE 2
Forest plot showing results from Mendelian randomization study to assess associations between special diets and osteoporosis (self-reported). nSNP, number of single-nucleotide polymorphisms; OR, odds ratio; CI, confidence interval; all, Eggs, dairy, wheat, sugar: I eat all of the above; gluten, Type of special diet followed: Gluten-free; nosugar, Never eat sugar: Sugar or foods/drinks containing sugar; nowheat, Never eat wheat: Wheat or products containing wheat.

Supplementary Table S5). Lastly, the MR-PRESSO Global Test identified no outliers in the four specific diets (refer to Supplementary Table S5). In summary, significant associations between these diets and osteoporosis (self-reported) were visually confirmed (shown in Supplementary Figures S1–S4).

In order to argue the study's credibility, a secondary outcome - osteoporosis diagnoses - was incorporated as a validation measure. Despite the smaller number of cases (1976) for diagnosed osteoporosis compared to self-reported osteoporosis (number of cases: 7,547), the clearly diagnosed osteoporosis patients provide high reliability to the sample's osteoporosis diagnosis. Supplementary Table S6 and Figure 3 indicate that although the 4 specialized diets are also linked to osteoporosis diagnoses, the strength of their association differs considerably from that of self-reported osteoporosis. Only GLUTEN exhibits a significant association with osteoporosis diagnoses. The sensitivity analyses were directionally consistent with the IVW method. MR-Egger intercept testing revealed horizontal pleiotropy in ALL and NOWHEAT (shown in Supplementary Table S7), indicating that there are unknown factors, other than ALL and NOWHEAT, that affect osteoporosis diagnoses. Consequently, we cannot establish a causal relationship between the two specialized diets and osteoporosis diagnoses. Finally, the association between GLUTEN, NOSUGAR, and osteoporosis diagnoses is visualized in Supplementary Figures S5, S6.

3.2 Special diet and bone mineral density

The BMD serves as a valuable indicator for the diagnosis of osteoporosis. In this study, we analyzed five distinct BMD sites separately to determine the specific impact of specialized diets on osteoporosis. Figure 4 presents the selected sites along with concise information.

As evidenced by Supplementary Table S8 and Figure 5, there was a suggestive association between genetically predicted ALL (OR: 3.735, 95%CI: 1.312–10.637, $p = 1.36E-02$) and an increase in Ultradistal forearm BMD. Cochran's Q test did not reveal any heterogeneity between the IVs of ALL and Ultradistal forearm BMD (shown in Supplementary Table S9). In conducting sensitivity analysis, the MR-Egger method yielded a point estimate that was consistent with that of the IVW method, and no horizontal pleiotropy was detected by the MR-Egger regression intercept (shown in Supplementary Table S9). Moreover, further global tests did not uncover any outliers (shown in Supplementary Table S9).

As per Supplementary Table S10 and Figure 6, we observed significant associations between heel BMD and ALL (OR: 0.801, 95%CI: 0.685–0.937, $p = 5.59E-03$), GLUTEN (OR: 0.562, 95%CI: 0.426–0.742, $p = 4.69E-05$), and NOWHEAT (OR: 0.683, 95%CI: 0.523–0.891, $p = 5.07E-03$) in the fixed-effects IVW method. However, heterogeneity was observed in all 3 special diets (PCochran's $Q < 0.05$), indicating a possible bias in the fixed-effects IVW estimation (Supplementary Table S11). On the other hand, the random-effects IVW method did not show any association between ALL, GLUTEN, NOWHEAT, and heel BMD.

The MR-Egger sensitivity analysis indicated a contradictory point estimation of the association between GLUTEN and heel BMD compared to the main analysis (IVW method), but no horizontal pleiotropy was identified in the MR-Egger intercept test (Supplementary Table S11). The MR-PRESSO Global Test detected outliers in all 3 special diets (Supplementary Table S11), and after their exclusion, there was no association observed either.

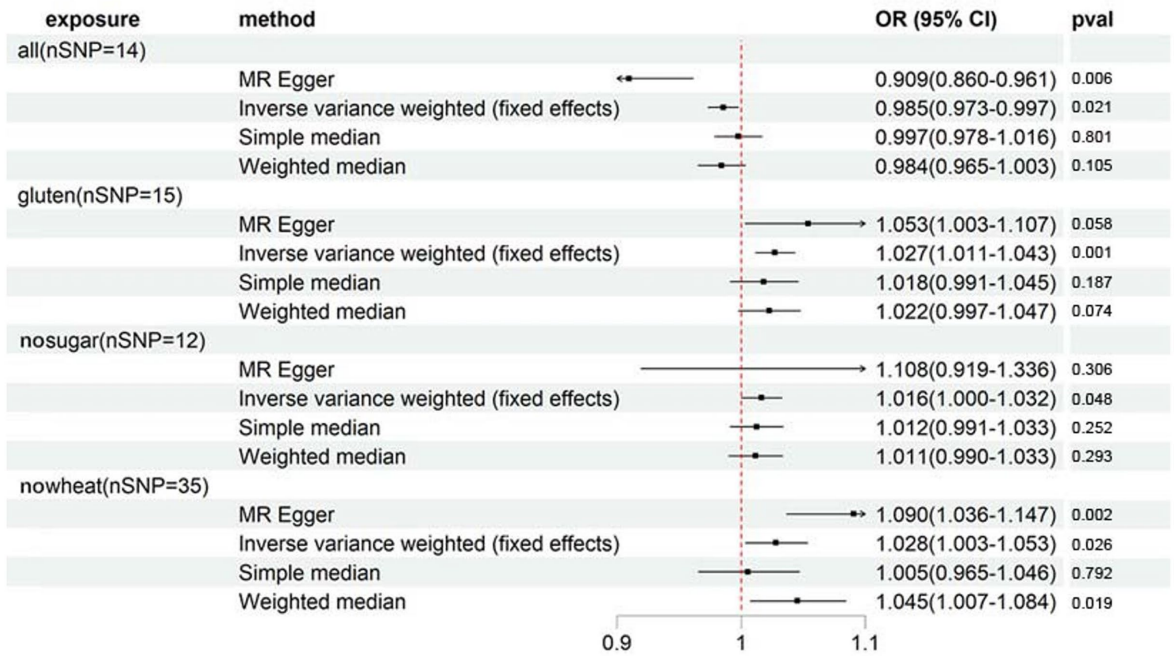


FIGURE 3
Forest plot showing results from Mendelian randomization study to assess associations between special diets and osteoporosis (diagnoses). nSNP, number of single-nucleotide polymorphisms; OR, odds ratio; CI, confidence interval; all, Eggs, dairy, wheat, sugar: I eat all of the above; gluten, Type of special diet followed: Gluten-free; nosugar, Never eat sugar: Sugar or foods/drinks containing sugar; nowheat, Never eat wheat: Wheat or products containing wheat.

There exists no correlation between the BMD of the residual 3 portions and specialized diets. Specific outcomes are exhibited in Supplementary Tables S12–S17.

4 Discussion

In this two-sample MR study, we explicated the correlation between 8 special diets and the incidence of osteoporosis or BMD. Also, we discovered a highly plausible relationship between GLUTEN and osteoporosis. Furthermore, we have also observed suggestive connections between ALL, NOSUGAR, and NOWHEAT, and osteoporosis.

Gluten-free diet (GFD) specifically eliminates gluten of diet, which is the chief protein constituent in wheat, rye, and barley (23). And it is also the primary cause of Celiac Disease (CD). Currently, the sole effective treatment for CD is a stringent lifelong GFD (24). As the implementation of a specialized GFD has been shown to be fraught with challenges and difficulties (23, 25), we deem it unlikely for individuals to undertake stringent GFD autonomously without medical guidance. Therefore, in this study, we believe that the crowd of GFD overlaps with the crowd of CD. And CD's various complications, including osteoporosis.

The main cause for the association between CD and low BMD lies primarily in the characteristic malabsorption, resulting in deficiencies in vitamin D and intestinal calcium absorption. In addition, given the close hormonal interrelationship, deficiencies in calcium and vitamin D stimulate the secretion of parathormone (PTH), and hyperparathyroidism itself becomes another contributing factor, as elevated levels of PTH have been linked to bone mass loss through the activation of bone resorption (26). Combining with previous research (26–28), it is shown that GFD only exhibits significant improvement in BMD for CD patients initially presenting with secondary hyperparathyroidism, low serum calcium, and vitamin D. We can infer that gluten initiates the onset of CD in specific populations, and the occurrence of CD affects bone metabolism, leading to declining BMD and the manifestation of osteoporosis. According to this speculation, the elimination of the pathogenic source is the clearest approach, where lifelong abstinence from gluten should improve both CD and BMD simultaneously. Existing studies have also confirmed that while GFD cannot fully restore BMD to normal levels, it still exerts a positive effect on BMD improvement (29).

However, it is important to note that gluten merely acts as a "key" to trigger the onset of CD in specific populations, and the direct impact of gluten on the skeletal system has not been investigated. The establishment of steady-state in the skeletal system relies on the dynamic balance between bone formation and resorption (30). GFD blocks the entry of gluten to halt the destructive effects of CD on the skeletal system, reducing the outflow of bone mineral loss. However, if gluten is a component of bone formation, limiting its entry would impede new bone formation, making it challenging for BMD to fully recover to a normal state, which aligns with the aforementioned research findings (29). Similarly, the most significant correlation observed in this study is the promotive effect of GFD on the incidence of osteoporosis. Aligning with the superior strategy of GFD (gluten is the protein in wheat, so avoiding wheat will inevitably avoid gluten), the avoidance of wheat (NOWHEAT) exhibits the same outcome, while the consumption of wheat (ALL) in contrast demonstrates an

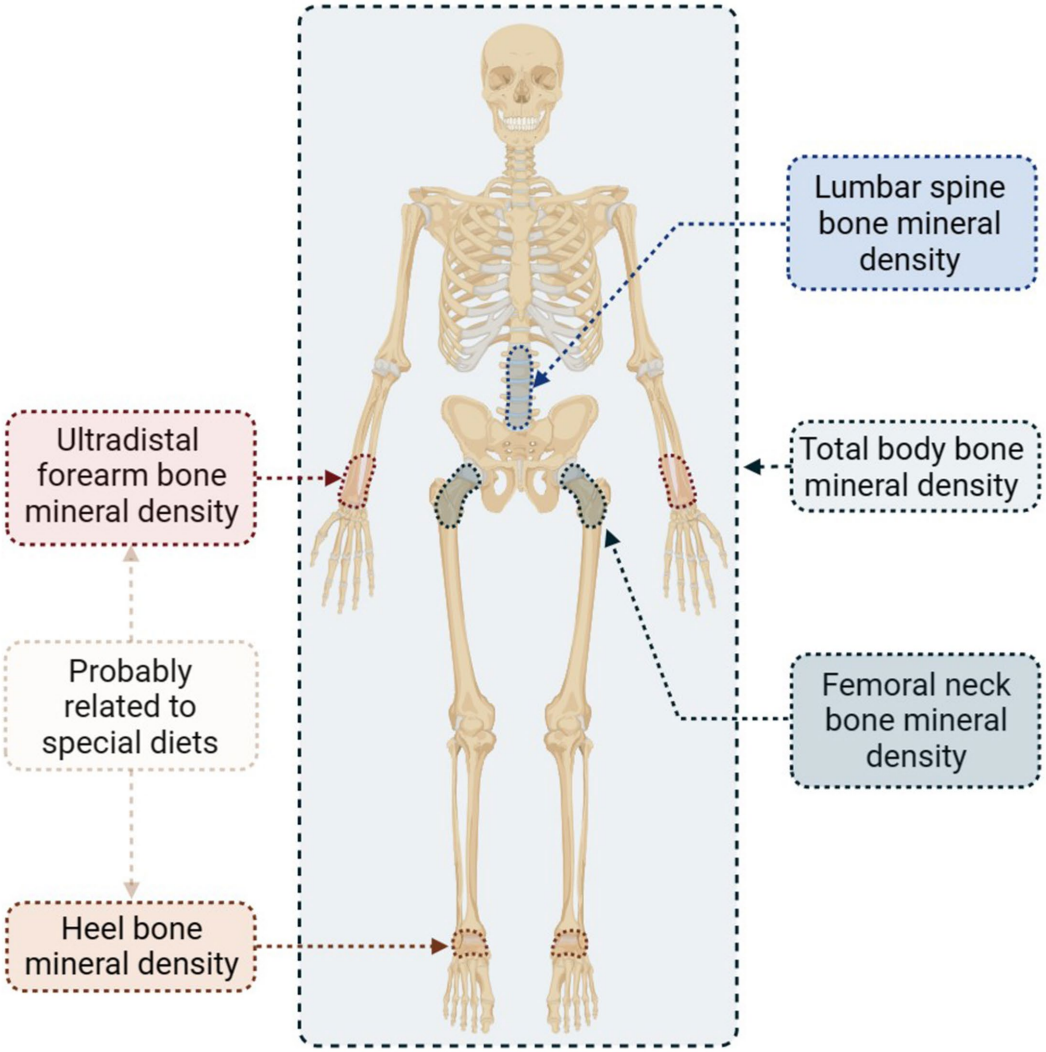


FIGURE 4
Bone mineral density selected sites and brief results.

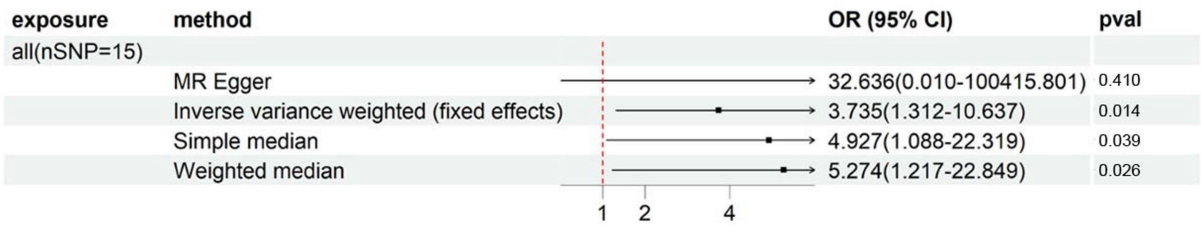


FIGURE 5
Forest plot showing results from Mendelian randomization study to assess associations between special diets and Ultradistal forearm BMD. nSNP, number of single-nucleotide polymorphisms; OR, odds ratio; CI, confidence interval; all, Eggs, dairy, wheat, sugar: I eat all of the above.

inhibitory effect on the risk of osteoporosis. It is thus reasonable to believe that gluten merely triggers the onset of CD in specific populations without direct bone resorption effects, and it may even have a role in bone formation or promoting osteogenesis.

In accordance with a systematic review conducted in 2018, excessive consumption of sugar potentially carries the risk for osteoporosis (31). This hypothesis was initially confirmed in 2023 through a cohort study of 6,620 young individuals aged between 18 and 23 in Brazil, which demonstrated a correlation between frequent intake of sugary drinks and low lumbar BMD (32). While there are currently no further clinical studies examining the impact of dietary sugar intake on osteoporosis, the effect of sugar on BMD is worth

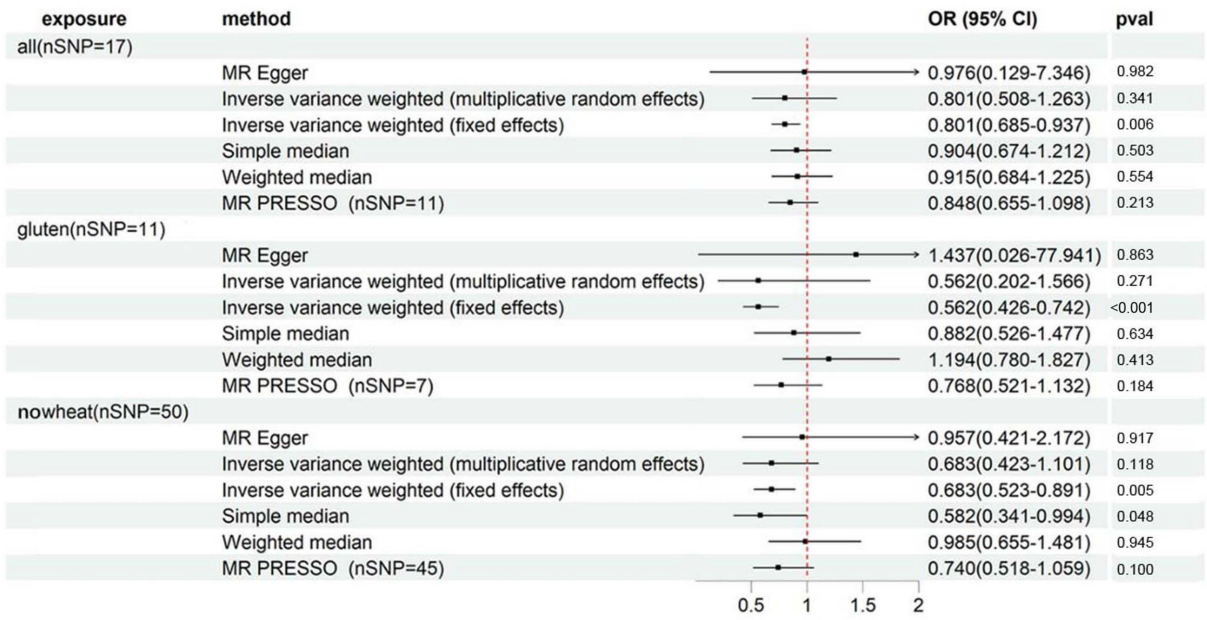


FIGURE 6
Forest plot showing results from Mendelian randomization study to assess associations between special diets and heel BMD. nSNP, number of single-nucleotide polymorphisms; OR, odds ratio; CI, confidence interval; all, Eggs, dairy, wheat, sugar: I eat all of the above; gluten, Type of special diet followed: Gluten-free; nowheat, Never eat wheat: Wheat or products containing wheat.

considering. Diabetes, a metabolic condition characterized by hyperglycemia (33), is believed to affect bone remodeling and turnover, leading to defects in bone material quality. Apart from other organs, diabetes affects bone through impairment of glucose metabolism, toxic effects of glucose oxidative derivatives, and impairment of bone microvascular and muscle endocrine function (34). Recent animal experiments have shown that the "high glucose and high-fat diet"-induced ferroptosis in osteoblasts may be the primary cause of osteoporosis in diabetes through the activation of the METTL3/ASK1-p38 signaling pathway (35, 36). Combining the preliminary results of the relationship between sugar intake and osteoporosis obtained in this study, it is apparent that both excess and abstain from sugar consumption can lead to the onset of osteoporosis. Given the essential relationship between sugar and BMD, we can further hypothesize that since there needs to be a steady state between sugar and BMD, sugar may have an effect on BMD, and bone may also have an impact on glucose metabolism. This conjecture was confirmed in a 2020 study (37). Consequently, for the management of diabetic patients, commencing with the improvement of the bone environment may be a novel and promising idea.

Contrary to conventional wisdom, which posits the bone-strengthening benefits of milk and dairy products (38, 39), this study yielded unexpected results by indicating no correlation between the avoidance of dairy products and osteoporosis. This finding can be interpreted in a number of ways. For instance, dietary supplements are sufficient in compensating for the nutritional deficiency caused by the rejection of dairy products or dairy products themselves have no impact on bone health. While certain studies have suggested that dairy products play an irreplaceable role in bone health (40), meta-analyses of numerous large-scale clinical cohorts have demonstrated that the positive effects of consuming milk and dairy products on osteoporosis and fracture risk, as reported in cross-sectional and case–control studies, were not found in cohorts. Due to the heightened reliability of cohort studies over case–control studies, it is not the case that there exists a link between dairy products and osteoporosis and fractures (41, 42). This discovery merits a comprehensive investigation into the relationship between dairy products and bone health.

The impact of ceasing egg intake on osteoporosis was not observed in this study, despite the fact that eggs constitute a primary source of daily protein intake. Nonetheless, in contrast to the equivocal role of dairy products, research has suggested that eggs may have a beneficial effect on bone health. A cross-sectional study found a favorable association between whole egg consumption and bone mineral density (43). Additionally, an oral peptide derived from egg yolk is believed to promote bone repair in mice (44), and the duck egg white-derived peptide VSEE (Val-ser-glu-glu) has been demonstrated to enhance bone repair through the wnt/β-catenin signaling pathway, as well as regulate bone and lipid metabolism through gut microbiota (45). Furthermore, a retrospective study in Spain demonstrated that eggs also regulate osteoporosis induced by vitamin D deficiency (46). In summary, while eggs may impact bone health, the mechanisms underlying their effects are multifaceted, and abstaining from egg consumption is not detrimental to bone health.

Some scholars contend that the vegetarian diet, which engender controversy, can lead to a deficiency of calcium and vitamin D, potentially resulting in adverse impacts on bone mineral density (47, 48). A cross-sectional study conducted in Poland has suggested that vegetarian diets may be associated with an increased risk of nutrient deficiencies, as well as decreased bone mineral content and height, although the nutrient deficiency was insignificant among vegetarians (49). However, recent studies have presented differing perspectives. One three-year retrospective survey found no link between vegetarianism and BMD, except for women aged 40–55 (50). Additionally, despite the distinct acid–base profiles of vegetarians and omnivores, no association was found between bone health and the range from alkaline to low acid load (51). Vegetarian diets typically contain many other micronutrients vital

for bone health, including vitamins C and K, carotenoids, potassium, and magnesium, among others (52). Thus, taking into account the conclusions of MR, this study proposes that there may be no association between a vegetarian diet and osteoporosis.

The study on the low-calorie diet is the most equivocal among investigations. Not only was there no correlation with osteoporosis in this study, but the inquiry into the relationship between calorie restriction (CR) and bone health has not been renewed for a prolonged duration. In 2014, a study alluded to the unfavorable effects of CR on trabecular and cortical bone (53), but in the updated systematic review of 2019, it was demonstrated that CR appears to decrease BMD, while it does not appear to impact bone integrity (54).

One of the merits of this study is the exploration of the relationship between osteoporosis and multiple special diets through MR analysis, which renders it the most extensive study to characterize the correlations between diet and osteoporosis. Moreover, the MR design itself remains impervious to residual clutter. By employing various MR methods to eliminate SNPs associated with multiple special diets, we have eliminated the effects of potential pleiotropy on the results, thus making it less likely for horizontal pleiotropy to disrupt our findings. Furthermore, the genetic variants in special diets and osteoporosis are derived from summary-level data from GWAS with large sample sizes, which is another advantage of this study.

However, this study also has some limitations. Firstly, although we have taken control measures, IVs may still have unmeasurable confounding and has affected the outcome as a result. Secondly, many IVs rely on monotonicity conditions, which means estimating the IVs effect under monotonicity often involves an unrecognized subgroup in the study population. Using subgroup results to guide decision-making is not an ideal method, and if more information is provided, the correlation between the subgroup effects will significantly increase (55). Our IVs are genetic variants identified from the United Kingdom Biobank, and we only know the size of the subgroup of IV origins, while the specific characteristics of this subgroup remain unknown to us. Additionally, it is difficult to quantify the sensitivity of effect estimation to monotonicity bias. Therefore, our analysis may violate monotonicity, which may render our results unsuitable for an extension to a larger population. Thirdly, while bone mineral density is the gold standard for the diagnosis of osteoporosis, only the Ultradistal forearm BMD suggested an association with special diets in this study. However, this index is usually not used in the clinical diagnosis of osteoporosis. Given that special diets are associated with osteoporosis, but almost not associated with its diagnostic criteria, we believe that a larger database should be used to verify the results. Finally, although the MR method can provide associational estimates, the results reported here cannot automatically be assumed to be causal because there is considerable room for other explanations. For example, GFD is not only limited to gluten but also other nutrients because of the elimination of certain grains. Some people use pre-prepared processed foods that are GF, which may have higher levels of sodium. Others might consume more GF starches such as potatoes and rice, therefore, overall nutrients from GFD could be quite variable and if not executed appropriately such diets could lead to nutrient deficiency beyond GF. Many people use GF diets even though they do not have CD either because they suspect they have gluten allergy or they think GF diets are healthier due to perhaps low carbohydrate levels. But we think this study, it is still one of the results with higher credibility and has considerable in-depth value.

Therefore, our findings should be interpreted with caution, and well-designed prospective studies are still needed to confirm our results in the future.

5 Conclusion

This work characterizes the correlations between genetically predicted special diets and osteoporosis. Our study preliminarily showed that simultaneous intake of eggs, dairy, wheat, and sugar could significantly reduce the risk of osteoporosis; and the abstain of gluten, wheat, and sugar could raise the risk of osteoporosis. Moreover, based on the results, a hypothesis was put forward that apart from CD, GFD for treating CD also caused osteoporosis. Our results should be interpreted carefully, and well-designed prospective studies are still needed to confirm our findings in the future.

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

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

Author contributions

CZ: Conceptualization, Methodology, Software, Investigation, Resources, Data curation, Writing – original draft, Project administration. LY: Validation, Visualization, Writing – review & editing. CL: Validation, Formal analysis, Writing - original draft. HM: Formal analysis, Writing – original draft. FY: Methodology, Validation, Funding acquisition, Writing – review & editing. LC: Conceptualization, Writing – review & editing, Supervision.

Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. This research was funded by the National Natural Science Foundation project (No. 81973889).

Acknowledgments

The completion of this research project would not have been possible without the generous support and contributions of various individuals and organizations. The authors would like to express our sincere gratitude to the creators and administrators of the IEU and UK Biobank databases for providing access to their extensive datasets. These resources played a vital role in the analysis and interpretation of our findings. Additionally, the authors would like to extend our heartfelt appreciation to Yang Xinyi from University College London for her invaluable academic translation services. Her meticulous and timely translations greatly enhanced the accuracy and clarity of our research.

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

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1364735/full#supplementary-material

References

1. Harris K, Zagar CA, Lawrence KV. Osteoporosis: common questions and answers. *Am Fam Physician*. (2023) 107:238–46.

2. Waldbaum JDH, Xhumari J, Akinsuyi OS, Arjmandi B, Anton S, Roesch LFW. Association between Dysbiosis in the gut microbiota of primary osteoporosis patients and bone loss. *Aging Dis*. (2023) 14:2081–95. doi: 10.14336/AD.2023.0425

3. Papadopoulou SK, Papadimitriou K, Voulgaridou G, Georgaki E, Tsotidou E, Zantidou O, et al. Exercise and nutrition impact on osteoporosis and sarcopenia-the incidence of Osteosarcopenia: a narrative review. *Nutrients*. (2021) 13:4499. doi: 10.3390/nu13124499

4. Muñoz-Garach A, García-Fontana B, Muñoz-Torres M. Nutrients and dietary patterns related to osteoporosis. *Nutrients*. (2020) 12:1986. doi: 10.3390/nu12071986

5. Kanellakis S, Moschonis G, Tenta R, Schaafsma A, van den Heuvel EG, Papaioannou N, et al. Changes in parameters of bone metabolism in postmenopausal women following a 12-month intervention period using dairy products enriched with calcium, vitamin D, and phylloquinone (vitamin K(1)) or menaquinone-7 (vitamin K (2)): the postmenopausal health study II. *Calcif Tissue Int*. (2012) 90:251–62. doi: 10.1007/s00223-012-9571-z

6. Larsson SCJCoil. Mendelian randomization as a tool for causal inference in human nutrition and metabolism. *Curr Opin Lipidol*. (2021) 32:1–8. doi: 10.1097/MOL.0000000000000721

7. Davey Smith G, Hemani G. Mendelian randomization: genetic anchors for causal inference in epidemiological studies. *Hum Mol Genet*. (2014) 23:R89–98. doi: 10.1093/hmg/ddu328

8. Emdin CA, Khera AV, Kathiresan S. Mendelian randomization. *JAMA*. (2017) 318:1925–6. doi: 10.1001/jama.2017.17219

9. Rusk N. The UK biobank. *Nat Methods*. (2018) 15:1001. doi: 10.1038/s41592-018-0245-2

10. Turley P, Walters RK, Maghzian O, Okbay A, Lee JJ, Fontana MA, et al. Multi-trait analysis of genome-wide association summary statistics using MTAG. *Nat Genet*. (2018) 50:229–37. doi: 10.1038/s41588-017-0009-4

11. Yan H, Jin X, Zhang C, Zhu C, He Y, Du X, et al. Associations between diet and incidence risk of lung cancer: a Mendelian randomization study. *Front Nutr*. (2023) 10:1149317. doi: 10.3389/fnut.2023.1149317

12. Kamat MA, Blackshaw JA, Young R, Surendran P, Burgess S, Danesh J, et al. PhenoScanner V2: an expanded tool for searching human genotype–phenotype associations. *Int Conf Intell Syst Mol Biol Proceed*. (2019) 35:4851–3. doi: 10.1093/bioinformatics/btz469

13. Burgess S, Thompson SGCRP CHD Genetics Collaboration. Avoiding bias from weak instruments in Mendelian randomization studies. *Int J Epidemiol*. (2011) 40:755–64. doi: 10.1093/ije/dyr036

14. Elsworth B, Lyon M, Alexander T, Liu Y, Matthews P, Hallett J, et al. (2020). The MRC IEU OpenGWAS data infrastructure. 2020.

15. Burgess S, Butterworth A, Thompson SG. Mendelian randomization analysis with multiple genetic variants using summarized data. *Genet Epidemiol*. (2013) 37:658–65. doi: 10.1002/gepi.21758

16. Bowden J, Davey Smith G, Haycock PC, Burgess S. Consistent estimation in Mendelian randomization with some invalid instruments using a weighted median estimator. *Genet Epidemiol Suppl*. (2016) 40:304–14. doi: 10.1002/gepi.21965

17. Burgess S, Thompson SG. Interpreting findings from Mendelian randomization using the MR-egger method. *Eur J Epidemiol*. (2017) 32:377–89. doi: 10.1007/s10654-017-0255-x

18. Verbanck M, Chen C-Y, Neale B, do R. Detection of widespread horizontal pleiotropy in causal relationships inferred from Mendelian randomization between complex traits and diseases. *Nat Genet*. (2018) 50:693–8. doi: 10.1038/s41588-018-0099-7

19. Greco M FD, Minelli C, Sheehan NA, Thompson JR. Detecting pleiotropy in Mendelian randomisation studies with summary data and a continuous outcome. *Stat Med*. (2015) 34:2926–40. doi: 10.1002/sim.6522

20. Bowden J, Del Greco MF, Minelli C, Davey Smith G, Sheehan N, Thompson J. A framework for the investigation of pleiotropy in two-sample summary data Mendelian randomization. *Stat Med*. (2017) 36:1783–02. doi: 10.1002/sim.7221

21. Bowden J, Davey Smith G, Burgess S. Mendelian randomization with invalid instruments: effect estimation and bias detection through egger regression. *Int J Epidemiol*. (2015) 44:512–25. doi: 10.1093/ije/dyv080

22. Hemani G, Zheng J, Elsworth B, Wade KH, Haberland V, Baird D, et al. The MR-base platform supports systematic causal inference across the human phenome. *eLife*. (2018) 7:e34408. doi: 10.7554/eLife.34408

23. Catassi C, Verdu EF, Bai JC, Lionetti E. Coeliac disease. *Lancet (London, England)*. (2022) 399:2413–26. doi: 10.1016/S0140-6736(22)00794-2

24. Caio G, Volta U, Sapone A, Leffler DA, De Giorgio R, Catassi C, et al. Celiac disease: a comprehensive current review. *BMC Med*. (2019) 17:142. doi: 10.1186/s12916-019-1380-z

25. Muhammad H, Reeves S, Jeanes YM. Identifying and improving adherence to the gluten-free diet in people with coeliac disease. *Proc Nutr Soc*. (2019) 78:418–25. doi: 10.1017/S002966511800277X

26. Ballestero-Fernández C, Varela-Moreiras G, Úbeda N, Alonso-Aperte E. Nutritional status in Spanish adults with celiac disease following a long-term gluten-free diet is similar to non-celiac. *Nutrients*. (2021) 13:1626. doi: 10.3390/nu13051626

27. Kemppainen T, Kröger H, Janatuinen E, Arnala I, Lamberg-Allardt C, Kärkkäinen M, et al. Bone recovery after a gluten-free diet: a 5-year follow-up study. *Bone*. (1999) 25:355–60. doi: 10.1016/S8756-3282(99)00171-4

28. Valdimarsson T, Toss G, Löfman O, Ström M. Three years' follow-up of bone density in adult coeliac disease: significance of secondary hyperparathyroidism. *Scand J Gastroenterol*. (2000) 35:274–80. doi: 10.1080/003655200750024146

29. Oliveira DDC, da Silva DCG, Kawano MM, de Castro CT, Pereira M. Effect of a gluten-free diet on bone mineral density in children and adolescents with celiac disease: systematic review and meta-analysis. *Crit Rev Food Sci Nutr*. (2022) 1–11. doi: 10.1080/10408398.2022.2153103

30. Ensrud KE, Crandall CJ. Osteoporosis. *Ann Intern Med*. (2017) 167:ITC17. doi: 10.7326/AITC201708010

31. DiNicolantonio JJ, Mehta V, Zaman SB, O'Keefe JH. Not salt but sugar as Aetiological in osteoporosis: a review. *Mo Med*. (2018) 115:247–52.

32. Bragança M, Bogea EG, de Almeida Fonseca Viola PC, dos Santos Vaz J, Confortin SC, Menezes AMB, et al. High consumption of sugar-sweetened beverages is associated with low bone mineral density in Young people: the Brazilian birth cohort consortium. *Nutrients*. (2023) 15:324. doi: 10.3390/nu15020324

33. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. (2013) 36:S67–74. doi: 10.2337/dc13-S067

34. Lecka-Czernik B. Diabetes, bone and glucose-lowering agents: basic biology. *Diabetologia*. (2017) 60:1163–9. doi: 10.1007/s00125-017-4269-4

35. Lin Y, Shen X, Ke Y, Lan C, Chen X, Liang B, et al. Activation of osteoblast ferroptosis via the METTL3/ASK1-p38 signaling pathway in high glucose and high fat (HGHF)-induced diabetic bone loss. *FASEB J*. (2022) 36:e22147. doi: 10.1096/fj.202101610R

36. Ma H, Wang X, Zhang W, Li H, Zhao W, Sun J, et al. Melatonin suppresses Ferroptosis induced by high glucose via activation of the Nrf2/HO-1 signaling pathway in type 2 diabetic osteoporosis. *Oxidative Med Cell Longev*. (2020) 2020:1–18. doi: 10.1155/2020/9067610

37. Cipriani C, Colangelo L, Santori R, Renella M, Mastrantonio M, Minisola S, et al. The interplay between bone and glucose metabolism. *Front Endocrinol*. (2020) 11:122. doi: 10.3389/fendo.2020.00122

38. LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, et al. The clinician's guide to prevention and treatment of osteoporosis. *Osteoporosis Int J*. (2022) 33:2049–102. doi: 10.1007/s00198-021-05900-y

39. Rizzoli R. Dairy products and bone health. *Aging Clin Exp Res*. (2022) 34:9–24. doi: 10.1007/s40520-021-01970-4

40. Ratajczak AE, Zawada A, Rychter AM, Dobrowolska A, Krela-Kaźmierczak I. Milk and dairy products: good or bad for human bone? Practical dietary recommendations for the prevention and Management of Osteoporosis. *Nutrients*. (2021) 13:1329. doi: 10.3390/nu13041329

41. Malmir H, Larijani B, Esmaillzadeh A. Consumption of milk and dairy products and risk of osteoporosis and hip fracture: a systematic review and Meta-analysis. *Crit Rev Food Sci Nutr*. (2020) 60:1722–37. doi: 10.1080/10408398.2019.1590800

42. Matía-Martín P, Torrego-Ellacuría M, Larrad-Sainz A, Fernández-Pérez C, Cuesta-Triana F, Rubio-Herrera M. Effects of Milk and dairy products on the prevention of osteoporosis and osteoporotic fractures in Europeans and non-Hispanic whites from North America: a systematic review and updated Meta-analysis. *Adv Nutr*. (2019) 10:S120–43. doi: 10.1093/advances/nmy097

43. Pujia R, Ferro Y, Maurotti S, Mare R, Arturi F, Montalcini T, et al. Relationship between osteoporosis, multiple fractures, and egg intake in healthy elderly. *J Mid-Life Health*. (2021) 12:287–93. doi: 10.4103/jmh.jmh_118_21

44. Kitaura Y, Nakamura U, Awada C, Yamaguchi M, Kim M, Ikeda Y, et al. Orally administrable peptides derived from egg yolk promote skeletal repair and ameliorate degenerative skeletal disorders in mouse models. *Regenerative Ther*. (2022) 21:584–95. doi: 10.1016/j.reth.2022.11.002

45. Guo D, Liu W, Zhang X, Zhao M, Zhu B, Hou T, et al. Duck egg white-derived peptide VSEE (Val-Ser-Glu-Glu) regulates bone and lipid metabolisms by Wnt/β-catenin signaling pathway and intestinal microbiota. *Mol Nutr Food Res*. (2019) 63:e1900525. doi: 10.1002/mnfr.201900525

46. Rodríguez-Rodríguez E, Aparicio Vizuete A, Sánchez-Rodríguez P, Lorenzo Mora AM, López-Sobaler AM, et al. Vitamin D deficiency in Spanish population. Importance of egg on nutritional improvement. *Nutricion Hospitalaria*. (2019) 36:3–7. doi: 10.20960/nh.02798

47. Ambroszkiewicz J, Klemarczyk W, Gajewska J, Chełchowska M, Franek E, Laskowska-Klita T. The influence of vegan diet on bone mineral density and biochemical bone turnover markers. *Pediatr Endocrinol Diabetes Metab*. (2010) 16:201–4.

48. Iguacel I, Miguel-Berges ML, Gómez-Bruton A, Moreno LA, Julián C. Veganism, vegetarianism, bone mineral density, and fracture risk: a systematic review and meta-analysis. *Nutr Rev*. (2019) 77:1–18. doi: 10.1093/nutrit/nuy045

49. Desmond MA, Sobiecki JG, Jaworski M, Płudowski P, Antoniewicz J, Shirley MK, et al. Growth, body composition, and cardiovascular and nutritional risk of 5- to 10-y-old children consuming vegetarian, vegan, or omnivore diets. *Am J Clin Nutr*. (2021) 113:1565–77. doi: 10.1093/ajcn/nqaa445

50. Chuang TL, Koo M, Chuang MH, Lin CH, Huang CH, Wang YF. Changes in bone mineral density and trabecular bone score over time between vegetarian and non-vegetarian middle-aged and older women: a three-year retrospective medical record review. *Int J Environ Res Public Health*. (2022) 19:2445. doi: 10.3390/ijerph19042445

51. Penczynski KJ, Remer T, Menzel J, Abraham K, Weikert C. Urinary potential renal acid load (uPRAL) among vegans versus omnivores and its association with bone health in the cross-sectional risks and benefits of a vegan diet study. *Nutrients*. (2022) 14:4668. doi: 10.3390/nu14214468

52. Galchenko A, Gapparova K, Sidorova E. The influence of vegetarian and vegan diets on the state of bone mineral density in humans. *Crit Rev Food Sci Nutr*. (2023) 63:845–61. doi: 10.1080/10408398.2021.1996330

53. Ahn H, Seo DH, Kim HS, Choue R. Calorie restriction aggravated cortical and trabecular bone architecture in ovariectomy-induced estrogen-deficient rats. *Nutr Res*. (2014) 34:707–13. doi: 10.1016/j.nutres.2014.07.006

54. Veronese N, Reginster JY. The effects of calorie restriction, intermittent fasting and vegetarian diets on bone health. *Aging Clin Exp Res*. (2019) 31:753–8. doi: 10.1007/s40520-019-01174-x

55. Swanson SA, Hernán MA. The challenging interpretation of instrumental variable estimates under monotonicity. *Int J Epidemiol*. (2018) 47:1289–97. doi: 10.1093/ije/dyx038

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 05 July 2024
DOI 10.3389/fpubh.2024.1403496

OPEN ACCESS

EDITED BY
Yun Gao,
Sichuan University, China

REVIEWED BY
Yi Zeng,
Zhongnan University of Economics and Law, China
Antonio Soares,
Pernambucana College of Health, Brazil

*CORRESPONDENCE
Józefa Dąbek
✉ jdabek@sum.edu.pl

RECEIVED 19 March 2024
ACCEPTED 24 June 2024
PUBLISHED 05 July 2024

CITATION
Dąbek J, Szynal M, Sierka O, Łebek E and Kulik H (2024) Has learning gone to waste?—Health-promoting behaviors of seniors. *Front. Public Health* 12:1403496. doi: 10.3389/fpubh.2024.1403496

Has learning gone to waste?—Health-promoting behaviors of seniors

Józefa Dąbek[1]*, Magdalena Szynal[1], Oskar Sierka[2], Ewelina Łebek[2] and Halina Kulik[3]

[1]Department of Cardiology, Faculty of Health Sciences in Katowice, Medical University of Silesia in Katowice, Katowice, Poland, [2]Doctoral School of the Medical University of Silesia in Katowice, Medical University of Silesia in Katowice, Katowice, Poland, [3]Department of Propaedeutics of Nursing, Faculty of Health Sciences in Katowice, Medical University of Silesia in Katowice, Katowice, Poland

Objective: Regardless of the fact that Universities of Third Age (UTA's) are becoming more and more popular among seniors there are not many available studies examining the impact of conducted educational activities on seniors' adherence to health-promoting activities. The aim of the study was to compare health behaviors (e.g.,: physical activity, eating habits, alcohol consumption, tobacco smoking, preventive tests performance) between seniors attending and not attending UTA's classes.

Methods: The study involved 631 (100%) seniors aged 60–92 years (x =70.28 ± 6.09 years). The majority of the study group were women (475; 75.28%). To conduct the study, a proprietary questionnaire was used, consisting of questions regarding the discussed topic and basic questions including: age, gender, place of residence and education. Polish versions of standardized questionnaire—*"My eating behaviors"* examine eating behaviors of the respondents. The Chi^2 test was used for qualitative data, and for quantitative data—the Mann-Whitney U test (No normal distribution: T S-W< 0.001). Linear and logistic regression models were used to check whether the associations would remain after adjustments for potential cofounders. The level of statistical significance was set at $\alpha < 0.05$.

Results: Number of seniors participating in UTA's activities was higher in terms of engaging in: actively spending free time (261; 73.73% vs. 93; 26.27%; $p < 0.001$), regular physical activity (270; 76.27% vs. 133; 48.01%; $p < 0.001$), self-assessment of physical activity (259; 73.16% vs. 95; 26.84%; $p = 0.004$), duration of physical activity (<0.001), past tobacco smoking (133; 37.57 vs. 76; 27.44%; $p = 0.007$) and alcohol consumption depending on the habit frequency ($p < 0.001$). Number of seniors not participating in UTA's classes was lower in terms of: regular annual dental controls (161; 58.12%; vs. 265; 74.86%; $p < 0.001$), regular self-examination of breasts/testicles (148; 53.43% vs. 218; 61.58%; $p = 0.04$) and regular laboratory tests (232; 83.75% vs. 318; 89.83%; $p = 0.02$).

Conclusions: Health-promoting behaviors of seniors attending classes at the UTA's were more correct in terms of physical activity, adequate attendance with preventive test and worst in terms of alcohol consumption. Overall picture allows to conclude that participation in UTA's classes seems to have a positive impact on the examined health-promoting behaviors of the surveyed seniors.

KEYWORDS

seniors, healthy behavior, Universities of Third Age, education, aging

Introduction

The World Health Organization (WHO) has defined health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" (1, 2).

According to Lalonde's concept of "health fields", it can be clearly seen that lifestyle has the greatest impact on human health and constitutes 50% of the factors determining it. Other factors are: the environment (all external elements surrounding a person)−−20%, the biology of the human body (sex, age, genetic factors)−−20% and the organization of medical care−10% (3–6).

In every age group, including seniors, prevention is particularly important in order to eliminate harmful risk factors for many diseases, including the circulatory system and cancer (7). The diseases mentioned are the most common diseases in the world. Elements of an unhealthy lifestyle including: improper diet, overweight/obesity, smoking, little or no physical activity and alcohol abuse strongly contribute to their development (8).

The above-mentioned information has become the basis for the development of health promotion worldwide, and the concept of "healthy lifestyle"—conscious action aimed at improving or maintaining health—has gained popularity (3). A healthy lifestyle includes, among others: diet, physical activity, not using stimulants (not smoking, limiting alcohol consumption) and monitoring one's own health by e.g., performing regular preventive test.

According to available studies adherence to health behaviors among seniors is not good enough and the importance and need of behavioral interventions in this area were highlighted in the literature (9, 10). Liu et al. in their study regarding adherence to health promoting behaviors of seniors ≥60 years of age stated that full adherence rate to blood pressure monitoring among 19,800 participants was lover than 20% (11). Agrawal S. et al. showed in their study of numerous health-promoting activities that out of 1,000 adult Poles examined, the percentage of people performing blood lipid tests was approximately 59.1%, and controlling glucose concentration 65.8% (12). Whereas, Calas et al. found that among 2,620 participants of their study, only about 49% engaged in physical activity and Zaragoza-Marti et al. in the group of 341 respondents older than 60 years, found that many of them has nutritional deficits e.g., in in the case of vitamin D, essential for maintaining good bone health, and iodine, important for endocrine–metabolic control (13, 14).

In Poland, the founder of the first University of the Third Age (UTA's) established in 1975 in Warsaw was prof. Halina Szwarc. It was a part of the Postgraduate Center for Medical Staff Education. Its assumptions were: the possibility of educating seniors who could not receive education in their youth and improving the quality of their lives, as well as implementing a continuing education program and conducting gerontological research.

Thanks to participation in UTA's classes, seniors can develop and pursue their youthful interests and passions through various forms of self-education, including: getting to know the environment, being in a group, acceptance, expanding knowledge and skills, filling free time, learning new technologies and ways of communicating. UTA's also help meet the psychosocial and health needs of seniors (15). In addition, they counteract the marginalization of seniors, and participation in the offered activities ensures good wellbeing, stress reduction and increased physical activity (16, 17). Many UTA's offer classes on health education and learning healthy habits, which are very popular among seniors. UTA's also organizes many meetings with experts and other events on health prevention, from which participants can gain knowledge about a healthy lifestyle (18).

Regardless of the fact that UTA's is becoming more and more popular among seniors there are not many available studies examining the impact of educational activities on seniors' adherence to health-promoting activities.

The aim of the study was to compare health behaviors (e.g.,: physical activity, eating habits, alcohol consumption, tobacco smoking, preventive tests performance) between seniors attending and not attending UTA's classes.

Materials and methods

The cross-sectional study was conducted after obtaining consent from the Bioethics Committee of the Medical University of Silesia in Katowice (PCN/0022/KB1/36/21). All methods used in this study were consistent with applicable guidelines and regulations on conducting scientific research, and all seniors gave their informed consent to participate in it.

The participants inclusion criteria for the study included: voluntary, informed consent to participate in the study, ability to follow instructions, ability to read and no need for help from other people in completing the questionnaire.

The study involved 631 (100%) seniors from Silesia Voivodeship, Poland. Participants were recruited from Polish Universities of Third Age attendees (354 seniors) and among researcher's families' members and friends, as well as the researchers' neighbors (277 seniors) who did not participate in Universities of Third Age classes/lectures. The above-mentioned respondents who did not attend UTA's classes were also asked to give the study sets, described below, to their friends and families' members. It can therefore be concluded that the snowball method was used to recruit the seniors not attending UTA's classes. Data were collected from 2019 to 2020.

To conduct the study, an original survey questionnaire was used, consisting of questions regarding the discussed topic and basic questions including: age, gender, place of residence and level of education. Questions assessing health-promoting behaviors in the field of: how to spend free time, regularity of physical activity, self-assessment of physical activity, data on smoking, alcohol consumption and regularity of diagnostic tests and visits to the doctor were the proprietary questions designed by authors. Eating behaviors were assessed using a Polish standardized questionnaire—"*My Eating Behaviors*" (19). The internal consistency of the questionnaire was examined using the Cronbach's alpha coefficient—alfa = 0.82.

Respondent form UTA's "+" group were invited to participate in the study before and during breaks in UTA's classes. Each respondent, who gave informed consent to participate, received the survey questionnaire in an unmarked white envelope (study set) and sat at a prepared table at a distance that made it impossible to see the responses of another survey participant

10.3389/fpubh.2024.1403496

or communicate. After completing the survey, the respondent placed the paper questionnaire in the above-mentioned white unmarked envelope, which was sealed and placed in a prepared closed box. After filling the box with envelopes, the researchers transported them to the science lab, where the box was opened. Then, the researchers opened individual envelopes, took out the completed questionnaires and entered the selected answers into the database. A similar procedure applied to UTA"–" participants. After obtaining their informed consent to participate in the study, they received the study set and completed the questionnaires independently in their homes. They also passed mentioned sets to their family members and friends. Sealed envelopes with answers and signed informed consents were handed over to the researchers and transported to the science lab. The further procedure was the same as for UTA"+" participants. As mentioned before completing the study questionnaire was completely anonymous and voluntary. The methods used to collect the questionnaires (placing them in white unmarked envelopes after completing them, collecting the envelopes in one secured place, opening them only when entering the obtained results into the database) made it impossible to identify the participants of the study.

For the purposes of the analyses, the surveyed seniors were divided depending on their attendance at classes at UTA's. Statistica 13.3 (StatSoft Poland) was used to perform statistical analyses. The Chi^2 test was used for qualitative data, and for quantitative data—the Mann-Whitney U test (No normal distribution: T S-W < 0.001). Further analyses using multiple and logistic regressions models were used to identify whether the associations would remain after adjustments for potential cofounders (categorical: sex, place of residence, UTA's participation and continuous: age). There was no missing data. The level of statistical significance was set at $\alpha < 0.05$.

Results

Table 1 shows the general characteristics of the study group.

Participants were from 60 to 92 years of age ($\bar{x} = 70.28 \pm 6.09$ years). The majority of the surveyed group were women (475; 75.28%), and most respondents had secondary education (292; 46.28%). Approximately 32% (195; 31.90%) of the surveyed seniors lived in rural areas, and over 55% (354; 65.10%) of the respondents declared that they participated in classes at UTA's.

Table 2 presents the characteristics of the study group of seniors, including physical activity according to the participation in the UTA's.

The proportion of seniors more often declaring spending their free time actively was higher among those attending UTA's classes than those who did not (261; 73.73% vs. 125; 45.13%). The Chi^2 test confirmed the statistical significance of the observed differences ($p < 0.001$). The above-mentioned test also confirmed that number of seniors participating in UTA's activities was higher in terms of engaging in regular physical activity (270; 76.27% vs. 133; 48.01%; $p < 0.001$) and describing themselves as physically active (259; 73.16% vs. 173; 62.45 %; $p = 0.004$).

Table 3 presents the characteristics of the studied group of seniors, including descriptive statistics and the results of the differences analysis depending on the time of physical activity undertaken, numbers of point obtained in the "My Eating Habits" questionnaire and participation in activities of UTA's.

TABLE 1 General characteristics of the study group ($n = 631$).

Variables	Data	
	n	%
Sex		
Male	156	24.72
Female	475	75.28
Age [years]		
60–70	373	59.11
71–80	220	34.87
≥81	39	6.18
Level of education		
Primary	37	5.86
Vocational	120	19.02
Secondary	292	46.28
Higher	182	28.55
Place of residence		
City	436	69.10
Village	195	31.90
Attending classes at Universities of the Third Age		
Yes	354	56.10
No	277	43.90
Marital status		
Single	26	4.12
Married	355	56.26
Widow/widower	224	35.50
Informal relationship	26	4.12
Residence		
Alone	206	32.65
With spouse	306	48.49
With family	109	17.27
In a nursing home	2	0.32
With a partner	8	1.27
Material situation		
Good	164	25.99
Average	313	49.60
Below average	126	19.97
Bad	23	3.65
Neither good, nor bad	5	0.79

Data are presented as absolute frequencies.

TABLE 2 Physical activity according to the participation in the University of the Third Age ($n = 631$).

Variables	UTA "+" ($n = 354$)		UTA "−" ($n = 277$)		*P*-value
	n	%	*n*	%	
Spending free time					
Active (e.g., walking, swimming)	261	73.73	125	45.13	<0.001
Passively (e.g., armchair/sofa)	93	26.27	152	54.87	
Regular physical activity					
Yes	270	76.27	133	48.01	<0.001
No	84	23.73	144	51.99	
Self-assessment of physical activity					
I am a physically active senior	259	73.16	173	62.45	0.004
I am not a physically active senior	95	26.84	104	37.55	

Data are presented as absolute frequencies, UTA "+"—seniors participating in classes at Universities of the Third Age, UTA "–"—seniors refusing to attend classes at Universities of the Third Age, P-value—statistical significance.

TABLE 3 Descriptive statistics and the results of the differences analyses depending on the time of physical activity undertaken, numbers of point obtained in the "My Eating Habits" questionnaire and participation in activities of Universities of the Third Age.

Variables	UTA "+" ($n = 354$)	UTA "−" ($n = 277$)	The entire study group
Time to engage in physical activity [minutes]			
Median	30	0	25
Lower quartile	10	0	0
Upper quartile	60	30	60
Number of points obtained in "My Eating Habits" questionnaire			
Median	10	10	10
Lower quartile	7	7	7
Upper quartile	13	12	13
Analysis of differences in the:			*P*-value
Duration of physical activity			<0.001
Number of points obtained in the "My Eating Habits" questionnaire			0.23

Data are presented as absolute and relative frequencies or median and interquartile range. UTA "+"—seniors participating in classes at Universities of the Third Age, UTA "–"—seniors refusing to attend classes at Universities of the Third Age, p-value—statistical significance.

The Mann-Whitney U test showed that the analyzed groups of seniors differed significantly in terms of time spent on physical activity during the day ($p < 0.001$), but not in terms of the points obtained in the "My Eating Habits" questionnaire ($p = 0.23$).

Table 4 presents the characteristics of the study group of seniors, including alcohol and tobacco smoking habits according to the participation in the in the UTA's.

Tobacco smoking was declared by only 57 (9.03%) seniors in total, and the difference in the number of respondents consuming alcohol depending on the frequency was statistically significant ($p < 0.001$) and showed that daily alcohol consumption was declared by more respondents in the group not participating in classes at UTA's.

Table 5 presents the characteristics of the study group, including rregular preventive examinations according to the participation in UTA's classes and Table 6 presents the characteristics of the performance of preventive tests recommended for women according to the participation in the UTA's.

Over 85% of seniors participating and not participating in UTA's activities were under the constant care of a family doctor, while regular dental check-ups were not carried out by approximately ¼ (89; 14%) and over 40% (116; 41.88%) of them, respectively. The Chi^2 test showed statistically significant differences in the number of seniors who regularly check their teeth ($p < 0.001$), perform self-examination of their breasts/testicles ($p = 0.04$) and perform regular laboratory tests ($p = 0.02$) over respondents attending and not attending UTA's classes.

Regular gynecological check-ups were declared by over 60% (191; 62.83%) of women participating in UTA's and approximately 55% (93; 54.39%) of those who denied the above-mentioned activity, and regular cytological tests were declared by approximately 60% (178; 58.55%) women attending and just over 50% (89; 52.05%) of those not attending UTA's. The observed differences in the numbers of individual groups were not statistically significant ($p = 0.07$ and $p = 0.17$).

Tables 7, 8 present the characteristics of the study group, including the procedure of logistic and multiple regression analyzes of the impact of sex, age, place of residence and participation in UTA's on studied health-promoting activities.

All logistic regression models created for individual health-promoting behaviors in order to determine the impact of gender, age, place of residence and attending classes at UTAs on the likelihood of engaging in health-promoting behaviors vs. not engaging in them turned out to be statistically significant. Only models describing the impact of additional factors on tobacco smoking in the past ($p = 0.143$), regular laboratory tests ($p = 0.808$) and regular self-examination of breast/testicles ($p = 0.994$) showed no impact of attending UTA's classes.

TABLE 4 Alcohol and tobacco smoking habits according to the participation in the in the University of the Third Age ($n = 631$).

Variables	UTA "+" ($n = 354$)		UTA "−" ($n = 277$)		*P*-value
	n	%	*n*	%	
Currently tobacco smoking					
Yes	30	8.47	27	9.75	0.580
No	324	91.53	250	90.25	
Tobacco Smoking in the past					
Yes	133	37.57	76	27.44	0.007
No	221	62.43	201	72.56	
Passive tobacco smoking					
Yes	54	15.25	56	20.21	0.103
No	300	84.75	221	79.78	
Alcohol consumption					
At all	121	34.18	131	47.29	<0.001
Every day	8	2.26	21	7.58	
2–3x a week	32	9.04	19	6.86	
Once a month	88	24.86	44	15.88	
Several times a month	27	7.63	19	6.86	
Several times a year	78	22.03	43	15.52	

Data are presented as absolute and relative frequencies or median and interquartile range, UTA "+"—seniors participating in classes at Universities of the Third Age, UTA "−"—seniors refusing to attend classes at Universities of the Third Age, p-value—statistical significance.

TABLE 5 Regular preventive examinations according to the participation in Third Age Universities classes ($n = 631$).

Variables	UTA "+" ($n = 354$)		UTA "−" ($n = 277$)		*P*-value
	n	%	*n*	%	
Regular controls by family doctor					
Yes	314	88.70	241	87.00	0.52
No	40	11.30	36	13.00	
Regular annual dental controls					
Yes	265	74,86	161	58,12	<0.001
No	89	25,14	116	41,88	
Regular self-examination of breasts/testicles					
Yes	218	61.58	148	53.43	0.04
No	136	38.42	129	46.57	
Regular laboratory tests controls					
Yes	318	89.83	232	83.75	0.02
No	36	10.17	45	16.25	

Data are presented as absolute and relative frequencies, UTA "+"—seniors participating in the activities of the Universities of the Third Age, UTA "−"—seniors refusing to participate in the activities of the Universities of the Third Age, p-value—statistical significance.

We tested if sex, age, place of residence and attendance for UTA's classes significantly predicted participants' time spent on physical activity. The results of the regression indicated the three predictors explained 7.7% of the variance ($R^2 = 0.077$, $F = 12.292$, $p < 0.001$). It was found that sex ($\beta_1 = -8.189$, $p < 0.027$), age ($\beta_2 = -1.213$, $p < 0.001$) and attendance for UTA's classes/lectures significantly predicted longer duration of physical activity ($\beta_3 = -11.104$, $p < 0.01$).

Discussion

Conducted study proved positive impact of UTA's attendance at examined healthy behaviors.

Seniors attending UTA's classes were more active considering all physical activity indicators, probably because they had the opportunity to participate in physical activities organized by the UTA's to which they belonged, and also because thanks

TABLE 6 Performance of preventive tests recommended for women according to the participation in the University of the Third Age ($n = 475$).

Variables	UTA "+" ($n = 304$)		UTA "−" ($n = 171$)		*P*-value
	n	%	*n*	%	
Regular gynecological control					
Yes	191	62.83	93	54.39	0.07
No	113	37.17	78	45.61	
Regular cytological tests					
Yes	178	58.55	89	52.05	0.17
No	126	41.45	82	47.95	
Regular mammograms					
Yes	217	71.38	108	59.65	0.06
No	87	28.62	63	36.84	

Data are presented as absolute and relative frequencies, UTA "+"—seniors participating in the activities of the Universities of the Third Age, UTA "-"—seniors refusing to participate in the activities of the Universities of the Third Age, p-value—statistical significance.

to the knowledge acquired during classes, they managed their free time more effectively (15). Similar results were obtained in our other study conducted in a group of seniors living in the cities of the Silesian agglomeration (20). Regular physical activity affects, among other things: increasing the efficiency of the circulatory system, lowering blood pressure, increasing the stroke volume of the heart and improving the elasticity of blood vessels and reducing the risk of developing atherosclerosis and its complications, reducing the risk of stroke, improving metabolism, and consequently therefore, treatment of obesity and overweight, reduction of stress, improvement of cognitive functions and improvement of logical thinking processes, as well as concentration of attention and memory (21–24). Research shows that regular physical activity promotes a better quality of life and even its extension (22, 25).

Our study also examined the use of stimulants by seniors. Less than 10% of the respondents declared that they smoked tobacco. However, Bartoszek et al. showed that almost 30% of the seniors they surveyed had contact with tobacco (26). As can be read in the 2019 Research Communication of the Public Opinion Research Center "Cigarette smoking", one fourth of adult Poles (26%) smoked tobacco. Among them, regular smokers constituted 82%, and occasional smokers-−18%, and the quoted result has not changed since 2012, similar research was conducted (27). However, according to the Report from a nationwide survey on attitudes toward smoking, prepared by Kantar for the Chief Sanitary Inspectorate—(also in 2019), over one fifth of Poles (21%) admitted to smoking tobacco every day (28). Tobacco smoking is a risk factor for the development of cancer and is also a classic cardiovascular risk factor (29). There are many reports in the literature regarding the prevalence of smoking among young and middle-aged people, but not among seniors (30–32). Observed lack of differences both in passive and active smoking could be due to: small number of study group participants who smoked (giving up the addiction in the past -significant differences in respondents numbers) or were exposed to passive smoking. Moreover, age-related limitations, such as: increased time spent at home and reduced time spent in the company of smokers or lack of funds to buy tobacco could have played role in shaping of the results (33).

Daily alcohol consumption was declared by more seniors among the participants who did not take part in the activities of the UTA's. Observed results are disturbing and might be caused by various factors. One of them can be worst knowledge about the dangers of drinking alcohol. The study by Bartoszek et al. cited above showed that as many as 83.6% of seniors drank alcohol, although they indicated that they drank alcohol occasionally (26). Mihailovic et al. showed that the prevalence of alcohol consumption among people over 55 years of age in Serbia and Hungary was 41.5% and 62.5%, respectively. In both countries, alcohol was consumed more often by men than women (34). According to analyzes by the Organization for Economic Co-operation and Development (OECD), one Pole consumes on average 11.7 liters of pure alcohol per year. Taking into account gender, it should be noted that men in our country consumed 18.4 liters of pure alcohol per year, and women−5.6 liters (35). According to WHO, the average consumption of pure alcohol in Poland exceeds the European average. Alcohol abuse not only leads to the development of many cardiovascular diseases, cancer, gastrointestinal and endocrine problems and many others, but also leads to severe addictions, injuries and aggression. Mortality caused by alcohol consumption is higher than by diseases such as tuberculosis or AIDS (36).

As indicated by the results of the European Health Interview Survey (EHIS), older people often undergo basic preventive examinations (37). More than 85% of all surveyed seniors were under the constant care of a family doctor, while seniors participating in UTA's classes were more regular in performing breast/testicular self-examination, regular laboratory tests, and checking their teeth, compared to seniors not participating in the above-mentioned classes. Regular performance of the above-mentioned health-promoting activities and the observed differences between UTA "+" and UTA "–" seniors may result from the information presented during the classes and the knowledge acquired during them. Therefore, it can be concluded that UTA's students had better knowledge of health prevention and the benefits of regular examinations. Similar results were obtained in our previously cited other studies conducted in a group of seniors.

10.3389/fpubh.2024.1403496

TABLE 7 Characteristic of study group taking into account logistic regression results.

Variables	β	SE	Wald's χ^2	*p*	OR (95% CI)
Spending free time					
Sex	−0.492	0.204	5.801	0.016	0.611 (0.409–0.913)
Age	0.055	0.015	14.353	<0.001	1.057 (1.027–1.088)
Place of residence	−0.429	0.240	3.189	0.074	0.651 (0.406–1.0437)
Attendance for UTA's classes	1.382	0.229	36.297	<0.001	3.982 (2.538–6.248)
Model $\chi^2 = 76.556$; $p < 0.001$. Model fit measure (−2log): for this model = 765.437, constant term = 841.993.					
Regular physical activity					
Sex	−0.076	0.208	0.134	0.714	0.926 (0.615–1.395)
Age	0.063	0.015	18.520	<0.001	1.066 (1.035–1.097)
Place of residence	0.050	0.234	0.045	0.832	1.051 (0.664–1.665)
Attendance for UTA's classes	1.205	0.228	28.058	<0.001	3.337 (2.135–5.217)
Model $\chi^2 = 73.192$; $p < 0.001$. Model fit measure (−2log): for this model = 751.486, constant term = 824.678.					
Self-assessment of physical activity					
Sex	0.130	0.212	0.380	0.538	1.139 (0.752–1.726)
Age	0.023	0.014	2.508	0.113	1.023 (0.995–1.053)
Place of residence	−0.597	0.241	6.114	0.013	0.551 (0.343–0.884)
Attendance for UTA's classes	0.867	0.226	14.759	<0.01	2.380 (1.528–3.706)
Model $\chi^2 = 17.432$, $p = 0.002$. Model fit measure (−2log): for this model = 768.454, constant term = 785.887.					
Tobacco smoking in the past					
Sex	−0.679	0.209	10.597	0.001	0.507 (0.337–0.764)
Age	−0.033	0.015	4.823	0.028	0.968 (0.940–0.997)
Place of residence	−0.483	0.253	3.633	0.057	0.617 (0.375–1.015)
Attendance for UTA's classes	−0.339	0.231	2.149	0.143	0.713 (0.453–1.122)
Model $\chi^2 = 24.409$; $p < 0.001$. Model fit measure (-2log): for this model = 774.798, constant term = 799.207.					
Alcohol consumption					
Sex	−0.757	0.212	12.767	<0.001	0.469 (0.309–0.711)
Age	−0.034	0.014	5.999	0.014	0.966 (0.940–0.993)
Place of residence	0.089	0.233	0.148	0.701	1.094 (0.693–1.726)
Attendance for UTA's classes	−0.789	0.221	12.755	<0.001	0.454 (0.295–0.701)
Model $\chi^2 = 30.660$; $p < 0.001$. Model fit measure (−2log): for this model = 816.517, constant term = 847.177.					
Regular annual dental controls					
Sex	−0.261	0.212	1.501	0.221	0.771 (0.507–1.170)
Age	−0.051	0.014	12.466	<0.001	0.950 (0.923–0.978)
Place of residence	−0.051	0.236	0.047	0.828	0.950 (0.598–1.509)
Attendance for UTA's classes	−0.783	0.227	11.898	<0.001	0.457 (0.293–0.714)
Model $\chi^2 = 33.320$; $p < 0.001$. Model fit measure (−2log): for this model = 761.577, constant term = 794.897.					
Regular self-examination of breasts/testicles					
Sex	−1.191	0.203	34.243	<0.001	0.304 (0.204–0.453)
Age	0.067	0.015	21.402	<0.001	1.070 (1.039–1.101)
Place of residence	0.068	0.189	0.131	0.717	1.071 (0.738–1.553)

(Continued)

TABLE 7 (Continued)

Variables	β	SE	Wald's χ^2	*p*	OR (95% CI)
Attendance for UTA's classes	<0.001	0.011	<0.001	0.994	1.000 (0.978–1.022)
Model $\chi^2 = 64.266$; $p < 0.001$. Model fit measure (−2log): for this model = 792.512, constant term = 856.778.					
Regular laboratory tests controls					
Sex	−0.846	0.262	10.416	0.001	0.429 (0.257–0.718)
Age	−0.007	0.020	0.120	0.729	0.993 (0.954–1.034)
Place of residence	0.604	0.333	3.296	0.069	1.829 (0.952–3.514)
Attendance for UTA's classes	−0.082	0.338	0.059	0.808	0.921 (0.475–1.788)
Model $\chi^2 = 20.183$; $p < 0.001$. Model fit measure (−2log): for this model = 463.231, constant term = 483.414.					

TABLE 8 Characteristic of study group taking into account multiple regression results of time spent on physical activity.

Duration of physical activity				
Variables	β	SE	t-statistics	*p*
Coefficient	149.757	19.173	7.811	<0.001
Sex	−8.188	3.690	−2.219	0.027
Age	−1.213	0.256	−4.739	<0.001
Place of residence	−8.010	4,328	−1.851	0,064
Attendance for UTA's classes	−11.104	4.045	−2.745	<0.01

R = 0.277.
R-squared = 0.077.
Adjusted R-squared = 0.071.
F = 12.929.
P ≤ 0.001.
Estimation error = 38.078.

However, there it was mainly due to living in cities and better access to medical services (20).

Regular gynecological check-ups were declared by over 60% of women participating in UTA's activities. Preventing reproductive system diseases in women requires regular check-ups with a doctor. In the study conducted in a group of younger women than in our study (age over 40), on average every third woman (41; 36%) had regular check-ups. Respondents reported for cytological examination at similar intervals as for check-up visits to a gynecologist—most often once a year (44; 39%) (38). Similar data were also obtained by Bojar et al. in a study on a group of 304 women, most of whom underwent cytology once a year (39). In Stanisławska's research, as many as 93.9% of respondents declared that they performed gynecological examinations once a year (40). In Poland, the cervical cancer prevention program, which includes cytological examination every 3 years, is addressed to women aged 25 to 64. After this time, you can consider stopping regular testing, but only if the results are in normal ranges.

Our study did not show a difference in the number of women regularly undergoing mammography examinations depending on their attendance at UTA's classes. Observed result can be caused by women age or lack in the knowledge of the importance of mammography. Pivot et al., in a group of French women aged 40–74, showed that the surveyed women underwent regular examinations. Similar results can be found in the Report of the Central Statistical Office (GUS), however, both of these studies were conducted in groups of younger women than our own studies (41, 42). Mammography is a recognized diagnostic method for the early detection of breast cancer. Population-based breast cancer prevention programs are aimed at women over 50 years of age. Similarly to cytology, in Poland the breast cancer prevention program, which includes mammography every 2 years, is addressed to women aged 45 to 74. After this time, you can consider quitting the regular test, but only if the results were correct, which may also affect the results obtained in your own study.

According to many studies and reports, Poles' eating habits are bad. The National Institute of Public Health of the National Institute of Hygiene (NIZP-PZH) in the study entitled: "The health situation of the Polish population and its determinants in 2020" revealed that: in the years 2010–2018, the amount of bread and flour eaten among Poles decreased by over 30%, the consumption of potatoes decreased by 35%, other vegetables—by 6%, and fruit consumption—increased by 6%. During the mentioned period, Poles increased their consumption of red meat products by as much as 120%. As it also turned out, an average Pole ate from 120 to 129 g of red meat and various meat products per day, meanwhile, according to the World Cancer Research Found (WCRF) and the American Institute for Cancer Research (AICR), the consumption of red meat for an adult should not exceed 71 grams. Fish consumption also decreased by as much as 40%. However, the number of confectionery products eaten by Poles, as well as crispbread, rice wafers and other bakery products, increased by 20% (43, 44). Our study showed that the analyzed groups of seniors did not differ significantly from each other in terms of the points

obtained in the My Eating Habits questionnaire. The results of the current study indicated that participating in UTA activities might not influence eating habits. The lack of differences in eating habits could be caused by the occurrence of selected diseases for which specialized diet is an element of treatment and tertiary prevention, both among UTA's"+" and UTA "–" respondents. Compliance with the diet by at least some of the respondents could have influenced the obtained results.

In the regression models we found out a statistically significant impact of the factors included in the models (sex, age, place residence, attendance for UTA's classes) on health-promoting behaviors under study. Presented regression models showed that attendance in UTA's classes influenced taking health-promoting activities in the discussed areas.

Limitations of the study include but are not limited to: relatively small sample size, self-reported data by the participants, possible occurrence of Hawthorne's effect when obtaining answers and examined scope limited only to few health behaviors and possibly influencing them variables. Another limitation of the study is the fact that the authors did not analyze the exact content of the classes/lectures in which the surveyed seniors participated. This was due to restrictions on third parties wanting to take part in classes/lectures and the copyright of speaker's classes/lectures on a given topic. However, it was checked whether in a given academic year, classes on all the discussed health-promoting activities were held at a given University of Third Age.

Taking into account obtained results, UTA's future activities should focus on further education and making seniors and the constantly aging society aware of the benefits of adopting health-promoting behaviors, with particular emphasis on their impact on the quality and length of life.

Further research conducted in this area, on larger groups of respondents, should focus on further exploration of health-promoting behaviors undertaken in various groups of seniors, taking into account additional factors, such as existing diseases. The results obtained on the basis of this and further research regarding the positive effect of UTA's on the lives of seniors may support people managing various educational and local governmental institutions to take actions related to managing an increasing number of UTA's not only in Poland but also in other countries.

Conclusions

Health-promoting behaviors of seniors attending classes at the UTA's were more correct in terms of physical activity, adequate attendance with preventive test and worst in terms of alcohol consumption. Overall picture allows to conclude that participation in UTA's classes seems to have a positive impact on the examined health-promoting behaviors of the surveyed seniors. Nevertheless, there is a need to conduct educational activities to promote the benefits of participating in the activities of UTA's, contributing to an active and health-promoting lifestyle and, consequently, extending and improving its quality.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Bioethics Committee of the Medical University of Silesia in Katowice (PCN/0022/KB1/36/21). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

JD: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. MS: Data curation, Formal analysis, Investigation, Methodology, Resources, Validation, Writing – original draft, Writing – review & editing. OS: Formal analysis, Resources, Writing – original draft, Writing – review & editing. EŁ: Data curation, Methodology, Writing – original draft. HK: Data curation, Resources, Software, Writing – original draft.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

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

References

1. Constitution of the World Health Organization. (2024). Available online at: https://www.afro.who.int/sites/default/files/pdf/generic/who_constitution_en.pdf (accessed February 23, 2024).

2. Główny Urzad Statystyczny. *Pojecia stosowane w statystyce publicznej*. Available online at: https://stat.gov.pl/metainformacje/slownik-pojec/pojecia-stosowane-w-statystyce-publicznej/896,pojecie.html (accessed February 23, 2024).

3. Lalonde M. *A New Perspective on the Health of Canadians*. Ottawa, ON: Minister of Supply and Services Canada Public Health Agency of Canada Available online at: http://wwwphac-aspcgcca/ph-sp/pdf/perspect-engpdf (accessed February 22, 2024).

4. Wozniak M, Brukwicka I, Kopański Z. Zdrowie jednostki i zbiorowości. *J Clini Healthc*. (2015) 4:1–3.

5. Syrek E. Styl życia w rodzinie – konteksty socjalizacji w obszarze zdrowia. *Pedagogika Społeczna Nova*. (2023) 2:55–68. doi: 10.14746/psn.2022.4.03

6. Kasperczyk T. Pola zdrowotne Lalonde'a– mity czy rzeczywistość. *Promocja Zdrowia i Ekologia*. (2018) 1–2:16–20.

7. Babatunde AO, Shobanke HA, Akinade AA, Michael AJ, Osadare M, Akanbi OK, et al. Enhancing preventive medicine over curative medicine: role of telemedicine. *Public Health Pract (Oxf)*. (2021) 2:100130. doi: 10.1016/j.puhip.2021.100130

8. Zhang X, Zhang L, Liu Y, Lin Y, Yang X, Gong L, et al. The relationship between unhealthy lifestyle patterns and depressive symptoms among residents in Beijing, China: a community-based cross-sectional study. *Front Public Health*. (2023) 11:1055209. doi: 10.3389/fpubh.2023.1055209

9. Yusuf S, Joseph P, Rangarajan S, Islam S, Mente A, Hystad P, et al. Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. *Lancet*. (2020) 395:795–808. doi: 10.1016/S0140-6736(19)32008-2

10. Li D, Jia Y, Yu J, Liu Y, Li F, Liu Y, et al. Adherence to healthy lifestyle and the risk of function limitations in late life: the atherosclerosis risk in communities study. *Front Aging Neurosci*. (2021) 13:698699. doi: 10.3389/fnagi.2021.698699

11. Liu F, Chang H, Liu X. Adherence behaviors and related factors among elderly hypertensive patients in china: evidence from the china health and retirement longitudinal study. *Patient Prefer Adherence*. (2023) 17:3539–53. doi: 10.2147/PPA.S445789

12. Agrawal S, Gołebiowska J, Makuch S, Mazur G. Prevalence of use of preventive services in Poland: result from a population-based nationwide study. *J Clin Med*. (2021) 10:2084. doi: 10.3390/jcm10102084

13. Calas L, Subiros M, Ruello M, Hassani Y, Gabet A, Angue M, et al. Hypertension prevalence, awareness, treatment and control in 2019 in the adult population of Mayotte. *Eur J Public Health*. (2022) 32:408–14. doi: 10.1093/eurpub/ckac015

14. Zaragoza-Martí A, Ruiz-Robledillo N, Sánchez-SanSegundo M, Albaladejo-Blázquez N, Hurtado-Sánchez JA, Ferrer-Cascales R. Eating habits in older adults: compliance with the recommended daily intakes and its relationship with sociodemographic characteristics, clinical conditions, and lifestyles. *Nutrients*. (2020) 12:446. doi: 10.3390/nu12020446

15. Borczyk W, Nalepa W, Knapik B, Knapik W. Standardy działania Uniwersytetów Trzeciego Wieku w Polsce. In: *Ogólnopolska Federacja Stowarzyszeń Uniwersytetów Trzeciego Wieku, Fundacja Rozwoju Ziem Górskich*. Nowy Sącz: National Federation of Associations of Universities of the Third Age (2014).

16. Marcinkieiwcz A. The University of the Third Age as an institution counteracting marginalization of older people. *J Educ Cult Soc*. (2011) 2:38–44. doi: 10.15503/jecs20112.38.44

17. Dabek J, Szynal M, Łebek E, Sierka O. Selected elements of the lifestyle of Silesian seniors, taking into account their participation in the activities of the Third Age Universities. *Front Public Health*. (2024) 12:1375238. doi: 10.3389/fpubh.2024.1375238

18. Gierszewski D, Kluzowicz J. The role of the University of the Third Age in meeting the needs of older adult learners in Poland. *Gerontol Geriatr Educ*. (2021) 42:437–51. doi: 10.1080/02701960.2021.1871904

19. Ogińska-Bulik N, Putyński L. Kwestionariusz Moje Nawyki Żywieniowe: konstrukcja i własności psychometryczne. *Acta Universitatis Lodziensis Folia Psychologica*. (2020) 4:25–33.

20. Szynal M, Dabek J. The quality of aging of seniors living in the cities of the silesian conurbation. *Health Prob Civilizat*. (2023). doi: 10.5114/hpc.2023.133730

21. Czarnecki D, Skalski W, Kowalski D, Graczyk M, Kindzer B, Gaynulina,I. Pozytywny wpływ ruchu i aktywności fizycznej na organizm człowieka. *Rehabil Recreat*. (2022) 12:113–20. doi: 10.32782/2522-1795.2022.12.16

22. Zarnigor D, Davlatov O, Salim S. *Physical Activity and Its Impact on Human Health and Longevity*. (2022). p. 82. Available online at: https://cyberleninka.ru/article/n/physical-activity-and-its-impact-on-human-health-and-longevity (accessed February 24, 2024).

23. Chastin SFM, Abaraogu U, Bourgois JG, Dall PM, Darnborough J, Duncan E, et al. Effects of regular physical activity on the immune system, vaccination and risk of community-acquired infectious disease in the general population: systematic review and meta-analysis. *Sports Med*. (2021) 51:1673–86. doi: 10.1007/s40279-021-01466-1

24. Anderson E, Durstine JL. Physical activity, exercise, and chronic diseases: a brief review. *Sports Med Health Sci*. (2019) 1: 3–10. doi: 10.1016/j.smhs.2019.08.006

25. Andrieieva O. Effects of physical activity on aging processes in elderly persons. *J Physi Educ Sport*. (2019) 19:1308–14. doi: 10.7752/jpes.2019.s4190

26. Bartoszek A, Kocka K, Zielonka E, Łuczyk M, Rzaca M, Deluga A, et al. The problem of the use of drugs among seniors living in the home environment. *J Educ Health Sport*. (2016) 6:235–44.

27. Komunikat z Badań. *CBOS "Palenie papierosów"*. Warsaw: Public Opinion Research Center (2019).

28. *Raport z ogólnopolskiego badania ankietowego na temat postaw wobec palenia tytoniu*. Kantar: Główny Inspektorat Sanitarny (2019).

29. Wiszniewska M, Lipińska-Ojrzanowska A, Witkowska A, Tymoszuk D, Kleniewska A, Kluszczyński D, et al. Choroby nowotworowe pochodzenia zawodowego – epidemiologia i aspekty orzecznicze. *Med Pr*. (2018) 69:93–108. doi: 10.13075/mp.5893.00620

30. Medina J. Regional Effects of perceived risks of harm on cigarette smoking among U.S. high school seniors: evidence from monitoring the future. *Int J Environ Res Public Health*. (2021) 18:9120. doi: 10.3390/ijerph18179120

31. Lindson N, Theodoulou A, Ordóñez-Mena JM, Fanshawe TR, Sutton AJ, Livingstone-Banks J, et al. Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses. *Cochrane Database Syst Rev*. (2023) 9:CD015226. doi: 10.1002/14651858.CD015226.pub2

32. Sokol NA, Feldman JM. High school seniors who used e-cigarettes may have otherwise been cigarette smokers: evidence from monitoring the future (United States, 2009-2018). *Nicotine Tob Res*. (2021) 23:1958–61. doi: 10.1093/ntr/ntab102

33. Fakoya OA, McCorry NK, Donnelly M. Loneliness and social isolation interventions for older adults: a scoping review of reviews. *BMC Public Health*. (2020) 20:129. doi: 10.1186/s12889-020-8251-6

34. Mihailovic N, Szollosi GJ, Rancic N, János S, Boruzs K, Nagy AC, et al. Alcohol consumption among the elderly citizens in Hungary and Serbia-comparative assessment. *Int J Environ Res Public Health*. (2020) 17:1289. doi: 10.3390/ijerph17041289

35. Raport Organizacji Współpracy Gospodarczej i Rozwoju. (2021). Available online at: https://data.oecd.org/healthrisk/alcohol-consumption.htm (accessed February 24, 2024).

36. WHO. *Global Status Report on Alcohol and Health 2018*. Geneva: World Health Organization. (2018).

37. Information on the situation of older people based on data from the Central Statistical Office. Warsaw: Central Statistical Office. (2018). Available online at: https://stat.gov.pl/obszary-tematyczne/osoby-starsze/osoby-starsze/informacja-o-sytuacji-osob-starszych-na-podstawie-badan-glownego-urzedu-statystycznego,1,2.html (accessed February 22, 2024).

38. Dabek J, Popken-Haładus B, Kulik H, Szynal M, Jeleń M. *Profilaktyka raka szyjki macicy i raka piersi w grupie kobiet po 40. roku życia oraz ich wiedza w tym zakresie. W: Zachowania prozdrowotne jako element aktywności życiowej człowieka*. Białystok: Uniwersytet Medyczny w Białymstoku. (2020). p. 55–79.

39. Bojar I, Woznica I, Holecki T, Diatczyk J. Dostepność badań cytologicznych oraz poziom wiedzy kobiet na temat ich znaczenia w profilaktyce chorób nowotworowych narzadu rodnego. *Medycyna Ogólna*. (2010) 16:77—89.

40. Stanisławska J, Janikowska K, Stachowska M, Talarska D, Drozd-Gajdus E, Szewczyczak M. Ocena wiedzy kobiet w zakresie profilaktyki raka piersi i raka szyjki macicy. *Problemy Higieny i Epidemiologii*. (2016) 97:38–44.

41. Raport: Zdrowie Kobiet 2004-2009. *Główny Urzad Statystyczny w Krakowie*. Cracow: Central Statistical Office - Statistical Office in Cracow (2012).

42. Pivot X, Eisinger F, Blaye JY, van Coscas Y, Calazel-Benqueh A, Viguieri J, et al. Mammography utilization in women aged 40–49 years: the French EDIFICE survey. *Eur J Cancer Prevent*. (2011) 20:16–9. doi: 10.1097/01.cej.0000391565.41383.ba

43. *Sytuacja zdrowotna ludności Polski i jej uwarunkowania*. Warsaw: National Institute of Public Health National Institute of Hygiene - National Research Institute (2020).

44. "Porozmawiajmy szczerze o otyłości" campaign (2021). Available online at: https://ootylosci.pl/ (accessed February 24, 2024).

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 10 July 2024
DOI 10.3389/fpubh.2024.1412842

OPEN ACCESS

EDITED BY
Yun Gao,
Sichuan University, China

REVIEWED BY
Irma Ruslina Defi,
Padjadjaran University, Indonesia
Giuseppe Murdaca,
University of Genoa, Italy
Joseph Atia Ayariga,
Alabama State University, United States

*CORRESPONDENCE
Sha Liu
1198967756@qq.com;
643363075@qq.com
Wanmeng Xiao
2983835392@qq.com;
hello_xwm@hotmail.com
Muhan Lü
yangtao20232023@163.com

RECEIVED 05 April 2024
ACCEPTED 17 June 2024
PUBLISHED 10 July 2024

CITATION
Yang T, Liu Z, Xiu M, Qing X, Liu S, Xiao W and Lü M (2024) Sarcopenia-related traits and 10 digestive system disorders: insight from genetic correlation and Mendelian randomization.
Front. Public Health 12:1412842.
doi: 10.3389/fpubh.2024.1412842

Sarcopenia-related traits and 10 digestive system disorders: insight from genetic correlation and Mendelian randomization

Tao Yang[1], Zheng Liu[1], Mingzhu Xiu[1], Xiaoman Qing[1], Sha Liu[1]*, Wanmeng Xiao[2,3]* and Muhan Lü[2,3]*

[1]Department of Gastroenterology, The Affiliated Hospital of Southwest Medical University, Luzhou, China, [2]The Affiliated Hospital of Southwest Medical University, Luzhou, China, [3]Human Microecology and Precision Diagnosis and Treatment of Luzhou Key Laboratory, Luzhou, China

Introduction: Despite observational studies suggest hypotheses indicating a potential link, the precise causal connection between sarcopenia and digestive system illnesses has not been clearly defined.

Methods: We first use Linkage Disequilibrium Score Regression (LDSC) testing to determine the genetic correlation of traits associated with sarcopenia and 10 specific gastrointestinal diseases. Subsequently, we performed a set of bidirectional Mendelian Randomization (MR) analyses to gauge the genetic inclination towards sarcopenia-related traits in relation to each gastrointestinal condition, individually, across the FinnGen, UK Biobank, and other extensive collaborative consortia. The analytical outcomes were synthesized using a fixed-effects meta-analytic model. For outcomes indicating substantial causal impacts, mediation MR analyses were executed. Additionally, a battery of sensitivity analyses was conducted to evaluate the study's strength and dependability.

Results: Our findings established a strong causal link between appendicular lean mass and gastroesophageal reflux disease (OR = 0.8607; 95% CI: 0.8345–0.8877; $p < 0.0001$) and a noteworthy correlation with nonalcoholic fatty liver disease (OR = 0.7981; 95% CI: 0.7281–0.8749; $p < 0.0001$), as per the meta-analysis data. We also evaluated the intermediary role of metabolic disorders in the association between appendicular lean mass and the aforementioned diseases. The intermediary effect towards gastroesophageal reflux disease is quantified as 0.0087 (95% CI, 8e-04, 0.0183), accounting for 5.9398% (95% CI, 0.5462, 12.4940%) of the overall effect. For non-alcoholic fatty liver, the intermediary impact is 0.0150 (95% CI, 0.0050, 0.0270), representing 19.7808% (95% CI, 6.5936, 35.6055%) of the total effect.

Conclusion: The findings posit that augmenting muscle mass may serve as a preventative strategy against gastroesophageal reflux disease and non-alcoholic fatty liver, highlighting the critical role of metabolic disorder management in reducing the risks of these sarcopenia-related conditions.

KEYWORDS

sarcopenia, digestive system disorders, genetic correlation, Mendelian randomization, GWAS

1 Introduction

Sarcopenia, a systemic and progressive condition affecting skeletal muscles, is characterized by a rapid decline in both muscle mass and strength (1). This condition is linked to numerous negative outcomes including increased risk of falls, reduced mobility, frailty, and mortality. Predominantly impacting the older demographic, it is a common issue among seniors, with estimates suggesting that it impacts between 10 and 16% of the older adult worldwide (2, 3). Sarcopenia can also develop in individuals during middle age and is associated with various health conditions. Although prior research in epidemiology has hinted at a possible link between sarcopenia and a range of gastrointestinal disorders, such as gastroesophageal reflux disease (GERD) (4), non-alcoholic fatty liver disease (NAFLD) (5) and gastrointestinal cancers (6), the existence of a causal relationship remains to be conclusively proven. This is largely due to the ongoing challenges posed by confounding factors and the risk of measurement errors.

In order to surmount these constraints, (7) devised a dependable technique for establishing causal connections between modifiable risk factors and health consequences. This approach utilizes genetic variants that are closely associated with the exposure in question as instrumental variables, a strategy known as Mendelian Randomization (MR). This technique has successfully navigated the common obstacles of confounding factors, the risk of reverse causality, and regression dilution bias, and it has become a favored method in the realm of observational epidemiology (8, 9).

To our knowledge, comprehensive MR studies that explore the causal links between sarcopenia and various gastrointestinal conditions, such as digestive tract tumors, have not yet been extensively undertaken. This study employs a bidirectional MR method to rigorously evaluate the causal relationship between sarcopenia and 10 distinct digestive system conditions, aiming to clarify the hypotheses from previous observational studies concerning their causal linkage. Elucidating the relationship between sarcopenia and digestive system diseases is crucial, as it could guide the development of preventive and treatment strategies. It is particularly important to determine if addressing sarcopenia could reduce the risk of gastrointestinal diseases, which could have a profound impact on the evolution of preventive medical approaches.

2 Materials and methods

2.1 Study design

As outlined in Figure 1, the design of our study commenced with the calculation of genetic correlations among traits associated with sarcopenia and 10 distinct gastrointestinal disorders. Following this, we carried out a series of bidirectional MR analyses to quantify the genetic predispositions to sarcopenia-related traits in relation to each gastrointestinal disease, separately within the FinnGen, UK Biobank, and additional large-scale collaborative groups. The results of these analyses were pooled using a fixed-effects meta-analytic model. Subsequently, for those outcomes demonstrating significant causal effects, we conducted mediation MR analyses. It is important to note that all research studies included herein had received approval from the appropriate ethics committees, and all participants had given their informed consent.

2.2 Data source for sarcopenia-related traits

Building on the knowledge from prior MR studies, we pinpointed appendicular lean mass (representing muscle mass), low grip strength (a measure of muscular power), and walking pace (indicative of muscle function) as critical sarcopenia metrics. For our analysis, we obtained instrumental variables for appendicular lean mass (ALM) from a Genome-Wide Association Study (GWAS) within the UK Biobank, which comprised 450,243 participants. ALM was quantified via bioelectrical impedance analysis (BIA), representing the total mass of the limbs excluding fat. We also identified instrumental variables for low grip strength from a GWAS meta-analysis involving 256,523 participants, with thresholds set at under 30 kg for men and under 20 kg for women. In addition, we sourced genetic instrumental variables for walking speed from GWAS data within the UK Biobank, which included 459,915 participants.

2.3 Data source for 10 digestive system disorders and metabolic disorders

Our study encompassed a comprehensive examination of ten distinct gastrointestinal disorders, categorized into four conditions affecting the upper gastrointestinal tract (GERD, esophageal cancer, gastric cancer, and gastroduodenal ulcer), one condition of the lower gastrointestinal tract (colorectal cancer), two pancreatic conditions (chronic pancreatitis and pancreatic cancer), and three liver-related diseases (NAFLD, liver cirrhosis, and liver cancer). The genetic associations at the summary level were obtained from studies conducted by the FinnGen consortium and the UK Biobank. Supplementary GWAS data were incorporated from multiple studies, such as those on gastroesophageal reflux disease by (10) (with 129,080 cases and 473,524 controls, as well as 20,381 cases and 464,217 controls), chronic pancreatitis (1,424 cases and 476,104 controls), esophageal cancer (98 cases and 475,308 controls), gastric cancer (1,029 cases and 475,087 controls), pancreatic cancer (1,196 cases and 475,049 controls), non-alcoholic fatty liver disease by (11) (8,434 cases and 770,180 controls), and liver cirrhosis (122 cases and 347,284 controls). Additionally, we considered metabolic disorders as possible mediators, and the pertinent findings are available through the FinnGen consortium. Supplementary Table S1 provides comprehensive details regarding the sources of the data presented.

2.4 Instruments selection

In our endeavor to ensure the accuracy and dependability of our dataset, we implemented a rigorous preprocessing protocol. We pinpointed independent Single Nucleotide Polymorphisms (SNPs) with a high degree of specificity ($r2 < 0.001$ and a clumping window of 10,000 kb) to act as instrumental variables for traits related to sarcopenia. These SNPs were chosen based on genome-wide

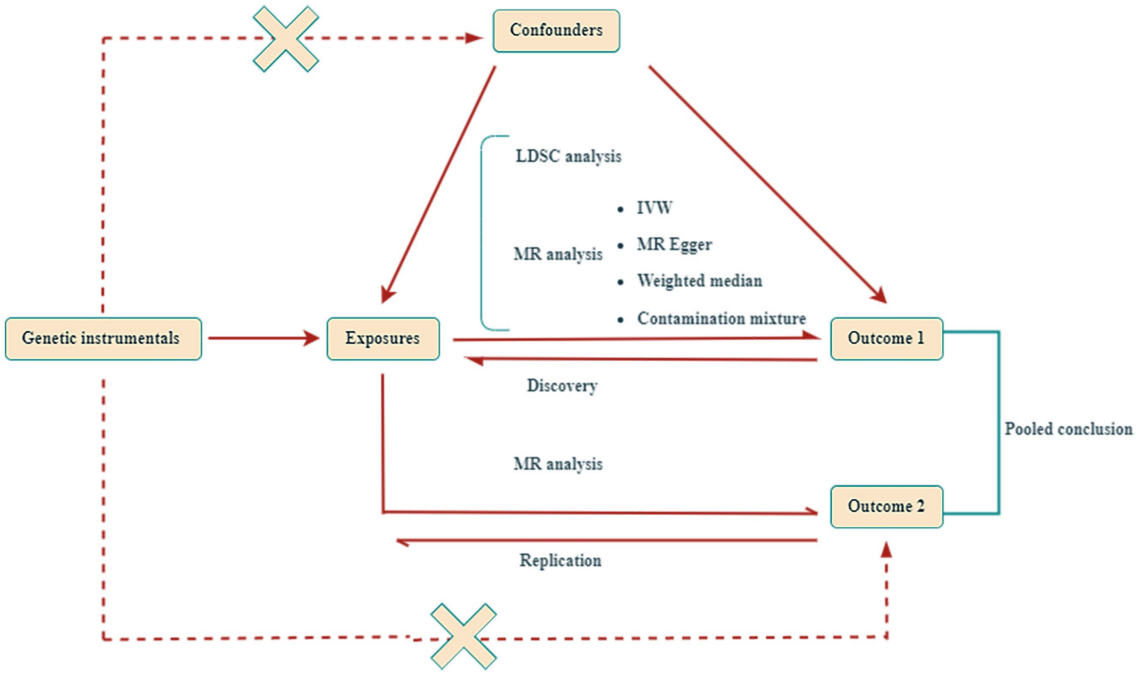


FIGURE 1
Design of this Mendelian randomization (MR) study. This study utilized two independent genome-wide association studies (GWAS) datasets for gastrointestinal diseases. LDSC, Linkage Disequilibrium Score; IVW, inverse-variance weighted.

significance ($p < 5.0 \times 10$^-8) and a minimum minor allele frequency (MAF) of 0.01. We excluded palindromic SNPs from our set of instrumental variables and evaluated their suitability by calculating the *F*-statistic for each SNP linked to sarcopenia traits. The *F*-statistic was determined using the formula $((N-k-1)/k) * (R2 /(1-R2))$, with N denoting the number of samples and k being the number of SNPs (12). SNPs with an *F*-statistic below 10 were excluded from our Mendelian Randomization (MR) analysis to reduce the likelihood of weak instrument bias. Conversely, for the reverse MR analysis, we applied a less stringent significance threshold of $p < 5.0 \times 10$^-6 to detect SNPs associated with the ten gastrointestinal diseases, considering the scarcity of SNPs meeting the genome-wide significance threshold ($p < 5.0 \times 10$^-8).

2.5 Statistical analysis

2.5.1 Genetic correlation analysis

Employing the Linkage Disequilibrium Score (LDSC) test, we estimated the genetic correlation (rg) between traits associated with sarcopenia and a set of ten gastrointestinal disorders. The LDSC approach assesses the correlation by examining the relationship between test statistics and linkage disequilibrium, which helps to distinguish between genuine polygenic effects and potential biases (13, 14). This method entails the multiplication of z-scores from variants of one trait with those from another trait's variants. The genetic covariance is derived by regressing this multiplied value against the LD score. This covariance, when divided by SNP heritability, provides an estimate of the genetic correlation. We established a *p* value threshold of $p < 0.0019$ (0.05/27, applying the stringent Bonferroni correction) to denote statistical significance (15). *p* values ranging from 0.002 to 0.05 were taken as suggestive of a possible genetic correlation.

2.5.2 MR analysis

In our exploration of the causal relationships between sarcopenia-related traits and various digestive diseases, we deployed four distinct methodologies: inverse variance weighting (IVW), MR Egger, weighted median, and contamination mixture, with IVW serving as the primary analytical tool (16). Particularly, the contamination mixture method has proven its resilience and accuracy in MR analyses where instrumental variables may not be valid, showing the lowest mean square error among robust techniques in diverse real-world contexts (17). To ensure the credibility of our results, we measured the heterogeneity across different SNPs using Cochran's Q statistic (18). In cases where substantial heterogeneity was identified in the MR analysis, we employed the IVW random effects model. Additionally, we availed ourselves of the MR-PRESSO tool to address any residual and outlier values that could indicate MR pleiotropy (19). For both scenarios, a *p*-value below 0.05 indicated the existence of heterogeneity or horizontal pleiotropy. Moreover, we performed a leave-one-out analysis to evaluate the specific contribution of each SNP to the overall results of our study (20).

Our analysis involved a meta-synthesis aimed at assessing the overall causal link between traits associated with sarcopenia and a set of ten gastrointestinal diseases, combining outcomes from both the exploratory and confirmatory phases of MR investigations. From the analysis, we omitted results that indicated pleiotropy. The selection of the effect model was guided by the degree of heterogeneity present in the data; a fixed-effects model was applied when heterogeneity was negligible ($I2 \leq 50\%$), and a random-effects model was used in the presence of significant heterogeneity ($I2 > 50\%$). The findings from the

meta-synthesis were taken as the conclusive causal determinations. Nonetheless, in scenarios where there was a single MR result, that particular result was decisive for the final causal interpretation. Statistical significance was established at a *p*-value below 0.0004 (0.05/114, adhering to stringent Bonferroni correction), while *p*-values ranging from 0.0004 to 0.05 were viewed as suggestive of a potential causal correlation.

Previous studies have shown that muscle mass loss is closely related to metabolic syndrome (21), in order to evaluate the potential role of metabolic disorders as mediators in the causal pathway between ALM and diseases like GERD or NAFLD, we conducted a two-stage MR analysis. The first stage was dedicated to determining the causal influence of ALM on metabolic disorders through Univariate MR (UVMR), quantified by the coefficient β1. The second stage utilized both UVMR and Multivariate MR (MVMR) to gauge the causal effect of metabolic disorders on GERD and NAFLD, taking into account the influence of ALM, with the MVMR coefficients represented as β2. The mediation effect of metabolic disorders was ascertained by the ratio of β1 to β2, and the 95% confidence interval for this ratio was established using the Delta method (22, 23). All analyses were performed with R packages (Two Sample MR、MVMR and MR-PRESSO) in R 4.3.1.

3 Results

3.1 Genetic correlation

Employing the LDSC regression technique, we assessed the genetic links between sarcopenia-associated characteristics and a variety of gastrointestinal conditions. As illustrated in Figure 2, the LDSC regression disclosed a noteworthy genetic association between ALM and GERD with a correlation coefficient (rg) of-0.1388 and a highly significant *p*-value of less than 0.0001. Similarly, ALM showed a notable genetic relationship with chronic pancreatitis, with an rg of 0.2122 and a p-value of 0.0006. The analysis also hinted at a potential genetic link between ALM and colorectal cancer (rg = −0.1260, $p = 0.0028$), NAFLD (rg = −0.1747, $p = 0.0062$), and liver cirrhosis (rg = 0.1364, $p = 0.0043$). In the case of reduced grip strength, a substantial genetic correlation with GERD was observed (rg = 0.2389, $p < 0.0001$). Moreover, a significant genetic correlation was detected between walking speed and several conditions: GERD (rg = −0.5952, $p < 0.0001$), NAFLD (rg = −0.4302, $p < 0.0001$), gastroduodenal ulcer (rg = −0.3490, $p < 0.0001$), and liver cirrhosis (rg = −0.2116, $p = 0.0002$). For comprehensive details on all genetic correlation results, please refer to Supplementary Table S2.

3.2 MR analysis

3.2.1 Discovery results

Utilizing a discovery cohort, we delved into the causal interactions between characteristics associated with sarcopenia and a set of ten gastrointestinal diseases (refer to Supplementary Tables S3–S5 for specifics). The analysis uncovered a causal link where an increment in ALM per unit of log odds ratio (logOR) was correlated with four gastrointestinal conditions: GERD with an OR of 0.8598 (95% CI: 0.8220 to 0.8992; $p < 0.0001$), gastric cancer (OR: 1.1300; 95% CI: 1.0344 to 1.2343; $p = 0.0067$), colorectal cancer (OR: 0.7805; 95% CI: 0.6096 to 0.9992; $p = 0.0493$), and NAFLD (OR: 0.8124; 95% CI: 0.7342 to 0.8990; $p < 0.0001$). In addition, we detected a causal effect of diminished grip strength on GERD (OR: 1.2720; 95% CI: 1.0684 to 1.5145; $p = 0.0069$) and pancreatic cancer (OR: 1.7395; 95% CI: 1.1336 to 2.6693; $p = 0.0113$). Furthermore, a relationship was pinpointed between walking speed and several disorders: GERD (OR: 0.1184; 95% CI: 0.0819 to 0.1711; $p < 0.0001$), colorectal cancer (OR: 2.8346; 95% CI: 1.0351 to 7.7626; $p = 0.0426$), NAFLD (OR: 0.3961; 95% CI: 0.2111 to 0.7435; $p = 0.0039$), and gastroduodenal ulcer (OR: 0.9901; 95% CI: 0.9824 to 0.9979; $p = 0.0127$). The leave-one-out analysis revealed results that were consistent with the initial findings (Supplementary Figure S1). Sensitivity analyses indicated that certain findings displayed heterogeneity, yet no signs of pleiotropy were observed.

In the reverse MR analysis, we identified causal relationships between two types of digestive disorders and ALM, specifically gastroesophageal reflux disease (β: -0.0812; 95% CI: −0.1224 to-0.0400; $p = 0.0001$) and liver cancer (β: 9.7125; 95% CI: 1.500 to 17.9247; $p = 0.0204$). Additionally, we found a causal association between two types of digestive disorders and low grip strength, including gastroesophageal reflux disease (β: 0.1968; 95% CI: 0.1430 to 0.2506; $p < 0.0001$) and esophageal cancer (β: 0.0386; 95% CI: 0.0157 to 0.0616; $p = 0.0009$). Furthermore, a causal relationship was observed between two types of digestive disorders and walking pace, such as gastroesophageal reflux disease (β: -0.1329; 95% CI: −0.1456 to-0.1201; $p < 0.0001$) and liver cancer (β: -6.3579; 95% CI: −11.6900 to −1.0259; $p = 0.0194$). Analysis conducted through leave-one-out validation demonstrated outcomes that were analogous (Supplementary Figure S1). Sensitivity analysis indicated that some results displayed heterogeneity, with significant pleiotropy ($p = 0.0110$) detected only in the causal relationship between liver cancer and ALM. No pleiotropy was observed in the other causal relationships.

3.2.2 Replication results

In our replication cohort, we identified a causal relationship between ALM and two digestive disorders: GERD (OR: 0.8615; 95% CI: 0.8255 to 0.8991; $p < 0.0001$) and NAFLD (OR: 0.7350; 95% CI: 0.5911 to 0.9141; $p = 0.0057$). Furthermore, we observed associations between low grip strength and GERD (OR: 1.1363; 95% CI: 1.0119 to 1.2759; $p = 0.0307$), as well as between walking pace and GERD (OR: 0.3196; 95% CI: 0.2222 to 0.4595; $p < 0.0001$), and gastroduodenal ulcer (OR: 0.4050; 95% CI: 0.1646 to 0.9963; $p = 0.0491$). Sensitivity analysis indicated some heterogeneity in the findings, but no evidence of pleiotropy was observed. Contrary to our expectations, the reverse MR analysis failed to identify any causal relationships between the ten examined digestive diseases and traits related to sarcopenia. For comprehensive details on all MR analysis and sensitivity analyses results, please refer to Supplementary Tables S5, S6.

3.2.3 Combined results from the meta-analysis

The outcomes of our meta-analysis are detailed in Figures 3, 4 and Supplementary Table S6. We identified a robust causal relationship between ALM and GERD (OR = 0.8607; 95% CI: 0.8345–0.8877; $p < 0.001$), as well as a significant association with NAFLD (OR = 0.7981; 95% CI: 0.7281–0.8749; $p = 0.0001$). Additionally, the meta-analysis yielded suggestive evidence for a potential causal effect of ALM on gastric cancer (OR = 1.1300; 95% CI: 1.0344 to 1.2343; $p = 0.0067$). Evidence was also found suggesting that low grip strength may have a causal effect on GERD (OR = 1.1762; 95% CI: 1.0680 to 1.2955; $p = 0.0010$) and pancreatic

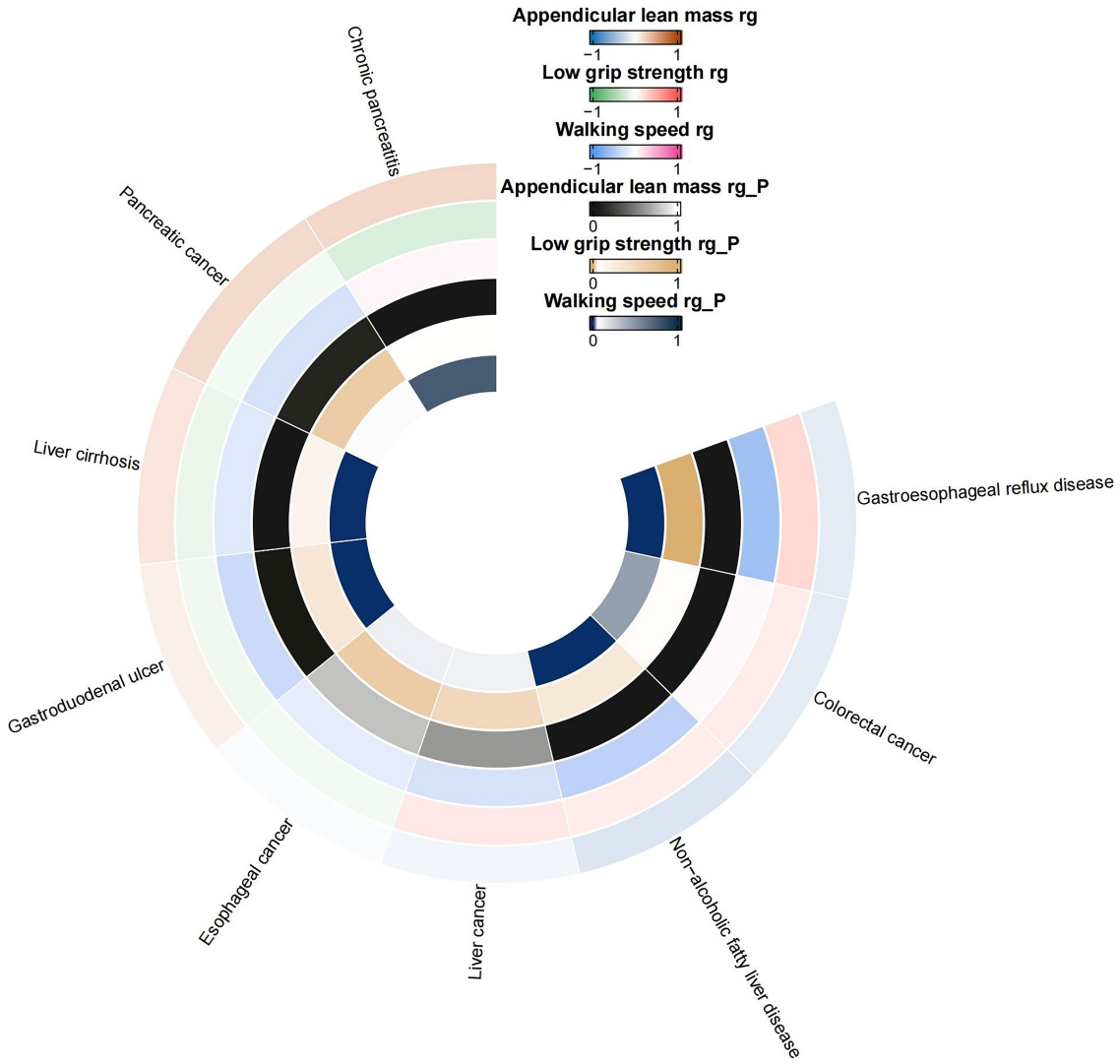


FIGURE 2
Circular heat map of suggestive genetic correlation between sarcopenia-related traits and 10 digestive system disorders. rg, genetic correlation.

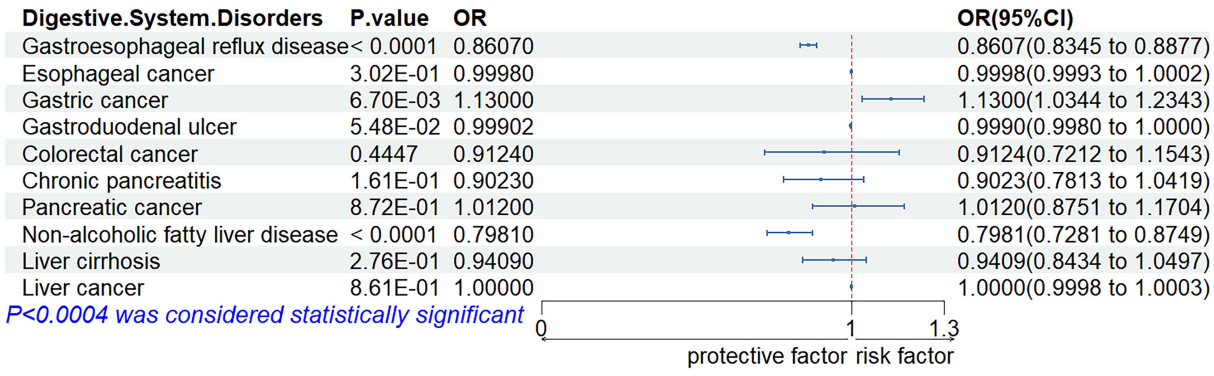


FIGURE 3
Associations of genetic liability to appendicular lean mass with digestive system disorders.

cancer (OR = 1.7706; 95% CI: 1.2193 to 2.5710; $p = 0.0027$). Moreover, our meta-analysis provided suggestive evidence for potential causal effects of walking speed on GERD (OR = 0.1946; 95% CI: 0.0736 to 0.5149; $p = 0.0010$) and colorectal cancer (OR = 0.4552; 95% CI: 0.2502 to 0.8282; $p = 0.0100$). In the reverse MR analysis, we observed suggestive evidence of potential causal relationships between chronic pancreatitis and walking speed ($\beta = -0.0031$; 95% CI: −0.0059 to −0.0004; $p = 0.0259$), as well as

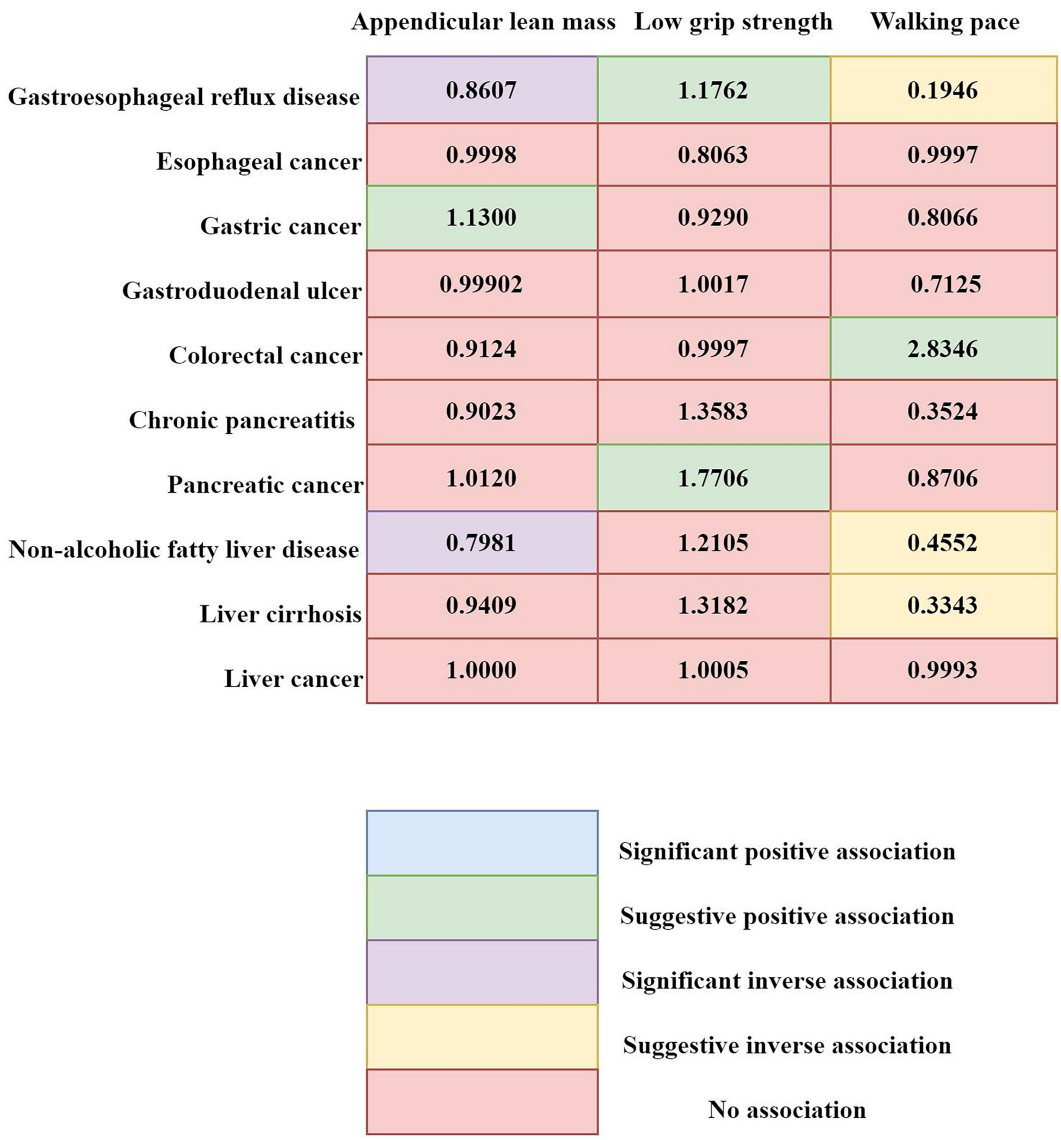


FIGURE 4
Summary of associations of genetically predicted sarcopenia-related traits and 10 digestive system disorders. Numbers in the boxes are ORs for associations of exposure and each gastrointestinal outcome. Statistical significance was established at a *p*-value <0.0004, while *p*-values ranging from 0.0004 to 0.05 were viewed as suggestive of a potential causal correlation.

between esophageal cancer and low grip strength (β = 0.0386; 95% CI: 0.0157–0.0616; p = 0.0010).

3.2.4 Mediation analysis

In our analysis, we assessed the mediating impact of metabolic disorders on the relationship between ALM and gastroesophageal reflux disease as well as non-alcoholic fatty liver. The mediating effect in the pathway to gastroesophageal reflux disease is 0.0087 (95% CI, 8e-04, 0.0183), representing 5.9398% (95% CI, 0.5462, 12.4940%) of the total effect. For the pathway to non-alcoholic fatty liver, the mediating effect is 0.0150 (95% CI, 0.0050, 0.0270), contributing to 19.7808% (95% CI, 6.5936, 35.6055%) of the total effect (refer to Supplementary Table S7 for specifics).

4 Discussion

This study, to our knowledge, is the first to delve into the genetic connections and causal relationships between traits associated with sarcopenia and a spectrum of ten digestive system disorders, using GWAS summary statistics. The research reveals the genetic ties between ALM and various conditions including GERD, chronic pancreatitis, colorectal cancer, NAFLD, and cirrhosis. It also brings to light the association between reduced hand grip strength and GERD, and points to a possible relationship between walking pace and a range of disorders such as GERD, NAFLD, gastroduodenal ulcers, and cirrhosis. The MR analysis provided strong causal evidence, suggesting that an increased ALM is significantly associated with a lower risk of GERD and NAFLD. Additionally, suggestive evidence proposes a causal link between sarcopenia-related traits and gastric cancer, pancreatic cancer, colorectal cancer, and cirrhosis. In the reverse MR analysis, we detected suggestive evidence that may link chronic pancreatitis to walking speed and esophageal cancer to reduced grip strength.

In a cohort study based on health check-ups, sarcopenia emerged as a distinct predictive element for the development of GERD (4). A separate five-year longitudinal cohort investigation highlighted that diminished back muscle strength and the presence of sarcopenia are key

contributors to the onset of GERD (24). Our research corroborates these findings. The genetic connection between traits associated with sarcopenia and GERD was also a significant discovery in this study. Further MR analyses have yielded robust evidence that genetically predicted elevated levels of ALM are inversely associated with a lower likelihood of GERD. Additionally, there is suggestive evidence that an individual's walking pace may serve as a protective factor against GERD, while a weak grip could potentially raise the risk. This MR study expands upon previous research on sarcopenia and gastroesophageal reflux disease by including not only the loss of muscle mass, which has traditionally been the focus, but also by considering gait speed and grip strength in its definition of sarcopenia. This approach addresses a notable gap in the literature. The findings indicate that the risk of gastroesophageal reflux is primarily influenced by muscle mass, rather than aspects of strength or functional performance. This novel insight suggests that interventions aimed at increasing muscle mass could be particularly effective in reducing the risk of GERD, offering a new perspective on the relationship between sarcopenia and gastroesophageal reflux.

Evidence from prior research has indicated a link between sarcopenia and GERD, potentially connected to metabolic syndrome (4). It has been documented that sarcopenia may lead to insulin intolerance, a hallmark of metabolic syndrome, establishing a reciprocal and detrimental relationship (25). Furthermore, the loss of muscle mass due to sarcopenia can result in reduced physical activity, which in turn can cause an escalation of visceral adiposity (26). Since skeletal muscles play a pivotal role in insulin sensitivity, sarcopenic patients are prone to the progression of metabolic syndrome, which may impair the functionality of the esophagus and stomach as mechanical barriers, thus precipitating GERD (4). Our advanced mediation analysis substantiates this link, highlighting the role of metabolic disorders in this context, especially the 5.9398% influence of ALM on GERD. Conversely, there is no supporting evidence that reduced grip strength or walking velocity have a mediating impact on GERD via metabolic pathways. These insights contribute to a clearer understanding of the mechanisms underlying the relationship between sarcopenia and GERD.

Previous inquiries, including both observational and MR studies, have sought to understand the connection between sarcopenia and NAFLD, yielding incongruent results. A cross-sectional analysis demonstrated a significant and solitary link between reduced muscle mass and strength with the prevalence of NAFLD (5). In parallel, an MR investigation established a causal effect of genetically driven muscle wasting on the likelihood of NAFLD (27). A recent synthesis of 19 observational studies, along with data from the National Health and Nutrition Examination Survey (NHANES), has corroborated these findings (28, 29). On the other hand, an MR study did not establish a causal link between sarcopenia and NAFLD (30). Our research has uncovered a genetic link between ALM, walking velocity, and the risk of NAFLD. MR studies have provided robust evidence that a higher genetically predicted ALM is associated with a reduced risk of alcoholic fatty liver. There is also suggestive evidence that faster walking speeds may lower the risk of NAFLD. Conversely, no genetic or causal ties have been identified between diminished grip strength and NAFLD. These findings suggest that the risk of NAFLD may be primarily influenced by muscle mass rather than strength or functional capacity, indicating that interventions aimed at increasing muscle mass could be most effective in the prevention of NAFLD.

Research has established that skeletal muscle, being the principal tissue for insulin-mediated glucose metabolism, is pivotal in the process of insulin signaling (31). A reduction in skeletal muscle mass is associated with the development of insulin resistance and dysregulation of blood glucose levels, which can ultimately result in NAFLD (32). Our subsequent mediation analysis supports this relationship, indicating that it is through the exacerbation of metabolic disorders that skeletal muscle mass influences NAFLD, with a notable 18% effect of ALM. The analysis also revealed that neither low grip strength nor walking speed have a significant mediating role in the development of NAFLD through metabolic pathways.

Indeed, the precise pathways through which sarcopenia contributes to the risk of NAFLD remain to be fully understood. Current hypotheses suggest a connection with inflammatory processes and oxidative stress (33–35). There is evidence to suggest that a deficiency in Vitamin D could be a common factor in the development of both sarcopenia and NAFLD, potentially influencing this relationship (36–38). Moreover, skeletal muscle, recognized as an endocrine tissue, releases myokines—peptides like interleukin-6 (IL-6) and irisin (33). The diminished production of these advantageous myokines due to muscle loss could be a contributing factor in the pathogenesis of NAFLD.

In a propensity score-matched Asian cohort investigation, sarcopenia was identified as a potential significant contributor to the risk of developing colorectal, pancreatic, gastric, esophageal, and hepatocellular carcinomas (6). Nevertheless, our research uncovered a mere hint of a genetic link between ALM and colorectal cancer, without establishing any genetic connection to other gastrointestinal cancers related to sarcopenia. Simultaneously, the MR study offered only preliminary insights, suggesting a possible connection between a rise in ALM and an elevated likelihood for gastric cancer. It also indicated that a weakened grip strength might be associated with a greater risk of pancreatic cancer, while an increased walking pace could potentially lower the chances of developing colorectal cancer. However, the study did not establish a direct causal relationship between genetically determined sarcopenia and the development of esophageal or hepatocellular carcinomas. Our findings do not align with those from prior Asian cohort research, which might be due to population-specific causal interactions. Given that the cohort research comprised solely of individuals from the Asian population, these results may not be directly relevant to Europeans. Currently, there is a dearth of observational studies on the interplay between sarcopenia and gastrointestinal cancers in the European demographic. Future research should prioritize the initiation of high-caliber cohort studies to confirm and expand upon our results.

Our analysis has yielded robust findings, indicating a genetic link between ALM and chronic pancreatitis, as well as between walking velocity and the occurrence of gastroduodenal ulcers. There is also suggestive data pointing to a genetic association with ALM, brisk walking, and the likelihood of liver cirrhosis. Concurrently, MR studies have provided suggestive evidence that an increased walking pace may lower the risk of cirrhosis. However, no direct causal link was observed between sarcopenia, determined by genetics, and either chronic pancreatitis or gastroduodenal ulcers. In the inverse MR studies, we identified only suggestive evidence for a potential causal effect of genetic predisposition to chronic pancreatitis on walking speed, and a genetic predisposition to esophageal cancer associated with reduced grip strength. For the remaining eight gastrointestinal conditions, no causal connections to sarcopenia were discerned. Observational research in the past has indicated that sarcopenia is associated with a notable rise in the occurrence of cirrhosis and gastroduodenal ulcers (39, 40). Additionally, gastrointestinal malignancies and chronic pancreatitis have been shown to markedly elevate the risk of developing sarcopenia (41, 42). Despite these findings, the observational nature of

most prior studies leaves the causality of these associations in question. In contrast, MR analysis offers a more robust approach by mitigating the influence of confounding elements and the issue of reverse causality, thus providing more dependable evidence regarding these relationships.

Our investigation offers a number of distinct benefits. Initially, this marks the inaugural use of MR to bidirectionally assess the causal links between sarcopenia and an array of gastrointestinal disorders. This MR approach, with its capacity to pinpoint causality, stands out over traditional observational studies by circumventing confounding influences and the potential for reverse causality. Secondly, the inclusion of a wide range of gastrointestinal conditions in our study allows for the most comprehensive evaluation yet of the association between sarcopenia and these diseases. Lastly, we have performed both discovery and replication analyses on gastrointestinal disease GWAS data from two distinct sources. By excluding pleiotropy and synthesizing the findings, we have ensured the dependability of our results.

We must concede that there are certain limitations to this research. Initially, the constraints on the number of accessible GWAS studies or the occurrence of significant pleiotropy in some findings result in conclusions derived from a single data source, which may compromise their strength. Furthermore, since the study's participants were primarily of European ancestry, the broader applicability of our findings to populations of different ethnicities is uncertain. It is imperative that these results be substantiated through further research involving a more heterogeneous group of individuals. In addition, although our study, through GWAS data aggregation, suggests the potential utility of augmenting muscle mass in preventing gastroesophageal reflux disease and non-alcoholic fatty liver disease, further comprehensive investigations are imperative to corroborate our findings and elucidate the underlying mechanisms.

5 Conclusion

To encapsulate the findings, this research discloses the causal relationships that sarcopenia has with a multitude of gastrointestinal conditions and the pivotal part that metabolic disorders play as mediators in these pathways. The study suggests that increasing muscle mass could be a constructive approach to preventing gastroesophageal reflux disease and non-alcoholic fatty liver, underscoring the significance of metabolic disorder management as a vital strategy in curbing the risks associated with these diseases that are linked to sarcopenia.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/Supplementary material.

Ethics statement

Written informed consent from the patients/participants or the patients'/participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

TY: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. ZL: Investigation, Writing – original draft. MX: Data curation, Formal analysis, Writing – review & editing. XQ: Software, Supervision, Writing – review & editing. SL: Resources, Supervision, Writing – review & editing. WX: Resources, Supervision, Writing – original draft. ML: Resources, Supervision, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. The research, authorship, and/or publication of this article have been financially supported. This work was supported by the Science and Technology Strategic Cooperation Project of Luzhou Municipal People's Government and Southwest Medical University (2020LZXNYDZ02, 2023LZXNYDJ001); the Science and Technology Plan Project of Sichuan Province (2022YFS0626); and the Science and Technology Plan Project of Luzhou City (2023RCM198).

Acknowledgments

We want to acknowledge the participants and investigators of the FinnGen study and the IEU Open GWAS Project.

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.2024.1412842/full#supplementary-material

References

1. Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet*. (2019) 393:2636–46. doi: 10.1016/s0140-6736(19)31138-9

2. Yuan S, Larsson SC. Epidemiology of sarcopenia: prevalence, risk factors, and consequences. *Metab Clin Exp*. (2023) 144:155533. doi: 10.1016/j.metabol.2023.155533

3. Zhang FM, Wu HF, Shi HP, Yu Z, Zhuang CL. Sarcopenia and malignancies: epidemiology, clinical classification and implications. *Ageing Res Rev*. (2023) 91:102057. doi: 10.1016/j.arr.2023.102057

4. Kim YM, Kim JH, Baik SJ, Jung DH, Park JJ, Youn YH, et al. Association between skeletal muscle attenuation and gastroesophageal reflux disease: a health check-up cohort study. *Sci Rep*. (2019) 9:20102. doi: 10.1038/s41598-019-56702-6

5. Gan D, Wang L, Jia M, Ru Y, Ma Y, Zheng W, et al. Low muscle mass and low muscle strength associate with nonalcoholic fatty liver disease. *Clin Nutr*. (2020) 39:1124–30. doi: 10.1016/j.clnu.2019.04.023

6. Sun MY, Chang CL, Lu CY, Wu SY, Zhang JQ. Sarcopenia as an independent risk factor for specific cancers: a propensity score-matched Asian population-based cohort study. *Nutrients*. (2022) 14:1910. doi: 10.3390/nu14091910

7. Smith GD, Ebrahim S. 'Mendelian randomization': can genetic epidemiology contribute to understanding environmental determinants of disease?. *Int J Epidemiol*. (2019) 32:1–22. doi: 10.1093/ije/dyg070

8. Lee K, Lim CY. Mendelian randomization analysis in observational epidemiology. *J Lipid Atheroscler*. (2019) 8:67–77. doi: 10.12997/jla.2019.8.2.67

9. Lawlor DA, Harbord RM, Sterne JA, Timpson N, Davey Smith G. Mendelian randomization: using genes as instruments for making causal inferences in epidemiology. *Stat Med*. (2008) 27:1133–63. doi: 10.1002/sim.3034

10. Sakaue S, Kanai M, Tanigawa Y, Karjalainen J, Kurki M, Koshiba S, et al. A cross-population atlas of genetic associations for 220 human phenotypes. *Nat Genet*. (2021) 53:1415–24. doi: 10.1038/s41588-021-00931-xIF:30.8.Q1

11. Ghodsian N, Abner E, Emdin CA, Gobeil É, TabaN, Haas ME, et al. Electronic health record-based genome-wide meta-analysis provides insights on the genetic architecture of non-alcoholic fatty liver disease. *Cell Rep Med*. (2021) 2:100437. doi: 10.1016/j.xcrm.2021.100437IF:14.3.Q1

12. Burgess S, Thompson SG. Avoiding bias from weak instruments in Mendelian randomization studies. *Int J Epidemiol*. (2011) 40:755–64. doi: 10.1093/ije/dyr036

13. Bulik-Sullivan BK, Loh PR, Finucane HK, Ripke S, Yang J, Patterson N, et al. LD score regression distinguishes confounding from polygenicity in genome-wide association studies. *Nat Genet*. (2015) 47:291–5. doi: 10.1038/ng.3211

14. ReproGen ConsortiumPsychiatric Genomics ConsortiumGenetic Consortium for Anorexia Nervosa of the Wellcome Trust Case Control Consortium 3Bulik-Sullivan B, Finucane HK, Anttila V, et al. An atlas of genetic correlations across human diseases and traits. *Nat Genet*. (2015) 47:1236–41. doi: 10.1038/ng.3406

15. Curtin F, Schulz P. Multiple correlations and Bonferroni's correction. *Biol Psychiatry*. (1998) 44:775–7. doi: 10.1016/s0006-3223(98)00043-2

16. Hemani G, Zheng J, Elsworth B, Wade KH, Haberland V, Baird D, et al. The MR-base platform supports systematic causal inference across the human phenome. *eLife*. (2018) 7:e34408. doi: 10.7554/eLife.34408

17. Burgess S, Foley CN, Allara E, Staley JR, Howson JMM. A robust and efficient method for Mendelian randomization with hundreds of genetic variants. *Nat Commun*. (2020) 11:376. doi: 10.1038/s41467-019-14156-4

18. Bowden J, Davey Smith G, Haycock PC, Burgess S. Consistent estimation in Mendelian randomization with some invalid instruments using a weighted median estimator. *Genet Epidemiol*. (2016) 40:304–14. doi: 10.1002/gepi.21965

19. Verbanck M, Chen CY, Neale B, Do R. Detection of widespread horizontal pleiotropy in causal relationships inferred from Mendelian randomization between complex traits and diseases. *Nat Genet*. (2018) 50:693–8. doi: 10.1038/s41588-018-0099-7

20. Burgess S, Bowden J, Fall T, Ingelsson E, Thompson SG. Sensitivity analyses for robust causal inference from Mendelian randomization analyses with multiple genetic variants. *Epidemiology*. (2017) 28:30–42. doi: 10.1097/ede.0000000000000559

21. Nishikawa H, Asai A, Fukunishi S, Nishiguchi S, Higuchi K. Metabolic syndrome and sarcopenia. *Nutrients*. (2021) 13:3519. doi: 10.3390/nu13103519

22. Carter AR, Sanderson E, Hammerton G, Richmond RC, Davey Smith G, Heron J, et al. Mendelian randomisation for mediation analysis: current methods and challenges for implementation. *Eur J Epidemiol*. (2021) 36:465–78. doi: 10.1007/s10654-021-00757-1

23. MacKinnon DP, Lockwood CM, Hoffman JM, West SG, Sheets V. A comparison of methods to test mediation and other intervening variable effects. *Psychol Methods*. (2002) 7:83–104. doi: 10.1037/1082-989x.7.1.83

24. Imagama S, Ando K, Kobayashi K, Machino M, Tanaka S, Morozumi M, et al. Increase in lumbar kyphosis and spinal inclination, declining back muscle strength, and sarcopenia are risk factors for onset of GERD: a 5-year prospective longitudinal cohort study. *Eur Spine J*. (2019) 28:2619–28. doi: 10.1007/s00586-019-06139-2

25. Gaster M, Vach W, Beck-Nielsen H, Schrøder HD. GLUT4 expression at the plasma membrane is related to fibre volume in human skeletal muscle fibres. *APMIS*. (2002) 110:611–9. doi: 10.1034/j.1600-0463.2002.1100903.x

26. Choi KM. Sarcopenia and sarcopenic obesity. *Endocrinol Metab*. (2013) 28:86–9. doi: 10.3803/EnM.2013.28.2.86

27. Ye C, Kong L, Wang Y, Zheng J, Xu M, Xu Y, et al. Causal associations of sarcopenia-related traits with cardiometabolic disease and Alzheimer's disease and the mediating role of insulin resistance: a Mendelian randomization study. *Aging Cell*. (2023) 22:e13923. doi: 10.1111/acel.13923

28. Cai C, Song X, Chen Y, Chen X, Yu C. Relationship between relative skeletal muscle mass and nonalcoholic fatty liver disease: a systematic review and meta-analysis. *Hepatol Int*. (2020) 14:115–26. doi: 10.1007/s12072-019-09964-1

29. Zhao X, Shi X, Gu H, Zhou W, Zhang Q. Association between handgrip strength, nonalcoholic fatty liver disease, advanced hepatic fibrosis and its modifiers: evidence from the NHANES database of the USA. *J Gastroenterol Hepatol*. (2023) 38:1734–42. doi: 10.1111/jgh.16150

30. Zhao ZH, Zou J, Huang X, Fan YC, Wang K. Assessing causal relationships between sarcopenia and nonalcoholic fatty liver disease: a bidirectional Mendelian randomization study. *Front Nutr*. (2022) 9:971913. doi: 10.3389/fnut.2022.971913

31. DeFronzo RA, Jacot E, Jequier E, Maeder E, Wahren J, Felber JP. The effect of insulin on the disposal of intravenous glucose. Results from indirect calorimetry and hepatic and femoral venous catheterization. *Diabetes*. (1981) 30:1000–7. doi: 10.2337/diab.30.12.1000

32. Bhanji RA, Narayanan P, Allen AM, Malhi H, Watt KD. Sarcopenia in hiding: the risk and consequence of underestimating muscle dysfunction in nonalcoholic steatohepatitis. *Hepatology*. (2017) 66:2055–65. doi: 10.1002/hep.29420

33. Joo SK, Kim W. Interaction between sarcopenia and nonalcoholic fatty liver disease. *Clin Mol Hepatol*. (2023) 29:S68–s78. doi: 10.3350/cmh.2022.0358

34. Beyer I, Mets T, Bautmans I. Chronic low-grade inflammation and age-related sarcopenia. *Curr Opin Clin Nutr Metab Care*. (2012) 15:12–22. doi: 10.1097/MCO.0b013e32834dd297

35. Wree A, Kahraman A, Gerken G, Canbay A. Obesity affects the liver - the link between adipocytes and hepatocytes. *Digestion*. (2011) 83:124–33. doi: 10.1159/000318741

36. Eliades M, Spyrou E, Agrawal N, Lazo M, Brancati FL, Potter JJ, et al. Meta-analysis: vitamin D and non-alcoholic fatty liver disease. *Aliment Pharmacol Ther*. (2013) 38:246–54. doi: 10.1111/apt.12377

37. Barchetta I, Angelico F, Ben MD, Baroni MG, Pozzilli P, Morini S, et al. Strong association between non alcoholic fatty liver disease (NAFLD) and low 25(OH) vitamin D levels in an adult population with normal serum liver enzymes. *BMC Med*. (2011) 9:85. doi: 10.1186/1741-7015-9-85

38. Visser M, Deeg DJ, Lips P. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): the longitudinal aging study Amsterdam. *J Clin Endocrinol Metab*. (2003) 88:5766–72. doi: 10.1210/jc.2003-030604

39. Choi YI, Chung JW, Park DK, Ko KP, Kim KO, Kwon KA, et al. Sarcopenia is independently associated with an increased risk of peptic ulcer disease: a Nationwide population-based study. *Medicina (Kaunas)*. (2020) 56:121. doi: 10.3390/medicina56030121

40. Cui Y, Zhang M, Guo J, Jin J, Wang H, Wang X. Correlation between sarcopenia and cirrhosis: a meta-analysis. *Front Nutr*. (2023) 10:1342100. doi: 10.3389/fnut.2023.1342100

41. Surov A, Wienke A. Prevalence of sarcopenia in patients with solid tumors: a meta-analysis based on 81,814 patients. *JPEN J Parenter Enteral Nutr*. (2022) 46:1761–8. doi: 10.1002/jpen.2415

42. Bundred J, Thakkar RG, Pandanaboyana S. Systematic review of sarcopenia in chronic pancreatitis: prevalence, impact on surgical outcomes, and survival. *Expert Rev Gastroenterol Hepatol*. (2022) 16:665–72. doi: 10.1080/17474124.2022.2091544

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 05 August 2024
DOI 10.3389/fpubh.2024.1406303

OPEN ACCESS

EDITED BY
Yun Gao,
Sichuan University, China

REVIEWED BY
Dongdong Qin,
Yunnan University of Chinese Medicine, China
Teresa Dianne Hawkes,
Applied Research Solutions, United States

*CORRESPONDENCE
Yang Pan
✉ panyang@sdu.edu.cn

RECEIVED 24 March 2024
ACCEPTED 19 July 2024
PUBLISHED 05 August 2024

CITATION
Chen J, Lu Y, Yao J, Zhang X and Pan Y (2024) The relationship between accelerometer-based physical activity, sedentary behavior, and seven common geriatric syndromes: a two-sample Mendelian randomization study.
Front. Public Health 12:1406303.
doi: 10.3389/fpubh.2024.1406303

The relationship between accelerometer-based physical activity, sedentary behavior, and seven common geriatric syndromes: a two-sample Mendelian randomization study

Jiping Chen[1], Yanyu Lu[1], JiaWei Yao[2], Xianliang Zhang[1] and Yang Pan[1]*

[1]School of Physical Education, Shandong University, Jinan, China, [2]Department of Physical Education Teaching and Research, Guangdong Dance and Drama College, Foshan, China

Introduction: To investigate the causal associations between accelerometer-based physical activity (PA), sedentary behavior (SB), and seven common geriatric syndromes (GSs) (frailty, falls, delirium, urinary incontinence, dysphagia, hearing loss, and visual impairment) by Mendelian randomization (MR) analysis.

Methods: Instrumental variables from a genome-wide association study were used for MR analysis. The exposure factors were three PA phenotypes (average acceleration, overall activity, and moderate-intensity activity) and one SB phenotype (SB). The outcome variables were seven common GSs. The inverse variance weighted (IVW) method was utilized for the primary MR analysis. Additionally, sensitivity, pleiotropy, and heterogeneity analyses were subsequently conducted to assess the robustness of the present study's findings.

Results: According to the primary MR results obtained using the IVW method, genetically predicted PA (average acceleration) decreased the risk of two GSs (frailty, $p = 0.01$; dysphagia, $p = 0.03$). Similarly, overall activity decreased the risk of two GSs (frailty, $p = 0.01$; delirium, $p = 0.03$), and moderate-intensity activity reduced the risk of three GSs (urinary incontinence, $p = 0.04$; hearing loss, $p = 0.02$; visual impairment, $p = 0.01$). Furthermore, SB was causally correlated with a greater risk for three GSs (frailty, $p = 0.03$; fall, $p = 0.01$; dysphagia, $p = 0.04$).

Conclusion: This study provided evidence that accelerometer-based PA may be causally associated with a lower risk of GSs, while SB may increase the risk of GSs.

KEYWORDS

accelerometer-based, physical activity, sedentary behavior, geriatric syndromes, mendelian randomization

1 Introduction

The term geriatric syndromes (GSs) refers to a group of medical conditions in the older adult, such as frailty, falls, delirium, and incontinence, associated with age increase (1, 2). Due to the complex pathogenesis involving dysregulated metabolism, immune system decline, and musculoskeletal dysfunction, the incidence of GSs has shown an upward trend consistently in recent years (3). According to recent epidemiological advancements, GSs affect approximately 10–33% of adults aged 65 and above worldwide, with more than 40% experiencing two or more symptoms simultaneously (4, 5). These conditions lead to long-term disability, emotional distress, and social isolation, all of which diminish the quality of life for the older adult and impose an economic burden on the whole society (6, 7). As reported, healthcare costs associated with GSs have been estimated to reach $164 billion annually in the US and over $182 billion in 18 European nations combined (7, 8). Therefore, GSs pose not only a medical issue but also a significant challenge to public health and socio-economic factors.

Physical activity (PA) has gained increasing attention in recent decades due to its lower cost and higher adherence than traditional strategies like medication, long-term nursing, and hospitalization (9, 10). There is strong evidence that PA was associated with a risk reduction in the incidence of GSs. A previous Longitudinal cohort study found that maintaining a regular frequency of PA is associated with frailty among European community-dwelling older adult (11). Another cross-sectional study conducted in Japan discovered a correlation between increased leisure-time PA and a reduced incidence of dysphagia, suggesting the potential protective role of PA on GSs (12). Conversely, insalubrious lifestyles such as sedentary behavior (SB) in older adults hurt muscle strength (13), bone health (14), and cognitive function (15). Several cohort studies investigating lifestyle factors and risk of GSs reported that SB was independently and positively associated with frailty and falls (16, 17). As two modifiable lifestyles, both PA and SB are strongly associated with several GSs. However, existing observational studies cannot eliminate the potential for reverse causation and confounding factors, hindering the establishment of causal relationships. Previous studies on PA and SB have primarily used self-reported activity measures instead of directly measuring overall mean acceleration with a wrist-worn accelerometer (18). This reliance on self-validated measures introduces the potential for information bias (19, 20). Therefore, the causal relationship between objectively measured PA, SB, and GSs remains uncertain.

Mendelian randomization (MR) study is a statistical method to infer potential causal relationships between exposure and outcome (21). Although MR methods have limitations, such as genetic variants only explaining a portion of the exposure variability and the possibility of unrecognized confounders still existing. An advantage of MR studies is their ability to strengthen result justification by minimizing the impact of confounding factors on result accuracy. Simultaneously, MR studies offer more robust evidence to ascertain the causal relationship between exposure and outcome (22). Therefore, this study used MR to investigate the causal relationship between accelerometer-based PA, SB, and GSs. These findings can potentially contribute novel strategies for preventing, diagnosing, and treating GSs.

2 Materials and methods

2.1 Study design

This study used two-sample MR to analyze the causal relationship between PA, SB, and GSs. A valid MR analysis must be supported by three key assumptions (23): (1) the selected genetic variants as instrumental variables (IVs) are robustly correlations with the exposure (24); (2) there were no unmeasured confounders for associations between genetic variants and outcomes (25); (3) the genetic variants affect the outcome only through their effect on the exposure of interest, that is, there is no horizontal pleiotropy between genetic variants and outcome (26). The overall design was shown in Figure 1.

For this MR study, we prioritized using IVs from Genome-Wide Association Studies (GWAS) databases over those from single-nation databases. This approach was chosen due to several advantages associated with GWAS databases (27): (1) GWAS databases include genetic data from a wide range of populations globally, providing a more comprehensive selection of SNPs. This ensures that our study captures a representative sample of genetic variations; (2) GWAS typically involve large-scale sample collections, resulting in higher statistical power and more reliable findings than smaller, single-nation studies; (3) the inclusion of diverse populations in GWAS helps to minimize regional and ethnic differences, enhancing the validity of our causal inferences.

In addition, we followed the Strengthening the Reporting of Observational Studies in Epidemiology–Mendelian Randomization (STROBE-MR) reporting guidelines in this study (28). All studies contributing data to these analyses obtained institutional review board approval from the respective countries, aligning with the Declaration of Helsinki (29). The present study did not need additional ethical approval since the original studies have received appropriate ethics and institutional review board approval.

2.2 Data sources

Three types of accelerometer-based PA and one type of accelerometer-based SB were included in our study as exposures, including acceleration average (AccAve), overall activity, moderate-intensity physical activity (MPA), and SB. GWAS for AccAve came from a recent study on PA among 377,234 participants from the UK Biobank (30). It required participants to wear an Axivity AX3 accelerometer for at least 72 h in a week, data <72 h or not completed every hour of the 24-h cycle, and other outliers were excluded (31). Overall activity, MPA, and SB were from another GWAS on PA and SB measured using wrist-worn accelerometers ($N = 91,105$); participants were asked to wear activity trackers over 7 days (32). Details of PA, SB, and accelerometers are in Supplementary Table S1.

Drawing from the GSs literature, this study focused on seven common GSs as outcomes, including frailty (4), urinary incontinence (2), dysphagia (33), delirium, fall (1), hearing loss and visual impairment (34). The source of GWAS for exposures and outcomes were shown in Table 1, and detailed information on each of the GSs is shown in Supplementary Table S2.

It is important to note that this part of the study was time-consuming for both the human subjects and the researchers due to the need for extended wear time and rigorous data collection protocols.

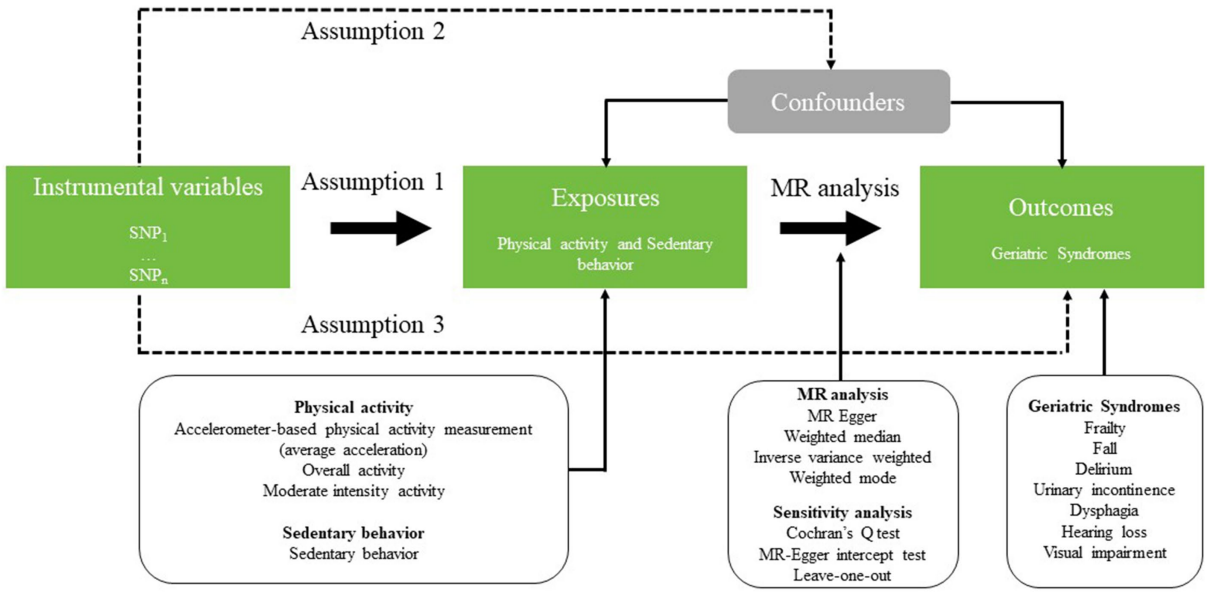


FIGURE 1
Schematic representation of the three hypotheses and study design.

TABLE 1 Characteristics and sources of data in this study.

Trait	Sample size	Population	No. of SNPs	GWAS ID	PMID
Frailty	175,226	European	7,589,717	ebi-a-GCST90020053	34431594
Fall	218,792	European	16,380,466	finn-b-FALLS	/
Delirium	218,792	European	16,380,466	finn-b-ALCODELIRIUM	/
Urinary incontinence	463,010	European	9,851,867	ukb-b-11531	/
Dysphagia	463,010	European	9,851,867	ukb-b-7073	/
Hearing loss	330,759	European	10,858,770	ebi-a-GCST90012115	32986727
Visual impairment	211,769	European	16,380,453	finn-b-H7_ BLINDANDVISIMPAIRMENT	/
AccAve	91,084	European	11,796,201	ebi-a-GCST006099	29899525
Overall activity	91,105	European	9,926,106	/	30531941
MPA	91,105	European	9,926,106	/	30531941
SB	91,105	European	9,926,106	/	30531941

2.3 Genetic instrumental variable selection

Inclusion criteria: (1) single nucleotide polymorphisms (SNPs) with complete genetic significance, ensuring independence and high correlation between exposure factors and outcome variables, were chosen as instrumental variables (35). In previous MR studies, accelerometer-based GWAS of PA identified only 2 independent genome-wide significant SNPs with 5–14% heritability of PA (19). Heritability estimates indicate that SNPs, not currently identified as genome-wide significant, may play a role in the variation of PA. Consequently, SNPs were chosen to achieve genome-wide significance ($p < 5e{-}06$). This approach of adjusting statistical thresholds for genetic tools has been employed in earlier MR studies where physical activity served as an exposure (19); (2) A criterion of $F > 10$ was employed to define a strong association. To evaluate the strength of the instrumental variables (IVs), the F statistic of an individual SNP was computed. If $F > 10$, it indicates a negligible possibility of weak instrumental variable bias (36); (3) to exclude the influence of gene pleiotropy on the results, the linkage disequilibrium coefficient r^2 was set to 0.001, and the width of the linkage disequilibrium region was set to 10,000 kb, to ensure the independence of each SNP (21, 37).

Exclusion criteria: given the close association of various confounding factors with the pathogenesis of sarcopenia, SNPs were scrutinized against the PhenoScanner database[1] to identify potential violations of independence and exclusivity assumptions. SNPs closely linked to the geriatric syndrome were then excluded. After screening

1 http://www.phenoscanner.medschl.cam.ac.uk/

based on inclusion and exclusion criteria, the detailed information on SNPs used as instrumental variables in the MR analyses is shown in Supplementary Tables S3–S6.

2.4 Statistical analysis

In this paper, we used the following four different methods to estimate the causal relationship between PA, SB, and GSs: (1) we used the inverse variance weighted (IVW) method as the main analysis, which is essentially a meta-analysis method. IVW assesses causality by meta-analyzing the Wald ratios for each of the included SNP (37, 38); (2) we used MR-Egger to detect several violations of the assumptions of the standard instrumental variables and provide estimates of effects that are unaffected by these violations. MR-Egger also provides a sensitivity analysis for the robustness of the results of MR studies (23); (3) we also used the weighted median approach because this method yields reliable estimates of causal effects, even though <50% of the information comes from the null instrument (25); (4) weighted mode is consistent when the largest subset of instruments which identify the same causal effect are valid instruments, even if the majority of others are invalid (39). The assessment of causality between exposure and outcome was quantified as odds ratios (OR) and their respective 95% confidence intervals (CI). Statistical significance was indicated by a $p < 0.05$.

In addition, we used Cochran's *Q*-test to detect heterogeneity among the selected SNPs, and if heterogeneity existed ($p < 0.05$) (40). To identify potential pleiotropy, we tested for MR-Egger-intercept horizontal pleiotropy, with a *p*-value for the intercept >0.05 indicating that no horizontal pleiotropy existed (41). Meanwhile, we removed individual SNPs one by one using the leave-one-out method and calculated the meta-effect estimates and confidence intervals for the remaining SNPs (42). It was used to test the effect of individual SNPs on causal inference.

In this study, R software (version 4.0.2) was used for all data analysis as well as for drawing statistical plots, mainly R packages (TwoSampleMR, Pacman, Matrix, and Mendelian randomization) were used for data analysis (43). These packages are free for free on the R Software website.[2]

3 Results

3.1 MR results

In the IVW analysis, we found a significant causal relationship between AccAve and a low risk of two GSs (frailty, OR = 0.99, 95% CI:0.98–0.99, $p = 0.01$; dysphagia, OR = 0.99, 95% CI: 0.99–0.99, $p = 0.03$; Figure 2). The weighted median, weighted mode, and MR-Egger analyses yielded similar patterns of effects (Supplementary Table S7). Similarly, there was a causal relationship between genetically predicted accelerometer-based "overall activity" PA and a low risk of two GSs (frailty, OR = 0.89, 95% CI: 0.81–0.98, $p = 0.01$; delirium, OR = 0.40, 95% CI: 0.16–0.95, $p = 0.03$; Figure 3) according to the IVW method. As shown in Figure 4, there was a significant causal relationship between accelerometer-based MPA and a low risk of three GSs (urinary incontinence, OR = 0.99, 95% CI: 0.99–1.00, $p = 0.04$; hearing loss, OR = 0.94, 95% CI: 0.90–0.99, $p = 0.02$; visual impairment, OR = 0.33, 95% CI: 0.13–0.80, $p = 0.01$).

Among the tested SB phenotypes, IVW analysis indicated that accelerometer assessed SB increased the risk for three GSs (frailty: $p = 0.039$, OR = 0.939, 95% CI: 0.885–0.997; fall: $p = 0.011$, OR = 2.28, 95% CI: 1.20–4.30; dysphagia: $p = 0.044$, OR = 1.004, 95% CI: 1.000–1.007, Figure 5). The results from other MR methods showed a consistent direction (Supplementary Table S7).

3.2 Sensitivity analysis

To assess the robustness of the above results, a series of sensitivity analyses, including Cochran's *Q*-test, MR Egger intercept test, and "leave-one-out," were conducted (Supplementary Table S8). All *p*-values of the MR-Egger intercept tests were >0.05, indicating that no horizontal pleiotropy existed. Meanwhile, heterogeneity was observed in the Cochran's *Q*-test between AccAve and Frailty ($Q = 54$, $p < 0.05$). Although heterogeneity was observed in specific findings, it did not render the MR estimations inaccurate as the random-effect IVW method used in this work has the potential to mitigate the overall variability.

In the "leave-one-out" approach (Supplementary Figures S1–S10), each line represents a single nucleotide polymorphism (SNP). Black dots represent the meta-effect estimates obtained when eliminating that particular SNP, while horizontal lines reflect the appropriate confidence intervals. The red line indicates the position of the zero effect. As depicted in the diagram, the total effect estimate remains mostly unchanged when eliminating each SNP. Additionally, all error lines are positioned either to the right or left of zero, indicating a higher level of reliability in the data.

4 Discussion

To the best of our knowledge, this is the first MR study to investigate the genetic association of PA, SB, and seven prevalent GSs (frailty, falls, delirium, urinary incontinence, dysphagia, hearing loss, and visual impairment). According to the data shown in the results, genetically predicted accelerometer-based PA (AccAve, overall activity, MPA) was associated with a lower risk of 6 out of 7 GSs (frailty, dysphagia, delirium, urinary incontinence, hearing loss, and visual impairment), and accelerometer-based SB was associated with an increased risk of GSs (frailty, falls, dysphagia). Sensitivity analyses also indicated that results were robust in general. These findings provided a better understanding that PA is, in general, superior to SB in the older adult and had clinical implications for patients and caregivers.

In a longitudinal cohort study involving 1,735 European community-dwelling older adults, regular PA was associated with preserving or enhancing frailty (11). In another prospective, single-center cohort study with 132 participants aged 60 and older, PA was linked to a decreased incidence of delirium, particularly among women (18). Furthermore, a cross-sectional questionnaire-based study investigated the association between dysphagia risk and daily PA, as well

2 https://www.r-project.org/

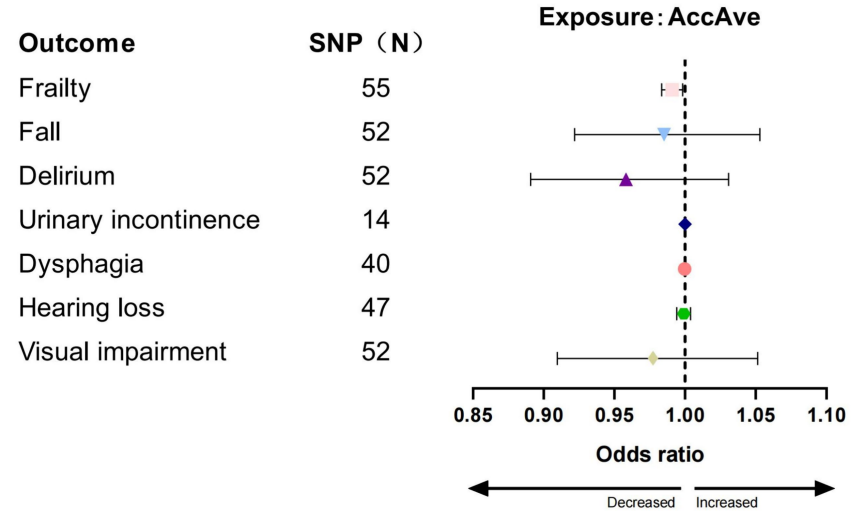


FIGURE 2
Association between AccAve and GSs by IVW method.

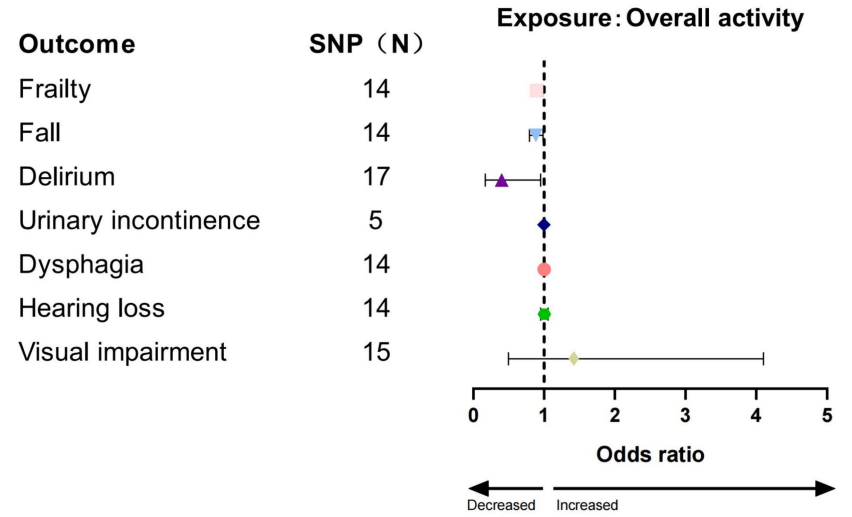


FIGURE 3
Association between overall activity and geriatric syndromes by IVW method.

as leisure-time exercise, in 3,070 community-dwelling Japanese older adults. The findings revealed that a higher level of leisure-time PA was associated with a reduced risk of dysphagia (12). However, research examining the relationship between PA and the mentioned three GS in older adults has yielded conflicting results. For instance, in a randomized controlled trial with 1,635 participants aged 70–89, the findings indicated that an MPA program did not correlate with a decreased risk of frailty (44). The present study aligns with this perspective. Additionally, a previous study identified a potential causal relationship between MPA and a reduced risk of urinary incontinence (45), hearing loss (46) and visual impairment in older adults (47). Our study, in supporting the aforementioned findings, further substantiates the potential causal relationship for them. Unfortunately, our study did not identify a potential causal relationship between accelerometer-based PA and fall risk. We have access to an explanation for this. In the MR study, SNPs associated with PA were used as instrumental variables to explore whether there is any link between exposure factors and outcome variables (48). This methodology enabled us to clearly and definitively determine the distinct influence of specific genetic variations on these outcomes, without any interference from other intricate elements (49). However, falls are not just attributed to individual genetic variations but also encompass intricate interplays between balance, muscle strength, environmental risk factors, and substance use (50, 51). Therefore, future research should look at the involvement of multiple SNPs and other complex factors in falls to provide a more complete approach to fall prevention in older persons.

There are various potential mechanisms can be used to illustrate the inverse association between PA and GSs. First, PA could induce

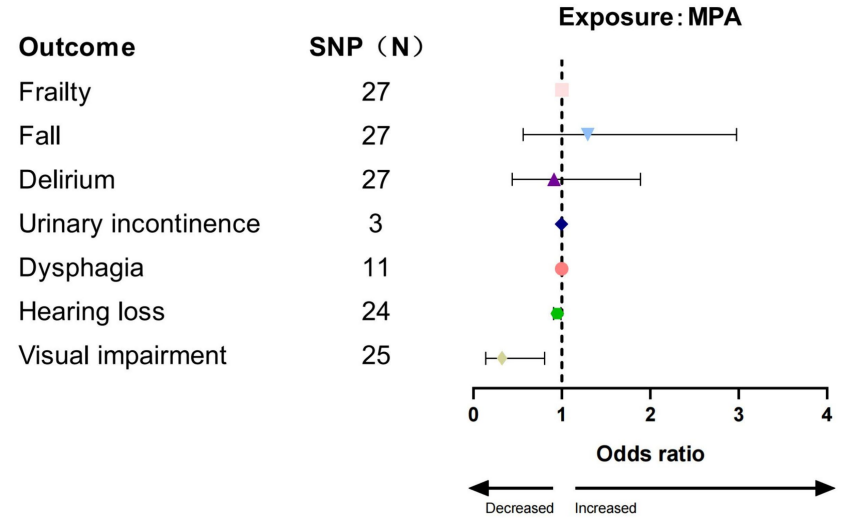


FIGURE 4
Association between MPA and GSs by IVW method.

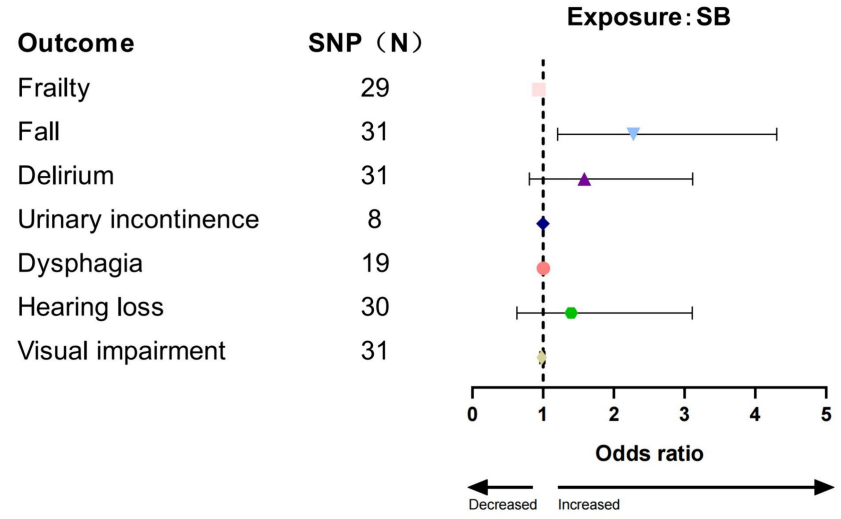


FIGURE 5
Association between SB and geriatric syndromes by IVW method.

several neuromuscular adaptations to slow down the aging-related decline in muscle function, which is suspected to be closely linked to the development of GSs (52, 53). Recent studies have shown that PA leads to the increase in peak firing frequencies of motoneurons and drives motor neuron activation, resulting in enhanced performance and function of the motor unit, which is the foundation for maintaining muscle strength in older adults (54, 55). Second, PA provides a healthy anti-inflammatory environment, largely by releasing muscle-derived myokines that accelerate myocardial regeneration and prevent age-related loss (56). Additionally, PA increases the availability of several growth factors to achieve delayed cognitive decline in the older adult and thus plays a protective role in GSs (57). According to reports, memory loss and cognitive impairment could be risk factors for GSs (58). Animal and human studies have shown that PA enhances brain health, and thus cognitive health, by increasing the availability of several growth factors in the neurotrophin family including BDNF, IGF-1, and VEGF (59, 60).

Another significant discovery in this MR study was the causal association between SB and a higher risk of three GSs (frailty, falls, dysphagia), which aligns with several investigations. A cross-sectional study in rural China revealed that older persons who spent 8 or more hours per day being sedentary were more susceptible to frailty than those who spent <4 h per day being sedentary (61). The adjusted analysis in another observational study with 411 participants demonstrated that there were independent associations between SB and frailty (62). Therefore, the older adult needed to enhance their awareness of reducing SB to control the GSs. In addition to frailty, previous observational studies have demonstrated that SB is associated

with an increased risk of falls for older adults living in the community (63, 64). Findings from a meta-analysis provided further evidence in favor of this perspective (65). This can be explained by the fact that SB causes muscle weakness (66), reduced bone mass (67), and sarcopenia in older adults, consequently heightening the risk of frailty and falls (68). Furthermore, this study presents new evidence suggesting a possible causative association between SB and dysphagia in older persons. Specifically, we found that SB was related to an increased risk of dysphagia. One possible explanation is that SB leads to progressive weakening of muscles throughout the body, including the laryngeal and neck muscles associated with swallowing (69). This may affect the coordination and efficiency of swallowing in older adults (70).

There are certain strengths of our study. Compared with previous observational studies, we employed an MR study design to assess the causal associations between genetically predicted PA, SB, and GSs (18, 71). This design could minimize the potential biases due to confounding and reverse causality in the observational studies. Another advantage of this study is that the measures of exposures were obtained using accelerometers, which helps to eliminate potential recall and reaction bias (72). Additionally, the population bias was avoided as the populations under study were all individuals of European ancestry.

However, several limitations in our study need to be addressed. First, the sample selection might introduce bias. Our data predominantly come from Europe, which may not fully represent the global population or specific populations. This geographic and demographic limitation could affect the generalizability of our findings. Second, the representativeness of the sample should be considered. Although we employed rigorous random sampling techniques, the inherent variability in genetic backgrounds and environmental exposures across different populations might influence the results. Future studies with more diverse and larger samples are warranted to confirm our findings. Third, accelerometers also possess some constraints. Measuring posture and other types of PA and SB such as inactive, light exercise, and non-ambulatory activity is challenging (73). Therefore, our study focused primarily on overall PA and SB metrics in the sample. Additional research is required to investigate the correlation between various forms of PA, SB, and GSs. Lastly, although we drew on the largest available GWAS, some identified few genome-wide significant SNPs, which could result in relatively weak genetic instruments. To address this, we incorporated thresholds established in previous MR studies, employed additional SNPs as instruments, and performed sensitivity analyses (19, 74, 75). This approach aimed to mitigate the potential influence of alternative thresholds on the outcomes, thus enhancing the reliability of our findings.

5 Conclusion

The present study used a genetic approach and revealed that PA (AccAve, overall activity, MPA) was potentially causally associated with a lower risk of some of the six GSs (frailty, dysphagia, delirium, urinary incontinence, hearing loss, and visual impairment), whereas the accelerometer-based SB was potentially causally associated with a greater risk of three GSs (frailty, falls, and dysphagia). Overall, this study supports the hypothesis that strengthening PA and reducing SB are effective strategies for reducing GSs.

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

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

Author contributions

JC: Conceptualization, Data curation, Formal analysis, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. YL: Writing – original draft, Supervision. JY: Writing – original draft, Supervision. XZ: Writing – original draft, Validation, Supervision. YP: Writing – original draft, Methodology, Project administration.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

Acknowledgments

The authors thank the collaborators of this study for their time and effort in our research.

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

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2024.1406303/full#supplementary-material

References

1. Inouye SK, Studenski S, Tinetti ME, Kuchel GA. Geriatric syndromes: clinical, research, and policy implications of a core geriatric concept. *J Am Geriatr Soc*. (2007) 55:780–91. doi: 10.1111/j.1532-5415.2007.01156.x

2. Akbarzadeh MA, Hosseini MS. Is COVID-19 really a geriatric syndrome? *Ageing Res Rev*. (2022) 79:101657. doi: 10.1016/j.arr.2022.101657

3. Wanigatunga AA, Cai Y, Urbanek JK, Mitchell CM, Roth DL, Miller ER, et al. Objectively measured patterns of daily physical activity and phenotypic frailty. *J Gerontol A Biol Sci Med Sci*. (2022) 77:1882–9. doi: 10.1093/gerona/glab278

4. Ahmed N, Mandel R, Fain MJ. Frailty: an emerging geriatric syndrome. *Am J Med*. (2007) 120:748–53. doi: 10.1016/j.amjmed.2006.10.018

5. Sanford AM, Morley JE, Berg-Weger M, Lundy J, Little MO, Leonard K, et al. High prevalence of geriatric syndromes in older adults. *PLoS One*. (2020) 15:e0233857. doi: 10.1371/journal.pone.0233857

6. Bishop AJ, Martin P, Poon L. Happiness and congruence in older adulthood: a structural model of life satisfaction. *Aging Ment Health*. (2006) 10:445–53. doi: 10.1080/13607860600638388

7. Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. *Arch Intern Med*. (2008) 168:27–32. doi: 10.1001/archinternmed.2007.4

8. Fong TG, Inouye SK. The inter-relationship between delirium and dementia: the importance of delirium prevention. *Nat Rev Neurol*. (2022) 18:579–96. doi: 10.1038/s41582-022-00698-7

9. Bernabei R, Landi F, Calvani R, Cesari M, Del Signore S, Anker SD, et al. Multicomponent intervention to prevent mobility disability in frail older adults: randomised controlled trial (SPRINTT project). *BMJ*. (2022) 377:e068788. doi: 10.1136/bmj-2021-068788

10. Leslie DL, Zhang Y, Bogardus ST, Holford TR, Leo-Summers LS, Inouye SK. Consequences of preventing delirium in hospitalized older adults on nursing home costs. *J Am Geriatr Soc*. (2005) 53:405–9. doi: 10.1111/j.1532-5415.2005.53156.x

11. Zhang X, Tan SS, Franse CB, Bilajac L, Alhambra-Borrás T, Garcés-Ferrer J, et al. Longitudinal association between physical activity and frailty among community-dwelling older adults. *J Am Geriatr Soc*. (2020) 68:1484–93. doi: 10.1111/jgs.16391

12. Maehara T, Nishimura R, Yoshitake A, Tsukamoto M, Kadomatsu Y, Kubo Y, et al. Association of daily physical activity and leisure-time exercise with dysphagia risk in community-dwelling older adults: a cross-sectional study. *Sci Rep*. (2023) 13:10893. doi: 10.1038/s41598-023-37605-z

13. Ramsey KA, Rojer AGM, D'Andrea L, Otten RHJ, Heymans MW, Trappenburg MC, et al. The association of objectively measured physical activity and sedentary behavior with skeletal muscle strength and muscle power in older adults: a systematic review and meta-analysis. *Ageing Res Rev*. (2021) 67:101266. doi: 10.1016/j.arr.2021.101266

14. Onambele-Pearson G, Wullems J, Doody C, Ryan D, Morse C, Degens H. Influence of habitual physical behavior-sleeping, Sedentarism, physical activity-on bone health in community-dwelling older people. *Front Physiol*. (2019) 10:408. doi: 10.3389/fphys.2019.00408

15. Hannan M, Collins EG, Phillips SA, Quinn L, Steffen A, Bronas UG. The influence of sedentary behavior on the relationship between cognitive function and vascular function in older adults with and without chronic kidney disease. *Nephrol Nurs J Am Nephrol Nurses Assoc*. (2021) 48:553–61. doi: 10.37526/1526-744X.2021.48.6.553

16. da Silva Coqueiro R, de Queiroz BM, Oliveira DS, das Merces MC, Oliveira Carneiro JA, Pereira R, et al. Cross-sectional relationships between sedentary behavior and frailty in older adults. *J Sports Med Phys Fitness*. (2017) 57:825–30. doi: 10.23736/S0022-4707.16.06289-7

17. Ozaki E, Matsui D, Kuriyama N, Tomida S, Nukaya Y, Koyama T. Association between sedentary time and falls among middle-aged women in Japan. *Healthcare*. (2022) 10:2354. doi: 10.3390/healthcare10122354

18. Lee SS, Lo Y, Verghese J. Physical activity and risk of postoperative delirium. *J Am Geriatr Soc*. (2019) 67:2260–6. doi: 10.1111/jgs.16083

19. Choi KW, Chen CY, Stein MB, Klimentidis YC, Wang MJ, Koenen KC, et al. Assessment of bidirectional relationships between physical activity and depression among adults: a 2-sample Mendelian randomization study. *JAMA Psychiatry*. (2019) 76:399–408. doi: 10.1001/jamapsychiatry.2018.4175

20. Strath SJ, Kaminsky LA, Ainsworth BE, Ekelund U, Freedson PS, Gary RA, et al. Guide to the assessment of physical activity: clinical and research applications: a scientific statement from the American Heart Association. *Circulation*. (2013) 128:2259–79. doi: 10.1161/01.cir.0000435708.67487.da

21. Davey Smith G, Hemani G. Mendelian randomization: genetic anchors for causal inference in epidemiological studies. *Hum Mol Genet*. (2014) 23:R89–98. doi: 10.1093/hmg/ddu328

22. Gupta V, Walia GK, Sachdeva MP. 'Mendelian randomization': an approach for exploring causal relations in epidemiology. *Public Health*. (2017) 145:113–9. doi: 10.1016/j.puhe.2016.12.033

23. Bowden J, Davey Smith G, Burgess S. Mendelian randomization with invalid instruments: effect estimation and bias detection through egger regression. *Int J Epidemiol*. (2015) 44:512–25. doi: 10.1093/ije/dyv080

24. Burgess S, Butterworth A, Thompson SG. Mendelian randomization analysis with multiple genetic variants using summarized data. *Genet Epidemiol*. (2013) 37:658–65. doi: 10.1002/gepi.21758

25. Bowden J, Davey Smith G, Haycock PC, Burgess S. Consistent estimation in Mendelian randomization with some invalid instruments using a weighted median estimator. *Genet Epidemiol*. (2016) 40:304–14. doi: 10.1002/gepi.21965

26. Gala H, Tomlinson I. The use of Mendelian randomisation to identify causal cancer risk factors: promise and limitations. *J Pathol*. (2020) 250:541–54. doi: 10.1002/path.5421

27. Marth G, Yeh R, Minton M, Donaldson R, Li Q, Duan S, et al. Single-nucleotide polymorphisms in the public domain: how useful are they? *Nat Genet*. (2001) 27:371–2. doi: 10.1038/86864

28. Skrivankova VW, Richmond RC, Woolf BAR, Davies NM, Swanson SA, Vander Weele TJ, et al. Strengthening the reporting of observational studies in epidemiology using mendelian randomisation (STROBE-MR): explanation and elaboration. *BMJ*. (2021) 375:n2233. doi: 10.1136/bmj.n2233

29. Goodyear MD, Krleza-Jeric K, Lemmens T. The declaration of Helsinki. *BMJ*. (2007) 335:624–5. doi: 10.1136/bmj.39339.610000.BE

30. Klimentidis YC, Raichlen DA, Bea J, Garcia DO, Wineinger NE, Mandarino LJ, et al. Genome-wide association study of habitual physical activity in over 377,000 UK biobank participants identifies multiple variants including CADM2 and APOE. *Int J Obes*. (2018) 42:1161–76. doi: 10.1038/s41366-018-0120-3

31. Guo W, Key TJ, Reeves GK. Accelerometer compared with questionnaire measures of physical activity in relation to body size and composition: a large cross-sectional analysis of UK biobank. *BMJ Open*. (2019) 9:e024206. doi: 10.1136/bmjopen-2018-024206

32. Doherty A, Smith-Byrne K, Ferreira T, Holmes MV, Holmes C, Pulit SL, et al. GWAS identifies 14 loci for device-measured physical activity and sleep duration. *Nat Commun*. (2018) 9:5257. doi: 10.1038/s41467-018-07743-4

33. Thiyagalingam S, Kulinski AE, Thorsteinsdottir B, Shindelar KL, Takahashi PY. Dysphagia in older adults. *Mayo Clin Proc*. (2021) 96:488–97. doi: 10.1016/j.mayocp.2020.08.001

34. Mueller YK, Monod S, Locatelli I, Büla C, Cornuz J, Senn N. Performance of a brief geriatric evaluation compared to a comprehensive geriatric assessment for detection of geriatric syndromes in family medicine: a prospective diagnostic study. *BMC Geriatr*. (2018) 18:72. doi: 10.1186/s12877-018-0761-z

35. Byrska-Bishop M, Evani US, Zhao X, Basile AO, Abel HJ, Regier AA, et al. High-coverage whole-genome sequencing of the expanded 1000 genomes project cohort including 602 trios. *Cell*. (2022) 185:3426–40. doi: 10.1016/j.cell.2022.08.004

36. Pierce BL, Ahsan H, Vanderweele TJ. Power and instrument strength requirements for Mendelian randomization studies using multiple genetic variants. *Int J Epidemiol*. (2011) 40:740–52. doi: 10.1093/ije/dyq151

37. Hemani G, Zheng J, Elsworth B, Wade KH, Haberland V, Baird D, et al. The MR-base platform supports systematic causal inference across the human phenome. *eLife*. (2018) 7:34408. doi: 10.7554/eLife.34408

38. Bowden J, Del Greco MF, Minelli C, Davey Smith G, Sheehan N, Thompson J. A framework for the investigation of pleiotropy in two-sample summary data Mendelian randomization. *Stat Med*. (2017) 36:1783–802. doi: 10.1002/sim.7221

39. Hartwig FP, Davey Smith G, Bowden J. Robust inference in summary data Mendelian randomization via the zero modal pleiotropy assumption. *Int J Epidemiol*. (2017) 46:1985–98. doi: 10.1093/ije/dyx102

40. Greco MF, Minelli C, Sheehan NA, Thompson JR. Detecting pleiotropy in Mendelian randomisation studies with summary data and a continuous outcome. *Stat Med*. (2015) 34:2926–40. doi: 10.1002/sim.6522

41. Burgess S, Thompson SG. Interpreting findings from Mendelian randomization using the MR-egger method. *Eur J Epidemiol*. (2017) 32:377–89. doi: 10.1007/s10654-017-0255-x

42. Nolte IM. Metasubtract: an R-package to analytically produce leave-one-out meta-analysis GWAS summary statistics. *Bioinformatics*. (2020) 36:4521–2. doi: 10.1093/bioinformatics/btaa570

43. Rasooly D, Peloso GM. Two-sample multivariable Mendelian randomization analysis using R. *Curr Protocols*. (2021) 1:e335. doi: 10.1002/cpz1.335

44. Trombetti A, Hars M, Hsu FC, Reid KF, Church TS, Gill TM, et al. Effect of physical activity on frailty: secondary analysis of a randomized controlled trial. *Ann Intern Med*. (2018) 168:309–16. doi: 10.7326/M16-2011

45. Lee AH, Hirayama F. Physical activity and urinary incontinence in older adults: a community-based study. *Curr Aging Sci*. (2012) 5:35–40. doi: 10.2174/1874609811205010035

46. Kuo PL, Di J, Ferrucci L, Lin FR. Analysis of hearing loss and physical activity among US adults aged 60-69 years. *JAMA Netw Open*. (2021) 4:e215484. doi: 10.1001/jamanetworkopen.2021.5484

47. Gleeson M, Sherrington C, Keay L. Exercise and physical training improve physical function in older adults with visual impairments but their effect on falls is unclear: a systematic review. *J Physiother*. (2014) 60:130–5. doi: 10.1016/j.jphys.2014.06.010

48. Didelez V, Sheehan N. Mendelian randomization as an instrumental variable approach to causal inference. *Stat Methods Med Res*. (2007) 16:309–30. doi: 10.1177/0962280206077743

49. Freidin MB, Stalteri MA, Wells PM, Lachance G, Baleanu AF, Bowyer RCE, et al. An association between chronic widespread pain and the gut microbiome. *Rheumatology*. (2021) 60:3727–37. doi: 10.1093/rheumatology/keaa847

50. Elliott S, Painter J, Hudson S. Living alone and fall risk factors in community-dwelling middle age and older adults. *J Community Health*. (2009) 34:301–10. doi: 10.1007/s10900-009-9152-x

51. Shapiro A, Melzer I. Balance perturbation system to improve balance compensatory responses during walking in old persons. *J Neuroeng Rehabil*. (2010) 7:32. doi: 10.1186/1743-0003-7-32

52. Taylor D. Physical activity is medicine for older adults. *Postgrad Med J*. (2014) 90:26–32. doi: 10.1136/postgradmedj-2012-131366

53. Taylor JA, Greenhaff PL, Bartlett DB, Jackson TA, Duggal NA, Lord JM. Multisystem physiological perspective of human frailty and its modulation by physical activity. *Physiol Rev*. (2023) 103:1137–91. doi: 10.1152/physrev.00037.2021

54. Nùñez-Lisboa M, Valero-Breton M, Dewolf AH. Unraveling age-related impairment of the neuromuscular system: exploring biomechanical and neurophysiological perspectives. *Front Physiol*. (2023) 14:1194889. doi: 10.3389/fphys.2023.1194889

55. Hunter SK, Pereira HM, Keenan KG. The aging neuromuscular system and motor performance. *J Appl Physiol*. (2016) 121:982–95. doi: 10.1152/japplphysiol.00475.2016

56. Vazquez-Guajardo M, Rivas D, Duque G. Exercise as a therapeutic tool in age-related frailty and cardiovascular disease: challenges and strategies. *Can J Cardiol*. (2024). doi: 10.1016/j.cjca.2024.01.005

57. Dao E, Hsiung GR, Liu-Ambrose T. The role of exercise in mitigating subcortical ischemic vascular cognitive impairment. *J Neurochem*. (2018) 144:582–94. doi: 10.1111/jnc.14153

58. Hopkins RO, Suchyta MR, Farrer TJ, Needham D. Improving post-intensive care unit neuropsychiatric outcomes: understanding cognitive effects of physical activity. *Am J Respir Crit Care Med*. (2012) 186:1220–8. doi: 10.1164/rccm.201206-1022CP

59. Choi JW, Jo SW, Kim DE, Paik IY, Balakrishnan R. Aerobic exercise attenuates LPS-induced cognitive dysfunction by reducing oxidative stress, glial activation, and neuroinflammation. *Redox Biol*. (2024) 71:103101. doi: 10.1016/j.redox.2024.103101

60. Farrukh S, Habib S, Rafaqat A, Sarfraz A, Sarfraz Z, Tariq H. Association of exercise, brain-derived neurotrophic factor, and cognition among older women: a systematic review and meta-analysis. *Arch Gerontol Geriatr*. (2023) 114:105068. doi: 10.1016/j.archger.2023.105068

61. Zhou Y, Yuan Y, Wang X, Qi K, Zhang S, Zhang Y, et al. Sedentary behavior and physical frailty among rural older adults in China: the moderating effect of social isolation. *J Am Med Dir Assoc*. (2023) 25:500–5. doi: 10.1016/j.jamda.2023.08.020

62. Santos ISD, Silva CFR, Ohara DG, Matos AP, Pinto A, Pegorari MS. Association between frailty syndrome and sedentary behavior among community-dwelling older adults in the Amazon region: a cross-sectional study. *Med J*. (2021) 139:226–33. doi: 10.1590/1516-3180.2020.0546.r1.14122020

63. Copeland JL, Ashe MC, Biddle SJ, Brown WJ, Buman MP, Chastin S, et al. Sedentary time in older adults: a critical review of measurement, associations with health, and interventions. *Br J Sports Med*. (2017) 51:1539. doi: 10.1136/bjsports-2016-097210

64. Gallibois M, Handrigan G, Caissie L, Cooling K, Hébert J, Jarrett P, et al. The effect of a standing intervention on falls in long term care: a secondary analysis of a randomized controlled trial. *Can Geriatrics J*. (2023) 26:247–52. doi: 10.5770/cgj.26.656

65. Jiang Y, Wang M, Liu S, Ya X, Duan G, Wang Z. The association between sedentary behavior and falls in older adults: a systematic review and meta-analysis. *Front Public Health*. (2022) 10:1019551. doi: 10.3389/fpubh.2022.1019551

66. Yang CW, Li CI, Li TC, Liu CS, Lin CH, Lin WY, et al. The joint association of insulin sensitivity and physical activity on the skeletal muscle mass and performance in community-dwelling older adults. *Exp Gerontol*. (2017) 95:34–8. doi: 10.1016/j.exger.2017.05.006

67. Zusman EZ, Dawes M, Fleig L, McAllister MM, Cook WL, Guy P, et al. Older Adults' sedentary behavior and physical activity after hip fracture: results from an outpatient rehabilitation randomized controlled trial. *J Geriatr Phys Ther*. (2001) 42:E32–8. doi: 10.1519/JPT.0000000000000193

68. da Silva VD, Tribess S, Meneguci J, Sasaki JE, Garcia-Meneguci CA, Carneiro JAO, et al. Association between frailty and the combination of physical activity level and sedentary behavior in older adults. *BMC Public Health*. (2019) 19:709. doi: 10.1186/s12889-019-7062-0

69. Pinto AJ, Bergouignan A, Dempsey PC, Roschel H, Owen N, Gualano B, et al. Physiology of sedentary behavior. *Physiol Rev*. (2023) 103:2561–622. doi: 10.1152/physrev.00022.2022

70. Panebianco M, Marchese-Ragona R, Masiero S, Restivo DA. Dysphagia in neurological diseases: a literature review. *Neurol Sci Off J Italian Neurol Soc Clin Neurophysiol*. (2020) 41:3067–73. doi: 10.1007/s10072-020-04495-2

71. Huang TY, Chou MY, Liang CK, Lin YT, Chen RY, Wu PF. Physical activity plays a crucial role in multidomain intervention for frailty prevention. *Aging Clin Exp Res*. (2023) 35:1283–92. doi: 10.1007/s40520-023-02412-z

72. Dowd KP, Szeklicki R, Minetto MA, Murphy MH, Polito A, Ghigo E, et al. A systematic literature review of reviews on techniques for physical activity measurement in adults: a DEDIPAC study. *The Int J Behav Nutr Phys Activity*. (2018) 15:15. doi: 10.1186/s12966-017-0636-2

73. Hu S, Xing H, Wang X, Zhang N, Xu Q. Causal relationships between Total physical activity and ankylosing spondylitis: a Mendelian randomization study. *Front Immunol*. (2022) 13:887326. doi: 10.3389/fimmu.2022.887326

74. Chen X, Hong X, Gao W, Luo S, Cai J, Liu G, et al. Causal relationship between physical activity, leisure sedentary behaviors and COVID-19 risk: a Mendelian randomization study. *J Transl Med*. (2022) 20:216. doi: 10.1186/s12967-022-03407-6

75. Zhuang Z, Gao M, Yang R, Li N, Liu Z, Cao W, et al. Association of physical activity, sedentary behaviours and sleep duration with cardiovascular diseases and lipid profiles: a Mendelian randomization analysis. *Lipids Health Dis*. (2020) 19:86. doi: 10.1186/s12944-020-01257-z

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 05 September 2024
DOI 10.3389/fpubh.2024.1407918

OPEN ACCESS

EDITED BY
Yun Gao,
Sichuan University, China

REVIEWED BY
Bhavesh Modi,
All India Institute of Medical Sciences, India
Chengxia Kan,
Affiliated Hospital of Shandong Second Medical University, China

*CORRESPONDENCE
Divya Sharma
✉ divya2809.sharma@gmail.com
Tanvi Kiran
✉ tanvikiran3@yahoo.com

†These authors have contributed equally to this work

RECEIVED 27 March 2024
ACCEPTED 26 August 2024
PUBLISHED 05 September 2024

CITATION
Mamgai A, Halder P, Behera A, Goel K, Pal S, Amudhamozhi KS, Sharma D and Kiran T (2024) Cardiovascular risk assessment using non-laboratory based WHO CVD risk prediction chart with respect to hypertension status among older Indian adults: insights from nationally representative survey. *Front. Public Health* 12:1407918. doi: 10.3389/fpubh.2024.1407918

Cardiovascular risk assessment using non-laboratory based WHO CVD risk prediction chart with respect to hypertension status among older Indian adults: insights from nationally representative survey

Anshul Mamgai[1†], Pritam Halder[1†], Ashish Behera[2], Kapil Goel[1], Saumyarup Pal[3], K. S. Amudhamozhi[1], Divya Sharma[1*] and Tanvi Kiran[1*]

[1]Department of Community Medicine and School of Public Health, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, [2]Department of Internal Medicine, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, [3]Department of Geriatric Medicine, All India Institute of Medical Sciences, New Delhi, India

Introduction: Knowledge of the risk of developing cardiovascular diseases (CVD) in the population is an important risk management strategy for the prevention of this disease. This is especially true for India, which has resource-restrained settings with an increased risk in a younger population for the development of the disease. An important modifiable risk factor for CVD is hypertension, with its influence on the development of CVD.

Methods: The data from the first wave of the Longitudinal Ageing Study in India (LASI) was used to calculate the 10-year CVD Risk Score among older adults ≥45 years using a WHO (2019) non-laboratory- based chart for South Asia. Univariate analysis was done using Pearson's chi-square test, and multivariable analysis using ordinal logistic regression. Categories of CVD risk score were considered as dependent variable. Socio-demographic variables, regular exercise, history of diabetes and hyperlipidaemia were considered as the independent variables. Relationship between CVD Risk score and hypertensives and self-reported hypertensives were presented using restricted cubic splines.

Result: Two-thirds (68.8%) of the population had a 10-year CVD risk of <10, and 2.8% had a risk of ≥20%. The self-reported hypertensives were distributed linearly in restricted cubic splines, with a more scattered distribution in higher scores, while actual hypertensives showed a sigmoid pattern. Urban residents (OR-0.88), being unmarried (OR-0.86), being in the richer (OR-0.94) and richest (OR-0.86) monthly *per capita* expenditure (MPCE) quintile and exercising regularly (OR-0.68) decreased the odds of being in a higher CVD risk score. Less than primary schooling (1.21) and diabetics (1.69) had higher odds for a higher CVD risk score.

Conclusion: In this population, two-thirds had <10% risk for the development of CVD. The study shows a higher risk among rural, poor, and those with a lower education and lower CVD risk for those undertaking physical activity. The sigmoid pattern in actual hypertensives highlights the need for early detection.

Even those with undiagnosed hypertension but with a higher BP had a similar risk for disease development, thus highlighting the need for an early detection of hypertension.

KEYWORDS

cardiovascular risk, non-laboratory based, WHO CVD risk prediction chart, risk prediction chart, hypertension, older Indian adults

Introduction

In 2019, of the nearly 2.5 billion healthy life years lost, 320.3 million were due to just two causes: ischemic heart disease and stroke (1). While the age-standardised deaths and Disability Adjusted Life Years (DALYs) decreased in 2019 compared to 2000, these two diseases alone added 50.2 million DALYs. The deaths due to these two diseases increased by 2.8 million from 2000 to 2019, ranking first and second respectively, throughout these years (2). Over 75% of these deaths occur in Low- and Middle- Income Countries (LMICs) (3). Simultaneously, while they face the largest burden of CVDs, they do not have sufficient resources to tackle the same (4). In India, Ischemic Heart Diseases (IHDs) and stroke account for 16.7 and 7.4% of the total deaths, respectively, and for 8 and 3.7% of the total DALYs (5). However, half the population faced catastrophic health expenditure due to hospitalization and 43% due to OPD care for cardiovascular diseases. The cost of caring for a patient with CVD in outpatient care or hospitalization is sufficient to push the population below the poverty line (6). In India, as in other LMICs, a younger working-age population is struck by cardiovascular disease, and there are more premature deaths (7, 8). Thus, it additionally leads to social and economic losses. CVD in India is estimated to cost US$ 1,044 billion by 2030 (9).

The development of cardiovascular diseases in an individual can be attributed to certain risk factors, including elevated blood pressure, tobacco consumption, obesity, poor dietary habits and a sedentary lifestyle, and increased levels of blood sugar or lipids (10). Additionally, the presence of multiple risk factors in an individual increases their risk compared to a single factor (11). Worryingly, there is a higher prevalence of CVD risk factors in the Indian population when compared to the high and upper middle-income countries (12). Prompt and appropriate interventions targeting these risk factors can mitigate the risk and also decrease the morbidity premature mortality, and disability associated with the disease and is a cost-saving strategy (10, 13). However, the identification and control of these risk factors remain limited and there is still room for improvement in adherence to cardiovascular guidelines for primary prevention (14).

The detection of levels of risk can enable the identification of a population that can benefit from treatment for CVD risk factors. A risk stratification approach is especially suitable for places with limited resources (10). The WHO has developed CVD Risk charts for 21 global regions, as delineated by the Global Burden of Disease (GBD). These charts facilitate a risk stratification approach to CVD management and are presented as laboratory-based and non-laboratory-based algorithms. This is a cost-effective strategy for preventing cardiovascular diseases in India. A two-stage screening using non-lab-based risk assessment for whole population and then screening those with ≥10% CVD risk using lab-based assessment is seen to be more cost-effective (15).

Among the modifiable risk factors for CVD, elevated blood pressure or hypertension is associated with the most compelling evidence for causation and also exhibits a high prevalence of exposure (16). Hypertension accounts for one-fifth of the CVD in the population, ranking among the highest across all income-level country groups (17). Blood pressure has a continuous, graded influence of blood pressure on the incidence and mortality of CVD (18). However, increased blood pressure rarely occurs in isolation; it is usually associated with other risk factors, further amplifying the risk due to elevated blood pressure (18). Moreover, increased blood pressure is a significant mediator for the risk of CVD due to factors such as overweight and obesity (16). Therefore, assessing the risk of CVD due to hypertension is the main theme of the present study. This study was thus done to decode the CVD risk score prescribed by the WHO and examine the influence of hypertension on this score in the Indian population using data from the Longitudinal Ageing Study in India (LASI). Further, the association of socio-demographic and disease factors with CVD Risk Score was also undertaken in the current study. The insights from this study can be utilized to develop and target interventions for the reduction of CVD. As the same population is envisioned to be followed up for the next 25 years, this study would also serve as a baseline assessment of CVD risk. This will facilitate tracking the progress over time and assess the impact of interventions and policy changes.

Methodology

Data source

The study utilized baseline data from the first wave of the Longitudinal Ageing Study in India (LASI). LASI surveyed older Indian adults over 45 and their spouses using a multistage stratified area probability cluster sampling design in 2017–18. Primary sampling units (PSUs) were selected based on factors like household numbers, female literacy, Scheduled Caste/Tribe population, and male non-agricultural engagement. Secondary Sampling Units (SSUs) were chosen from each PSU, proportionally allocated to rural and urban areas. A Census Enumeration Block (CEB) was randomly selected within each urban ward. Finally, households were systematically sampled from each village and CEB (19).

Outcome variable

The outcome variable for this analysis was the CVD Risk score as defined by the World Health Organisation (WHO) in the cardiovascular disease risk non-laboratory-based chart for South Asia,

published in 2019. It was calculated using the variables age, sex, smoking status, BMI category and Systolic Blood pressure category (20) (Supplementary Table S1).

The variables for the development of score were taken based on the questions asked and measurement was done as per the individual questionnaire of LASI. Age was asked as the age in completed years since their last birthday. Sex was determined by the interviewer or asked from the respondent if unclear. Those with an intake of tobacco ever were categorised as smokers. Weight was measured using digital weighing scale (Seca 803) in kilograms with 2 decimal places in light clothing. Single measurement of weight was taken as the final measurement. Height was measured using a stadiometer in centimetres standing straight without shoes and with feet together, chin tucked to chest slightly and looking straight ahead. Single measurement of height was taken. BMI was calculated using the weight and height measured during the survey. BMI was categorised as the WHO BMI Category. Blood pressure was measured using a digital BP monitor in left arm in a relaxed seating position (19). Three readings at 1 minute interval were taken and the average of the last two measures were taken as the systolic (and diastolic) blood pressure. Blood Pressure was categorised as per Joint National Commission (JNC)-8 guidelines.

A STATA .do file was developed (Supplementary material S1), to compute the WHO CVD Risk Score based on the aforementioned variables. Thus, calculated score was categorised as: < 5, 5% to <10, 10% to <20%, 20% to <30% and ≥ 30% (20, 21).

Independent variables

The data extracted from the LASI dataset included socio-demographic characteristics such as educational status, residence, marital status, socio-economic factors including monthly *per capita* expenditure (MPCE) quintiles and health-related factors including known history of diabetes and hyperlipidemia and physical activity. Physical activity was assessed based on questions about exercise and work of the individuals, including participation in vigorous activities, moderately energetic activities, yoga, meditation, pranayama, or playing outdoor sports every day or more than once a week.

Missing values and the final data selected

The Longitudinal Ageing Study in India (LASI) initially included a total of 73,396 individuals, comprising 31,135 males and 42,261 females. However, individuals aged below 45 years (6,790 individuals) and above 74 years (6,880 individuals) were excluded as the analysis was focused on the age group of 45 to 74 years. Furthermore, individuals with missing information for any of the variables used in developing the cardiovascular disease (CVD) risk score were also excluded (5,740 individuals). An additional 182 individuals with outliers in weight and height were removed from the study. Consequently, a total of 53,804 individuals were included in the final analysis (Figure 1). Additionally those with a known history of stroke and heart disease were excluded from the analysis (2,480 individuals). Finally, 51,324 individuals were included in the analysis.

Data analysis

Descriptive analysis was done using mean with standard deviation for continuous variables and frequencies with percentages. Univariate analysis was done using Pearson's Chi-square test. The risk factors used for the development of CVD risk score were presented separately between males and females due to differences in the risk between them. For examining the association between CVD risk and socio-demographic and disease factors, we applied ordinal regression using the logit model to determine the factors associated with CVD risk based on the WHO 2019 non-laboratory-based risk score. Age, sex, smoking status, BMI category and BP were not included in the ordinal logistic based regression analysis as these were considered for developing CVD Risk score. Restricted cubic splines were used to show the graphical relationship between CVD risk score vs. self-reported hypertensive and CVD risk score vs. hypertensive. All Analysis was done using STATA 17 (StataCorp, College Station, Texas, 2021).

Results

Supplementary Table S2 presents the socio-demographic characteristics in relation to hypertension status among males and females. It was found that 30.2% of females and 33.0% of males had high blood pressure, while 29.8% of females and 21.2% of males were known cases of hypertension. The prevalence of both high blood pressure measurements and self-reported hypertension was higher in the older age groups for both genders. The urban population exhibited a higher prevalence of self-reported hypertension and high blood pressure among both males (37.7 and 32.7% respectively) and females (28.1 and 37.1% respectively) (Supplementary Table S2). Among females, those with less than primary level schooling had the highest prevalence of high blood pressure (31.4%), while those with secondary school level of education had the highest prevalence of self-reported hypertension (36.2%). Among males, those with no schooling had the highest prevalence of high blood pressure (39.7%), while those with diploma or graduate and above had the highest prevalence of self-reported hypertension (31.5%). When classified by marital status, widowed, separated, or divorced individuals had the highest prevalence of high blood pressure and self-reported hypertension in both females (36.5 and 35.1% respectively) and males (38.8 and 23.1% respectively).

There was no significant difference in the prevalence of high blood pressure among females in the different MPCE quintiles, but the prevalence of self-reported hypertension increased from 23.3% in the poorest quintile to 35.1% in the richest quintile. Similar trends were observed for males. Both females and males who exercised regularly had a lower prevalence of high blood pressure (29.9 and 32.1%) and self-reported hypertension (28.8 and 20.0%) when compared to those who did not exercise regularly. Those with a history of smoking had a higher prevalence of high blood pressure in females (31.0%); the non-smokers had a higher prevalence in males (35.3%). The non-smokers also had a higher prevalence of self-reported hypertension in both females (30.5%) and males (25.6%). Self-reported hypertension was most prevalent among morbidly obese females (54.9%) and obese males (40.1%). A higher prevalence of high blood pressure was observed among obese individuals in both females

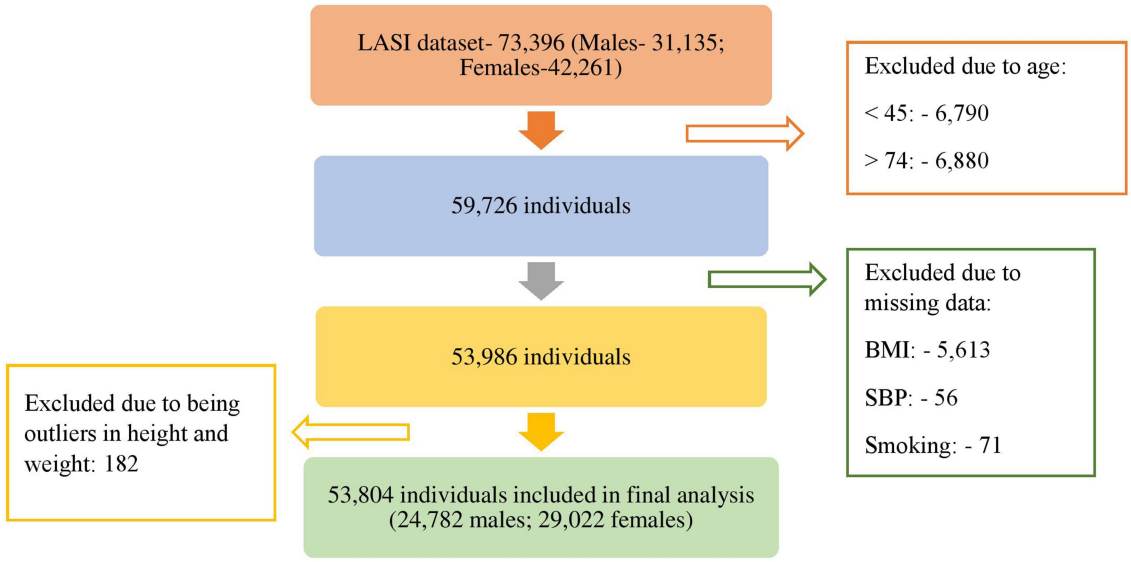


FIGURE 1
Selection of individuals for analysis.

(38.3%) and males (47.9%). Those with known diabetes had a higher prevalence of high blood pressure and self-reported hypertension among both females (38.9 and 62.4%) and males (40.9 and 53.0%), compared to those without any such history. A similar situation was observed with hypercholesterolemia.

Supplementary Table S3 shows the distribution of the study population with respect to the risk factors used for the development of the cardiovascular disease (CVD) risk score. Between one-fifth and one-fourth of the population, both females (23.7%) and males (22.4%), were 45–49 years old. Most females (80.5%) were non-smokers, while over half of the males (56.4%) were smokers. Most of the population, including both male and female subgroups, had a normal Body Mass Index (BMI). Two-fifths of the population had a systolic blood pressure of 120–139 mmHg.

Two-third (68.7%) of the population had a 10-year fatal and non-fatal cardiovascular disease (myocardial infarction and stroke) risk of <10% (with 29.8% having a risk of <5%), 28.5% of the participants had a risk of 10- < 20 and 2.7% had a risk of ≥20%. A CVD risk score of 30% or higher was observed in individuals aged above 65 years, smokers, and those with systolic blood pressure above 160 mmHg. This was distributed across both genders and all BMI categories. Compared to the rural population, the urban population had a slightly higher proportion in the <5% group, and slightly lower proportion in 5- < 10%, 10- < 20%, and 20- < 30% groups. Among education groups, individuals with less than primary level schooling had the lowest proportion in the less than 5% risk group (25.8%). Those educated up to higher secondary level had the highest proportion in the less than 5% risk group (38.6%) and the diploma holders of graduates and above had the highest proportion in the 5- < 10% risk group (36.1%).

Unmarried individuals had a higher proportion in the less than 5% risk group (37.2%) compared to married (32.5%) and widowed/separated/divorced individuals (19.3%). The population belonging to the richest MPCE quintile had the highest proportion in the less than 5% CVD risk score group (32.5%) in the population when divided by the MPCE quintile.

Those who exercised regularly had a higher proportion in the lower CVD risk score groups of <5% (31.8%) and 5- < 10% (39.5%) compared to those who did not exercise regularly. Diabetics and those with high cholesterol had a lower prevalence in these groups compared to those without these conditions (Table 1).

When categorised by sex, it was observed that most women aged between 45 and 49 years and 50–54 years had a risk of less than 5% (88.3%). Among men aged between 45 to 49 years, the majority (63.4%) had a risk of less than 5%, while one-fourth of men between 50–54 years had a risk of less than 5% (26.5%). Majority of females (65.6%) and males (63.6%) aged between 55 and 59 years had a risk of 5- <10. In the age group of 60–64 years, three-fourths of females had a risk between 5- < 10% (77.8%), while most males had a risk between 10- < 20% (58.8%). Half of females aged between 65 and 69 years (57.1%) and most males (83.4%) had a risk between 10% to less than 20%. Among those aged between 70 and 74 years, most females (89.2%) had a risk between 10- < 20%, while one-fourth of males (27.0%) had a risk between 20- < 30% (Supplementary Table S4).

Tables 2, 3 display the CVD risk among individuals with and without controlled blood pressure during the survey, categorised by their known hypertension status and age group. In the population with blood pressure below the hypertension level, a higher proportion (40.1%) was observed in the lowest risk group of less than 5% among those without a known history of hypertension, compared to those with a known history of hypertension (30.9%). However, in the age groups 45–49 and 50–54, a higher prevalence was seen in those with known hypertension. Among those with blood pressure above the hypertension range, a higher proportion in the lowest risk group of less than 5% was seen among those without a known history of hypertension (13.5%), compared to those with a known hypertension status (9.4%). In the age groups 45–49 years, those with a known hypertension; and in 50–54 years, those without any known history of hypertension had a higher proportion in the <5% Risk score category. Gender-wise

10.3389/fpubh.2024.1407918

TABLE 1 Distribution of participants as per CVD risk score.

Total	Total population	<5%, *N* (%)	5– < 10%, *N* (%)	10– < 20%, *N* (%)	20– < 30%, *N* (%)	≥30%, *N* (%)
Age group						
45–49	11,861 (23.1)	9,165 (77.3)	2,580 (21.8)	116 (1.0)	0	0
50–54	9,686 (18.9)	4,655 (48.1)	4,471 (46.2)	559 (5.8)	1 (0.0)	0
55–59	8,778 (17.1)	1,544 (17.6)	5,680 (64.7)	1,518 (17.3)	36 (0.4)	0
60–64	8,785 (17.1)	0	5,338 (60.8)	3,392 (38.6)	55 (0.6)	0
65–69	7,476 (14.6)	0	1,874 (25.1)	5,220 (69.8)	380 (5.1)	2 (0.0)
70–74	4,738 (9.2)	0	0	3,817 (80.6)	889 (18.8)	32 (0.7)
Gender						
Female	27,903 (53.9)	10,715 (38.4)	10,927 (39.2)	5,889 (21.1)	372 (1.3)	3 (0.0)
Male	23,418 (46.1)	4,649 (19.9)	9,016 (38.5)	8,733 (37.3)	989 (4.2)	31 (0.1)
Smoking status						
Non-Smoker	32,667 (63.7)	13,763 (42.1)	12,436 (38.1)	6,293 (19.3)	175 (0.5)	0
Smoker	18,657 (36.3)	1,601 (8.6)	7,507 (40.2)	8,329 (44.6)	1,186 (6.4)	34 (0.2)
BMI category						
< 20	14,906 (29.0)	3,957 (26.6)	6,125 (41.1)	4,413 (29.6)	408 (2.7)	3 (0.0)
20–24	21,025 (41.0)	6,591 (31.4)	7,820 (37.2)	6,132 (29.2)	474 (2.3)	8 (0.0)
25–29	11,606 (22.6)	3,442 (29.7)	4,653 (40.1)	3,105 (26.8)	387 (3.3)	19 (0.2)
30–35	3,137 (6.1)	1,156 (36.9)	1,103 (35.2)	797 (25.4)	77 (2.5)	4 (0.1)
≥ 35	650 (1.3)	218 (33.5)	242 (37.2)	175 (26.9)	15 (2.3)	0
Systolic blood pressure						
< 120	18,725 (36.5)	9,348 (49.9)	6,810 (36.4)	2,567 (13.7)	0	0
120–139	20,112 (39.2)	5,285 (26.3)	8,678 (43.2)	6,073 (30.2)	76 (0.4)	0
140–159	9,139 (17.8)	731 (8.0)	3,630 (39.7)	4,176 (45.7)	602 (6.6)	0
160–179	3,160 (6.2)	0	803 (25.4)	1,718 (54.4)	620 (19.6)	19 (0.6)
≥ 180	188 (0.4)	0	22 (11.7)	88 (46.8)	63 (33.5)	15 (8.0)
Residence						
Urban	17,373 (33.9)	5,474 (31.5)	6,657 (38.3)	4,829 (27.8)	403 (2.3)	10 (0.1)
Rural	33,951 (66.1)	9,890 (29.1)	13,286 (39.1)	9,793 (28.8)	958 (2.8)	24 (0.1)
Education						
No schooling	23,681 (46.1)	6,573 (27.8)	9,437 (39.9)	7,006 (29.6)	650 (2.7)	15 (0.1)
Less than primary (till 4)	5,841 (11.4)	1,505 (25.8)	2,240 (38.4)	1,904 (32.6)	186 (3.2)	6 (0.1)
Primary completed (5–7)	6,959 (13.6)	2,112 (30.4)	2,700 (38.8)	1,950 (28.0)	193 (2.8)	4 (0.1)
Middle completed (8–9)	5,136 (10.0)	1,741 (33.9)	2,003 (39.0)	1,277 (24.9)	110 (2.1)	5 (0.1)
Secondary school (10–11)	4,658 (9.1)	1,530 (32.9)	1,748 (37.5)	1,248 (26.8)	128 (2.8)	4 (0.1)
Higher secondary	2,255 (4.4)	870 (38.6)	807 (35.8)	530 (23.5)	48 (2.1)	0
Diploma or graduate and above	2,794 (5.4)	1,033 (37.0)	1,008 (36.1)	707 (25.3)	46 (1.7)	0
Marital status						
Unmarried	651 (1.3)	242 (37.2)	250 (38.4)	148 (22.7)	11 (1.7)	0
Married/ in live -in	40,420 (78.)	13,146 (32.5)	15,905 (39.4)	10,438 (25.8)	907 (2.2)	24 (0.1)
Widow/ separated/ divorced	10,252 (20.0)	1,976 (19.3)	3,787 (36.9)	4,036 (39.4)	443 (4.3)	10 (0.1)
MPCE quintile						
Poorest	10,286 (20.0)	2,904 (28.2)	4,029 (39.2)	3,048 (29.6)	301 (2.9)	4 (0.0)
Poorer	10,460 (20.4)	2,956 (28.3)	4,170 (39.9)	3,038 (29.0)	292 (2.8)	4 (0.0)
Middle	10,372 (20.2)	3,136 (30.2)	3,930 (37.9)	3,027 (29.2)	272 (2.6)	7 (0.1)

(Continued)

TABLE 1 (Continued)

Total	Total population	<5%, *N* (%)	5– < 10%, *N* (%)	10– < 20%, *N* (%)	20– < 30%, *N* (%)	≥30%, *N* (%)
Richer	10,264 (20.0)	3,135 (30.5)	3,963 (38.6)	2,879 (28.1)	274 (2.6)	13 (0.1)
Richest	9,942 (19.4)	3,233 (32.5)	3,851 (38.7)	2,630 (26.5)	222 (2.2)	6 (0.1)
Regular exercise						
No	13,298 (25.9)	3,264 (24.6)	4,933 (37.1)	4,600 (34.6)	484 (3.6)	17 (0.1)
Yes	38,026 (74.1)	12,100 (31.8)	15,010 (39.5)	10,022 (26.4)	877 (2.3)	17 (0.0)
Known diabetes						
No	45,262 (88.2)	14,092 (31.1)	17,567 (38.8)	12,427 (27.5)	1,147 (2.5)	29 (0.1)
Yes	6,046 (11.8)	1,267 (21.0)	2,369 (39.2)	2,191 (36.2)	214 (3.5)	5 (0.1)
Known hypercholesterolemia						
No	49,804 (97.1)	14,933 (30.0)	19,326 (38.8)	14,193 (28.5)	1,319 (2.7)	33 (0.1)
Yes	1,514 (2.9)	430 (28.4)	613 (40.5)	428 (28.3)	42 (2.8)	1 (0.1)
Total	51,324	15,364 (29.8)	19,943 (38.9)	14,622 (28.5)	1,361 (2.7)	34 (0.1)

classification of CVD Risk Score among participants with uncontrolled blood pressure was documented in Supplementary Tables S5, S6.

Figure 2 describes the graphical representation of Distribution of CVD risk score as per (A) self-reported hypertensive and (B) Actual hypertensive using restricted cubic splines. Both graphs showed upward trend. In the initial 0 to 10 score, self-reported hypertensives were distributed symmetrically. With increase in the scores later, the distribution was less steep and was more scattered from the expected line (A). For actual hypertension, as defined by their blood pressure level, the initial 0 to 5 score, the trend was upward which followed a gentle plateau from 6 to 12; later following a steep curve, hitting a plateau at 30: overall following a sigmoid pattern. The distribution of hypertensives was along the line and less dispersed (B).

As shown in Table 4, the urban residents had 12% lower odds of being in a higher CVD risk score category rather than a combined lower risk score category, compared to the rural population. When categorised by education status, individuals with less than primary education had 1.21 times higher odds of being in a higher CVD risk score category, compared to those with no schooling. However, those with middle-school, secondary school, higher secondary and diploma, and graduate and higher education had lower odds of being in a higher CVD risk score category. Compared to married individuals, unmarried individuals had 14% less odds of being in a higher category group, while widowed/separated/divorced individuals had 1.93 times higher odds for the same. When categorised by MPCE quintiles, the richer and richest quintiles had 6 and 14% lower odds, respectively of being in a higher CVD risk score category, compared to the poorest quintile. Those who exercised regularly had 32% lower odds of being in a higher risk score category than those who did not exercise regularly. Individuals with a known history of diabetes had 1.69 times higher odds of being in a higher CVD risk score category when compared to individuals without these conditions (Table 4).

Discussion

This study estimated the 10-year risk for fatal and non-fatal cardiovascular disease using the 2019 WHO Non-laboratory-based risk prediction tool in the Indian population of ≥45-years. It was observed that two-thirds of the population had a 10-year CVD risk of <10%, and only a minority had a risk of ≥20%. The results are comparable to a study conducted in rural Andhra Pradesh, where 83.1% of the total population had a risk score of <10%, although the proportion of the population with a high CVD risk score was much higher in that population, i.e., 7.8% (21). The CVD risk score in our population was seen to be comparable to studies in the neighbouring countries. In a hospital-based cross-sectional study in Nepal, two-thirds of the participants, including 80% of females and half of the males had a 10-year CVD risk score of <10% (22). A cross-sectional analysis of individuals in rural and urban Bangladesh showed that half of the population had a risk of <5%, with 15% of the population at risk of >10%. This included almost one-fifth of the male population and 8% of the female population (23).

While the WHO CVD Risk Score is commonly used, other risk scores have been utilized for Indian and other populations in LMICs. These include the Framingham Risk Score, the Globorisk and the older WHO/ ISH classification. A study using nationally representative data of individuals aged 30 to 74 in India showed that sizable number of females and males had a high risk of CVD when classified using the WHO/ISH risk score (24). In male individuals from Tamil Nadu, it was found that majority of the urban and of the rural population had a 10-year risk of <10%, using the Framingham Risk Score (25).

For self-reported hypertension, the distribution was seen to be more scattered from the expected line at a higher CVD risk score. This suggests that there is more uncertainty at this level of CVD risk score, implying that these may not be aware of their true hypertension status, i.e., those with a higher CVD risk score have less knowledge of their hypertension status.

In this population, while three-fourths of individuals aged 45–49 years had a CVD Risk Score of <5%, none of those aged 60 years and above had this risk. The risk of ≥30% was seen only in individuals 65 years and above. With ageing, the risk of CVD escalates due to changes in the heart caused by myocardial deterioration and degeneration (26). As expected, both males and females were shown to have an increased risk for CVD with increasing age.

TABLE 2 CVD risk among the participants with blood pressure below the diagnostic level of hypertension.

Age-group (years)	Self-reported hypertension present						Self-reported hypertension absent					
	Total	<5% (%)	5–9% (%)	10–19% (%)	20–29% (%)	≥30% (%)	Total	<5% (%)	5–9% (%)	10–19% (%)	20–29% (%)	≥30% (%)
45–49	1,287 (17.2)	1,114 (86.6)	173 (13.4)	0	0	0	7,651 (27.6)	6,543 (85.5)	1,103 (14.4)	5 (0.1)	0	0
50–54	1,288 (17.2)	897 (69.6)	387 (30.0)	4 (0.3)	0	0	5,611 (20.3)	3,316 (59.1)	2,280 (400.6)	15 (0.3)	0	0
55–59	1,301 (17.4)	296 (22.8)	888 (68.3)	117 (9.0)	0	0	4,707 (17.0)	1,235 (26.6)	3,015 (64.1)	457 (9.7)	0	0
60–64	1,404 (18.8)	0	1,070 (76.2)	334 (23.8)	0	0	4,328 (15.6)	0	3,111 (71.9)	2,039 (60.2)	0	0
65–69	1,330 (17.8)	0	474 (350.6)	854 (64.2)	2 (0.2)	0	3,385 (12.2)	0	1,346 (39.8)	2,039 (66.2)	0	0
70–74	869 (11.6)	0	0	840 (96.7)	29 (3.3)	0	2,018 (7.3)	0	0	1,979 (98.1)	39 (1.9)	0
All groups	7,479 (21.2)	2,307 (30.9)	2,992 (40.0)	2,149 (28.7)	31 (0.4)	0	27,700 (78.8)	11,094 (40.1)	10,855 (39.2)	5,712 (20.6)	39 (0.1)	0

TABLE 3 CVD risk among the participants with blood pressure above the diagnostic level of hypertension.

Age-group (years)	Self-reported hypertension present						Self-reported Hypertension absent					
	Total	<5% (%)	5–9% (%)	10–19% (%)	20–29% (%)	≥30% (%)	Total	<5% (%)	5–9% (%)	10–19% (%)	20–29% (%)	≥30% (%)
45–49	866 (14.9)	449 (51.9)	369 (42.6)	48 (5.5)	0	0	2,052 (19.9)	1,056 (51.5)	933 (45.5)	63 (3.1)	0	0
50–54	916 (15.7)	119 (13.0)	608 (66.4)	188 (20.5)	1 (0.1)	0	1,870 (18.1)	323 (17.3)	1,195 (63.9)	352 (18.8)	0	0
55–59	991 (17.0)	3 (0.3)	658 (66.4)	308 (31.1)	22 (2.2)	0	1,777 (17.2)	9 (0.5)	1,119 (63.0)	635 (35.7)	14 (0.8)	0
60–64	1,119 (19.2)	0	431 (38.5)	657 (58.7)	31 (2.8)	0	1,930 (18.7)	0	723 (37.5)	1,813 (61.3)	24 (1.2)	0
65–69	1,161 (20.0)	0	16 (1.4)	976 (58.7)	168 (14.5)	1 (0.1)	1,599 (15.5)	0	38 (2.4)	1,350 (84.4)	210 (13.1)	1 (0.1)
70–74	769 (13.2)	0	0	439 (57.1)	315 (41.0)	15 (2.0)	1,081 (10.5)	0	0	558 (51.6)	506 (46.8)	17 (1.6)
All groups	5,822 (35.9)	571 (9.8)	2,082 (35.8)	2,616 (44.9)	537 (9.2)	16 (0.3)	10,309 (64.1)	1,388 (13.5)	4,008 (38.9)	4,141 (40.2)	754 (7.3)	18 (0.2)

10.3389/fpubh.2024.1407918

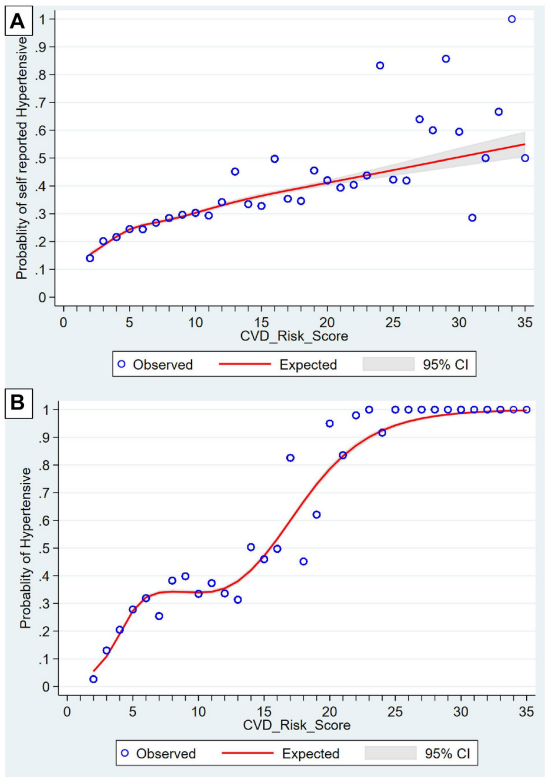


FIGURE 2
Distribution of CVD risk score as per **(A)** Self-reported hypertensive and **(B)** actual hypertensives using restrictive cubic splines.

The risk was higher among males compared to females, as observed in this study and in a national representative survey of individuals aged less than 49 years in the country, and in the study conducted in Andhra Pradesh (21, 27). The difference between sexes can be attributed to the presence of sex hormones and other sex chromosome complement. Pre-menopausal women are known to have a lower blood pressure and associated cardiovascular diseases due to modulation provided by sex hormones (28). Oestrogen has a cardioprotective effect due to its impact on the renin-angiotensin-aldosterone and the endothelin systems (28). However, these protections are lost in the post-menopausal women. In this study, the post-menopausal women too had a lower risk, which may partly be attributed to a much higher prevalence of tobacco use in males compared to females. Tobacco causes increased sympathetic activation leading to an increase in blood pressure. Endothelial dysfunction and reduced endothelial repair caused by smoking lead to an atherosclerotic environment in the vessels (29). Tobacco smokers are more likely to experience an acute cardiovascular event at a younger age and earlier in the course of their disease (30). In India, 28.6% of the population, including 42.4% of men and 14.2% of women, use tobacco in some form (31).

In this study, the urban population was observed to have a lower risk for developing cardiovascular disease compared to the rural population. Additionally, individuals in the richest quintile and those with higher education levels were seen to have a lower risk. Non-communicable diseases were previously more commonly seen in the affluent population. Lately, non-communicable diseases are seen to be prevalent among the poor in the Low- and Middle-Income Countries (32). This may be because of a higher prevalence of risk factors including tobacco use, alcohol consumption and an unhealthy diet consisting of fewer fruits, vegetables, fish, and fibre, when compared to their wealthier counterparts (33). Conversely, the presence of chronic diseases itself may drive them into poverty (32).

Physical activity decreases the risk of and mortality due to cardiovascular disease. It also reduces the risk of developing risk factors for CVD, including hypertension, diabetes and high cholesterol levels (34). Those without regular exercise and those with a history of diabetes were shown to have a higher risk of developing cardiovascular disease. The inflammatory state in obesity and diabetes and its effect on blood pressure, cholesterol, and sugar levels causes an increase in cardiovascular risk in these individuals (35). However, this study did not find any significant association between increased cholesterol levels and the risk of CVD. Excluding the individuals with known cardiovascular disease may be the reason of the non-significant association observed in this study.

This study has also categorised individuals into those with and without a known diagnosis of hypertension. In the population with blood pressure above the range to qualify as hypertension, two-thirds of the population did not have a diagnosis of hypertension. However, the CVD Risk did not differ significantly between these individuals. Additionally, hypertensive individuals who had their blood pressure under control had a similar risk as those without known hypertension in this study and a nationally representative survey (27). Management of a person should not just stop at controlling blood pressure; managing other factors would be equally important. This also indicates the importance of managing hypertension (27). This underscores the importance of regular health check-ups and maintaining a healthy lifestyle.

Some limitations do exist in this study. Since, it is a cross-sectional survey, causality between outcome and independent variables cannot be established. Since the LASI survey involved self-reported questions pertaining to CVD-risk, therefore chances of recall bias and social desirability bias cannot be neglected. These biases due to self-reported nature may result in under reporting or sometimes over reporting of the results (36). Despite these limitations, the present study has its own unique strengths. The large and representative sample in the survey enhances its generalizability to the Indian population. The standard methodology used in LASI and in the assessment of CVD risk score ensures consistency and reliability. Given that the same population will be followed up in the future waves of LASI, the study offers excellent replicability for the future research on CVD risk assessment. Thus, the study would be helpful for understanding and managing cardiovascular risk in India.

Policy implications

The World Health Organisation (WHO) has set worldwide objectives with respect to the Global Monitoring Framework for the control of non-communicable diseases (NCDs) especially in context of Low- and middle-income countries (LMICs) like India. Eighty percent of the country's basic affordable technologies and critical medications that are required to treat

10.3389/fpubh.2024.1407918

TABLE 4 Univariate and multivariable analysis between socio-demographic and disease factors with CVD risk score.

Variable	Total population, *N* (%)	Crude odds ratio (95% CI)	*p*-value	Adjusted odds ratio (95% CI)	*p*-value
Socio-demographic factors					
Residence					
Rural	33,951 (66.1)	Ref		Ref	
Urban	17,373 (33.9)	0.91 (0.88–0.94)	< 0.001	0.88 (0.85–0.91)	< 0.001
Education					
No schooling	23,681 (46.1)	Ref		Ref	
Less than primary (till 4)	5,841 (11.4)	1.14 (1.08–1.20)	< 0.001	1.21 (1.15–1.28)	< 0.001
Primary completed (5–7)	6,959 (13.6)	0.91 (0.87–0.96)	< 0.001	0.98 (0.94–1.03)	0.513
Middle completed (8–9)	5,136 (10.0)	0.77 (0.72–0.81)	< 0.001	0.86 (0.82–0.91)	< 0.001
Secondary school (10–11)	4,658 (9.1)	0.83 (0.79–0.88)	< 0.001	0.95 (0.89–1.00)	0.068
Higher Secondary	2,255 (4.4)	0.66 (0.61–0.71)	< 0.001	0.76 (0.70–0.83)	< 0.001
Diploma and graduate and above	2,794 (5.4)	0.70 (0.65–0.75)	< 0.001	0.85 (0.78–0.92)	< 0.001
Marital status					
Unmarried	651 (1.3)	0.82 (0.71–0.94)	0.006	0.86 (0.74–0.99)	0.038
Married/ in live -in	40,420 (78.)	Ref		Ref	
Widow/ separated/ divorced	10,252 (20.0)	2.00 (1.92–2.08)	<0.001	1.93 (1.85–2.00)	< 0.001
MPCE quintile					
Poorest	10,286 (20.0)	Ref		Ref	
Poorer	10,460 (20.4)	0.98 (0.93–1.03)	0.462	1.00 (0.95–1.05)	0.921
Middle	10,372 (20.2)	0.94 (0.89–0.98)	0.010	0.96 (0.91–1.01)	0.084
Richer	10,264 (20.0)	0.91 (0.86–0.96)	< 0.001	0.94 (0.89–0.99)	0.014
Richest	9,942 (19.4)	0.82 (0.78–0.87)	< 0.001	0.86 (0.81–0.90)	< 0.001
Disease factors					
Regular exercise					
No	13,298 (25.9)	Ref		Ref	
Yes	38,026 (74.1)	0.67 (0.64–0.69)	< 0.001	0.68 (0.66–0.71)	< 0.001
Known diabetes					
No	45,262 (88.2)	Ref		Ref	
Yes	6,046 (11.8)	1.59 (1.52–1.67)	< 0.001	1.69 (1.60–1.77)	< 0.001
Known hypercholesterolemia					
No	49,804 (97.1)	Ref		Ref	
Yes	1,514 (2.9)	1.03 (0.94–1.14)	0.459	1.00 (0.91–1.10)	0.943

severe NCDs, including CVDs, must be readily available in both rural and urban regions (37). Weak healthcare infrastructure and limited access to CVD treatment are major public health concerns. Adequate regulations ought to tackle the possibility of both under and overtreatment, since it is quite expensive for the patient and the healthcare system. The substantial proportion of adults with a low 10-year CVD risk (<10%) underscores the possibility of lowering CVD risk by means of population-wide public health policies and the provision of easily available preventive interventions. But care should be taken to make sure that risk stratification techniques aren't applied in unsuitable clinical situations, including those with severely uncontrolled hypertension (160/100 mm Hg) (24).

The sigmoid pattern in actual hypertensives highlights the need for early detection and initiation of treatments. Government of India has implemented population-based screening (PBS) as a part of implementation of comprehensive healthcare under National Program for Prevention and Control of Non-Communicable Diseases (NP-NCD) targeting population aged 30 years and above for screening for hypertension, diabetes, common cancers (breast, cervical and oral) implemented by trained frontline health professionals (ANM: Auxiliary Nurse Midwife; ASHA: Accredited Social Health Activist) (38). Camp-based screenings are practiced at regular intervals in the Indian community settings. Medical Officers at nearby Primary Health Centres (PHCs) receive suspicious patients and refer them for a second examination in the higher centres. The

program seeks to lower the burden of NCDs by allowing early detection and prompt care (39). We recommend to include evaluation of CVD risk score in the same approach. By early detection, the treatment can be implemented at national and subnational levels especially in geographically unapproachable population.

Conclusion

This study reveals that while the majority of the Indian population has a low risk of CVD, a small but significant proportion have a high risk. It also highlights the disparities among the different socio-economic and educational groups, with a shifting of the burden to the poorer population. It also emphasizes the protective role of physical activity against cardiovascular disease, suggesting the need for initiatives to encourage regular exercise. A large proportion of individuals with blood pressure in the levels of hypertension were undiagnosed but had a similar risk of developing cardiovascular disease. These findings highlight the importance of promoting regular health check-ups for early detection and management of 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 authors.

Ethics statement

The studies involving humans were approved by the original LASI study reports which were in compliance with research ethics. Informed written consent was obtained from the participants. Ethical clearance was permitted by the Indian Council of Medical Research (ICMR) and each collaborating bodies. Current study is based on secondary data analysis of Longitudinal Ageing Study in India (LASI) Wave- 1, India. This study was carried out in accordance with the Helsinki Declaration Principles (19). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

AM: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. PH: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. AB: Writing – original draft, Writing – review & editing. KG: Writing – original draft, Writing – review & editing. SP: Writing – original draft, Writing – review & editing. KA: Writing – original draft, Writing – review & editing. DS: Conceptualization, Data curation, Investigation, Methodology, Software, Supervision, Writing – original draft, Writing – review & editing. TK: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

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.2024.1407918/full#supplementary-material

References

1. WHO. The top 10 causes of death (2020). Available at: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death (accessed September 27, 2023).

2. The Global Health Observatory, WHO. Global Health estimates: Life expectancy and leading causes of death and disability (2023). Available at: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates (accessed September 27, 2023).

3. WHO South-East Asia India. Cardiovascular diseases (2023). Available at: https://www.who.int/india/health-topics/cardiovascular-diseases (accessed September 29, 2023).

4. Gheorghe A, Griffiths U, Murphy A, Legido-Quigley H, Lamptey P, Perel P. The economic burden of cardiovascular disease and hypertension in low- and middle-income countries: a systematic review. *BMC Public Health*. (2018) 18:975. doi: 10.1186/s12889-018-5806-x

5. Institute for Health Metrics and Evaluation. GBD India compare (2019). Available at: http://vizhub.healthdata.org/gbd-compare/india (accessed September 29, 2023).

6. Allarakha S, Yadav J, Yadav AK. Financial burden and financing strategies for treating the cardiovascular diseases in India. *Soc Sci Humanit Open*. (2022) 6:100275. doi: 10.1016/j.ssaho.2022.100275

7. Bowry ADK, Lewey J, Dugani SB, Choudhry NK. The burden of cardiovascular disease in low- and middle-income countries: epidemiology and management. *Can J Cardiol*. (2015) 31:1151–9. doi: 10.1016/j.cjca.2015.06.028

8. Kalra A, Jose AP, Prabhakaran P, Kumar A, Agrawal A, Roy A, et al. The burgeoning cardiovascular disease epidemic in Indians – perspectives on contextual factors and potential solutions. *Lancet Reg Health Southeast Asia*. (2023) 12:100156. doi: 10.1016/j.lansea.2023.100156

9. World Heart Federation. Factsheet: Cardiovascular diseases in India. Geneva: World Heart Federation (2021).

10. World Health Organization. HEARTS technical package for cardiovascular disease management in primary health care: Risk based CVD management. Geneva: World Health Organization (2020).

11. Biswas T, Townsend N, Gupta RD, Ghosh A, Rawal LB, Mørkrid K, et al. Clustering of metabolic and behavioural risk factors for cardiovascular diseases among the adult population in south and Southeast Asia: findings from WHO STEPS data. *Lancet Reg Health Southeast Asia*. (2023) 12:100164. doi: 10.1016/j.lansea.2023.100164

12. Vasan SK, Antonisamy B, Gowri M, Selliah HY, Geethanjali FS, Jebasingh FS, et al. Prevalence, incidence and predictors of cardiovascular risk factors: longitudinal data from rural and urban South India and comparison with global data. *BMJ Open Diabetes Res Care*. (2020) 8:e001782. doi: 10.1136/bmjdrc-2020-001782

13. Barton P, Andronis L, Briggs A, McPherson K, Capewell S. Effectiveness and cost effectiveness of cardiovascular disease prevention in whole populations: modelling study. *BMJ*. (2011) 343:d4044. doi: 10.1136/bmj.d4044

14. Tiffe T, Wagner M, Rücker V, Morbach C, Gelbrich G, Störk S, et al. Control of cardiovascular risk factors and its determinants in the general population– findings from the STAAB cohort study. *BMC Cardiovasc Disord*. (2017) 17:1–12. doi: 10.1186/s12872-017-0708-x

15. Sharma M, John R, Afrin S, Zhang X, Wang T, Tian M, et al. Cost-effectiveness of population screening programs for cardiovascular diseases and diabetes in low- and middle-income countries: a systematic review. *Front Public Health*. (2022) 10. doi: 10.3389/fpubh.2022.820750

16. Fuchs FD, Whelton PK. High blood pressure and cardiovascular disease. *Hypertension*. (2020) 75:285–92. doi: 10.1161/HYPERTENSIONAHA.119.14240

17. Yusuf S, Joseph P, Rangarajan S, Islam S, Mente A, Hystad P, et al. Modifiable risk factors, cardiovascular disease and mortality in 155,722 individuals from 21 high-, middle-, and low-income countries. *Lancet*. (2020) 395:795–808. doi: 10.1016/S0140-6736(19)32008-2

18. Kannel WB. Hypertensive risk assessment: cardiovascular risk factors and hypertension. *J Clin Hypertens (Greenwich)*. (2007) 6:393–9. doi: 10.1111/j.1524-6175.2004.03605.x

19. International Institute for Population Sciences (IIPS), NPHCE, MoHFW, Harvard T. H., Chan School of public health (HSPH), University of Southern Sciences. Longitudinal ageing study in India (LASI) Wave-1, 2017–18. India Report: Mumbai (2020). Available at: https://www.iipsindia.ac.in/sites/default/files/LASI_India_Report_2020_compressed.pdf (accessed July 21, 2023).

20. The WHO CVD Risk Chart Working Group. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. *Lancet Glob Health*. (2019) 7:e1332–45. doi: 10.1016/S2214-109X(19)30318-3

21. Halder P, Das S, Mamgai A, Nongkynrih B, Bisoi S, Chattopadhyay A, et al. Association of sleep disorders with non-lab-based CVD risk score among Indian population aged above 45 years: insight from longitudinal aging study in India. *Int J Commun Med Public Health*. (2024) 11:3113–21. doi: 10.18203/2394-6040.ijcmph20242172

22. Birhanu MM, Evans RG, Zengin A, Riddell M, Kalyanram K, Kartik K, et al. Absolute cardiovascular risk scores and medication use in rural India: a cross-sectional study. *BMJ Open*. (2022) 12:e054617. doi: 10.1136/bmjopen-2021-054617

23. Sitaula D, Dhakal A, Mandal SK, Bhattarai N, Silwal A, Adhikari P, et al. Estimation of 10-year cardiovascular risk among adult population in western Nepal using nonlaboratory-based WHO/ISH chart, 2023: a cross-sectional study. *Health Sci Rep*. (2023) 6:e1614. doi: 10.1002/hsr2.1614

24. Islam JY, Zaman MM, Moniruzzaman M, Shakoor SA, Hossain AHME. Estimation of total cardiovascular risk using the 2019 WHO CVD prediction charts and comparison of population-level costs based on alternative drug therapy guidelines: a population-based study of adults in Bangladesh. *BMJ Open*. (2020) 10:e035842. doi: 10.1136/bmjopen-2019-035842

25. Geldsetzer P, Manne-Goehler J, Theilmann M, Davies JI, Awasthi A, Danaei G, et al. Geographic and sociodemographic variation of cardiovascular disease risk in India: a cross-sectional study of 797,540 adults. *PLoS Med*. (2018) 15:e1002581. doi: 10.1371/journal.pmed.1002581

26. Sasikumar M, Marconi SD, Dharmaraj A, Mehta K, Das M, Goel S. Prevalence of risk factors and estimation of 10-year risk for cardiovascular diseases among male adult population of Tamil Nadu India-an insight from the National Family Health Survey–5. *Indian Heart J*. (2023) 75:251–7. doi: 10.1016/j.ihj.2023.06.003

27. Rodgers JL, Jones J, Bolleddu SI, Vanthenapalli S, Rodgers LE, Shah K, et al. Cardiovascular risks associated with gender and aging. *J Cardiovasc Dev Dis*. (2019) 6:19. doi: 10.3390/jcdd6020019

28. Jaiswal A, Pa SD, Singh G, Sathiyamoorthy R, Deori T, Dwarakanathan V, et al. Assessment of cardiovascular risk using WHO CVD risk prediction chart with respect to hypertension status among Indian population: a secondary analysis of National Family Health Survey (2015–16). *J Family Med Prim Care*. (2022) 11:5757. doi: 10.4103/jfmpc.jfmpc_158_22

29. Colafella KMM, Denton KM. Sex-specific differences in hypertension and associated cardiovascular disease. *Nat Rev Nephrol*. (2018) 14:185–201. doi: 10.1038/nrneph.2017.189

30. Kondo T, Nakano Y, Adachi S, Murohara T. Effects of tobacco smoking on cardiovascular disease. *Circ J*. (2019) 83:1980–5. doi: 10.1253/circj.CJ-19-0323

31. World Health Organization. Tobacco & Coronary Heart Disease. Geneva: World Health Organization (2023).

32. Ministry of Health and Family Welfare, Government of India, International Institute for Population Sciences (IIPS). National Fact Sheet of fourth round of global youth tobacco survey (GYTS-4) (2019). Available at: https://ntcp.mohfw.gov.in/assets/document/National_Fact_Sheet_of_fourth_round_of_Global_Youth_Tobacco_Survey_GYTS-4.pdf (accessed October 19, 2019).

33. Niessen LW, Mohan D, Akuoku JK, Mirelman AJ, Ahmed S, Koehlmoos TP, et al. Tackling socioeconomic inequalities and non-communicable diseases in low-income and middle-income countries under the sustainable development agenda. *Lancet*. (2018) 391:2036–46. doi: 10.1016/S0140-6736(18)30482-3

34. Allen L, Williams J, Townsend N, Mikkelsen B, Roberts N, Foster C, et al. Socioeconomic status and non-communicable disease behavioural risk factors in low-income and lower-middle-income countries: a systematic review. *Lancet Glob Health*. (2017) 5:e277–89. doi: 10.1016/S2214-109X(17)30058-X

35. Piercy KL, Troiano RP, Ballard RM, Carlson SA, Fulton JE, Galuska DA, et al. The physical activity guidelines for Americans. *JAMA*. (2018) 320:2020–8. doi: 10.1001/jama.2018.14854

36. Althubaiti A. Information bias in health research: definition, pitfalls, and adjustment methods. *J Multidiscip Healthc*. (2016) 9:211–7. doi: 10.2147/JMDH.S104807

37. World Health Organisation. NCD global monitoring framework (2024). Available at: https://www.who.int/publications/i/item/ncd-surveillance-global-monitoring-framework (accessed August 14, 2024).

38. Bhatt G, Goel S, Kiran T, Grover S, Medhi B, Singh G, et al. Estimating the cost of delivering tobacco cessation intervention package at noncommunicable disease clinics in two districts of North India. *Nicotine Tob Res*. (2023) 25:1727–35. doi: 10.1093/ntr/ntad105

39. Directorate General Of Health Services, Ministry of Health & Family Welfare, Government of India, Population Based Screening (PBS) (2024). Available at: https://dghs.gov.in/content/1363_3_NationalProgrammePreventionControl.aspx?format=Print (accessed April 10, 2024).

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 18 September 2024
DOI 10.3389/fpubh.2024.1403450

OPEN ACCESS

EDITED BY
Yun Gao,
Sichuan University, China

REVIEWED BY
Ruijie Xie,
University of South China, China
Alpesh Goyal,
All India Institute of Medical Sciences, India
Andre Luis Lacerda Bachi,
Universidade Santo Amaro, Brazil

*CORRESPONDENCE
Yongtao Mao
✉ maoyt@suda.edu.cn

RECEIVED 19 March 2024
ACCEPTED 30 August 2024
PUBLISHED 18 September 2024

CITATION
Wu X, Jin X, Xu W, She C, Li L and Mao Y (2024) Cardiometabolic index is associated with increased bone mineral density: a population-based cross-sectional study.
Front. Public Health 12:1403450.
doi: 10.3389/fpubh.2024.1403450

Cardiometabolic index is associated with increased bone mineral density: a population-based cross-sectional study

Xujin Wu, Xixin Jin, Wei Xu, Chang She, Liubing Li and Yongtao Mao*

Department of Orthopedics, The Second Affiliated Hospital of Soochow University, Suzhou, China

Background: Osteoporosis is a multifactorial bone disease in which lipid metabolism plays an important role. Bone Mineral Density (BMD) measured by Dual-energy X-ray Absorptiometry (DXA) is a critical indicator for diagnosing osteoporosis. The cardiometabolic index (CMI) is a novel metric that combines two quantitative indicators of blood lipids—triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C). This study explores the association between CMI and BMD and seeks to elucidate the role of lipid metabolism in the context of bone health.

Methods: Based on the data of the National Health and Nutrition Examination Survey (NHANES) 2017–March 2020-pre-pandemic, weighted multiple linear regression and smooth curve fitting were used to study the relationship between CMI and femoral BMD. Stratified analyses were also conducted for age, gender, BMI, ethnicity, diabetes and hypertension status. And, the saturation threshold effect of CMI was further analyzed using a two-stage linear regression model.

Result: This study enrolled a total of 1,650 participants (48.7% males), with an average age of 63.0 ± 8.6 years. After adjusting for multiple confounding factors, CMI was positively correlated with total femur BMD, trochanter BMD, and intertrochanter BMD, while the correlation with femur neck BMD was not statistically significant. In the fully adjusted model, each unit increase in CMI was associated with a 0.026 (g/cm^2) increase in total femur BMD, a 0.022 (g/cm^2) increase in trochanter BMD, and a 0.034 (g/cm^2) increase in intertrochanter BMD. Subjects in the highest quartile of CMI had a 0.034 (g/cm^2) increase in total femur BMD, a 0.035 (g/cm^2) increase in trochanter BMD, and a 0.039 (g/cm^2) increase in intertrochanter BMD in the fully-adjusted model compared to those in the lowest quartile. In addition, saturation was observed between CMI and total femur BMD, trochanter BMD and intertrochanter BMD, with saturation thresholds of 1.073, 1.431 and 1.073, respectively.

Conclusion: CMI is strongly associated with BMD, indicating its potential relevance in bone metabolism. However, the role of CMI in the context of bone health, especially regarding osteoporosis risk, requires further investigation in large-scale prospective studies.

KEYWORDS

CMI, BMD, osteoporosis, NHANES, cross-sectional study

Introduction

Osteoporosis (OP) is a systemic skeletal disease characterized by an increased risk of fractures (1). Approximately 200 million people worldwide are affected by osteoporosis, and according to NHANES data, more than 16.20% of the population in the United States suffers from osteoporosis, and as aging intensifies, this proportion will gradually increase (2, 3). Osteoporosis is characterized by a loss of bone mass and damage to the microstructure of the skeleton, significantly increases the incidence of fragility fractures (4, 5). Femoral BMD is an important indicator for the detection and diagnosis of osteoporosis. It is strongly associated with all-cause mortality in osteoporosis patients, with hip fractures due to decreased femoral BMD being even more devastating in the older adult population (6, 7). The World Health Organization (WHO) has proposed that Bone Mineral Density (BMD) measured by Dual Energy X-ray Absorptiometry (DXA) is the gold standard for diagnosing osteoporosis, which helps identify potential risk factors for bone health and plays a crucial role in the prevention and early detection of osteoporosis (8).

Recent research has revealed a close relationship between lipid metabolism and bone metabolism. Specifically, studies shown that osteoporosis is strongly associated with high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) (9, 10). Moreover, Gender differences significantly influence osteoporosis development and progression. Postmenopausal women are at heightened risk due to hormonal changes, particularly estrogen deficiency, which accelerates bone loss and adversely affects lipid metabolism, increasing osteoporosis risk (11, 12). However, there is a lack of consistent evidence on the relationship between lipid metabolism and osteoporosis.

Recent studies have observed increased bone mineral density and altered bone health in patients with high-risk cardiometabolic conditions, such as prediabetes, type 2 diabetes, and non-alcoholic fatty liver disease, suggesting a potential link between cardiometabolic risk factors and bone health (13–15). The cardiometabolic index (CMI) has been recognized as a new indicator of the distribution and dysfunction of visceral adipose tissue and primarily used to assess cardiovascular disease risk. CMI not only indicates an individual's degree of obesity but also reflects blood lipid levels (16, 17). However, its correlation with osteoporosis and BMD remains unclear. Therefore, this study used the National Health and Nutrition Examination Survey (NANES) database to examine the relationship between CMI and BMD at different sites in the femur, thereby investigating the link between lipid metabolism and osteoporosis.

Materials and methods

Reach publication

The NHANES database is the largest population-based national nutritional health survey in the world, managed by the U.S. National Center for Health Statistics (NCHS). The survey has been conducted biennially since 1999, utilizing a complex, stratified, multistage sampling design to select representative populations. More detailed information about the NHANES database can be found on the NHANES website: http://www.cdc.gov/nchs/nhanes/.

This study focuses on the 2017–2020-pre-pandemic NHANES database, which includes 15,560 participants, and aims to assess the nutritional and health status of Americans. Among these participants, 3,445 underwent DXA testing. After excluding subjects with missing relevant covariates, the study included a total of 1,650 subjects. The survey collected data through household questionnaires, telephone interviews, and examinations conducted by medical professionals and trained staff. Further details can be found at https://www.cdc.gov/nchs/nhanes/irba98.htm.

Variable

The independent variable in this study was CMI, which was derived from anthropometric indicators and blood samples. Data were collected based on standardized sampling protocols and rigorous laboratory tests and measurements to ensure validity and accuracy. Blood samples were typically collected in an investigative vehicle or at a designated sampling site and then processed and tested in a standard laboratory. Subjects' height and waist circumference were measured by certified health professionals in a mobile screening facility. Based on the above indicators, calculate WHtR and CMI:

$$\mathrm{WHtR} = \text{waist circumference}\,(\mathrm{cm}) / \text{height}\,(\mathrm{cm});$$

$$\mathrm{CMI} = \mathrm{TG}\,(\mathrm{mmol/L}) / \mathrm{HDL-C}\,(\mathrm{mmol/L}) \times \mathrm{WHtR}.$$

The dependent variable was BMD measured by NHANES DXA using a Hologic Discovery Model A densitometer with APEX 3.2. BMD (g/cm^2) was defined as bone mineral content (g) divided by bone area (cm^2). Specific data on BMD measurements using DXA can be found on the website: https://wwwn.cdc.gov/nchs/nhanes/Search/DataPage.aspx?Component=Examination, particularly in the chapter "Dual-Energy X-ray Absorptiometry—Whole Body."

Based on previous studies, confounders that could potentially affect BMD were selected to eliminate potential effects on outcomes (18, 19). We also analyzed these covariates for multicollinearity and no multicollinearity was detected. Finally, the following covariates were collected and adjusted for gender, age, race, PIR (Poverty Income Ratio), body mass index (BMI), blood urea nitrogen (mg/dl), creatinine (mg/dl), globulin (g/dl), total protein (g/dl), uric acid (mg/dl), glycohemoglobin (%), low-density lipoprotein cholesterol (mmol/L), serum phosphorus (mmol/l), serum iron (μmol/l), serum calcium (mmol/l), and smoking status, alcohol consumption, and the presence of hypertension or diabetes. For more information on covariates, see the NHANES website: http://www.cdc.gov/nchs/nhanes/.

Data analysis

Continuous variables were expressed as mean values with standard deviations (mean ± SD), while categorical variables were presented as percentages. The comparison of continuous variables was conducted using a weighted t-test, and for categorical variables, a chi-squared test was applied, with outcomes reported as counts (n) and percentages (%). Multivariate regression models were used to assess the relationship between CMI and BMD. To assess the

correlation between covariates and the analytical outcomes, three distinct models were formulated. Each model in the analysis progressively incorporated additional adjustments for covariates. The initial model remained unadjusted, while the second model included partial adjustments for age, gender and race. Model 3 represents the fully adjusted model, encompassing additional variables such as BMI, smoking habits, alcohol consumption, diabetes, hypertension and so on. Following this, subgroup analyses were executed to explore potential modifications in effect measures, including gender, ethnicity, age and BMI as potential influential factors. Finally, the saturation threshold effect of CMI was further analyzed using a two-stage linear regression model. Statistical analyses were conducted using R and Empower Stats, with significance set at $p < 0.05$ and strong significance at $p < 0.01$.

Ethics approval and consent to participate

NHANES participants were required to sign an informed consent form, and the data are now publicly available. The study was reviewed and approved by the Research Ethics Review Board of the National Center for Health Statistics (NCHS). The acquisition and dissemination of data within the NHANES database adhered to the principles of the Declaration of Helsinki, with the necessary approval from the Ethics Committee to ensure the ethical integrity of the data used in this investigation. The research methodology is based entirely on publicly available statistical data. All research activities complied with applicable laws and ethical standards in accordance with the guidelines for data usage and research practices.

Result

Baseline characteristic

A total of 1,650 subjects were included in this study, mean age: 63.0 ± 8.6 year, of which 48.7% were male and 51.3% female. Subjects included 5.1% Mexican American, 6.8% Other Hispanic, 69.8% Non-Hispanic White people, 9.3% Non-Hispanic Black people, 5.8% Non-Hispanic Asian and 3.3% Other Race—Including Multi-Racial.

As shown in Table 1, subjects were categorized into CMI quartiles: Q1 (0.041–0.283), Q2 (0.284–0.485), Q3 (0.486–0.831), and Q4 (0.832–24.483), based on the 25th, 50th, and 75th percentiles of the CMI distribution. Most of the covariates in each subgroup were significantly different from each other. We found that populations with higher CMI (Q4) were predominantly male, non-Hispanic white people, hypertensive, and non-diabetic. And with increasing CMI, there was a gradual increase in BMI, hip circumference, blood urea nitrogen, globulin, blood uric acid, glycated glycohemoglobin, total cholesterol, low-density lipoprotein cholesterol ($p < 0.001$), and a gradual increase in bone mineral density of the femur at all sites of the femur ($p < 0.001$) in the population. On the contrary, Serum iron gradually decreased with increasing CMI ($p < 0.001$).

Association between CMI and BMD

We used weighted multiple linear regression models to reveal the relationship between CMI and BMD. As shown in Table 2, in the simple adjustment model (Model2), there is a significant positive correlation between CMI and femoral BMD: total femoral BMD (0.019 (0.012, 0.025) <0.001), Femur neck BMD (0.009 (0.003, 0.016) 0.006), trochanter BMD (0.015 (0.009, 0.021) <0.001), intertrochanter BMD (0.022 (0.014, 0.030) <0.001). In the fully adjusted model (Model3), the positive correlation between CMI and femur neck BMD was not significant (0.001 (−0.014, 0.016) 0.904) but remained significant with total femur BMD (0.026 (0.010, 0.041) 0.001), trochanter BMD (0.022 (0.008, 0.035) 0.002) and intertrochanter BMD (0.034 (0.015, 0.053) <0.001) remained significantly positively correlated. It can be found that in the fully adjusted model (Model3), for each 1-unit increase in CMI, the corresponding increase in total femoral BMD was 0.026 g/cm^2, trochanter BMD was 0.015 g/cm^2, and intertrochanter BMD was 0.022 g/cm^2. When CMI was grouped according to quartiles using CMI Q1 as the reference, in the fully adjusted model (model3), the contribution of CMI to total femoral BMD (0.034 (0.013, 0.055) 0.001), trochanter BMD (0.035 (0.017, 0.054) <0.001) and intertrochanter BMD (0.039 (0.014, 0.065) 0.003) remained significant and the trend between each group is also statistically different (p for trend <0.05). In addition, the results of smoothed curve fitting (Figure 1) further demonstrated the positive correlation of CMI on total femoral BMD, trochanter BMD, and intertrochanter BMD, but the effect of CMI on femur neck BMD was not significant. Interestingly, as CMI increased, there was a brief period of decline in trochanter BMD followed by an upward trend.

Subgroup analysis

We performed subgroup analyses and interaction tests stratified by age, gender, race, BMI, diabetes status and hypertension status to evaluate whether the relationship between CMI and BMD is consistent in the general population, and the results are shown in Tables 3–8. When analyzed stratified by gender, the positive effect of CMI on BMD was predominantly seen in the female population ($p < 0.05$), particularly in Total femur BMD and Intertrochanter BMD ($p < 0.01$). When analyzed stratified by race, the positive correlation effect of CMI between total femoral BMD, trochanter BMD, and intertrochanter BMD was predominantly seen in non-Hispanic white people ($p < 0.01$). When analyzed stratified by age, the positive effect of CMI on total femoral BMD and Intertrochanter BMD was concentrated in people aged ≥60 years ($p < 0.01$). In contrast, the positive effect of CMI on trochanter BMD was concentrated in people aged <60 years. Furthermore, the positive correlation between CMI and BMD was significantly affected by age (P for interaction: 0.024). When analyzed stratified by BMI, the positive correlation of CMI on femoral BMD was mainly concentrated in people with BMI ≥30, particularly in Total femur BMD, Trochanter BMD and Intertrochanter BMD ($p < 0.01$). And the positive correlation of CMI on total femoral BMD and trochanter BMD was significantly influenced by the effect of BMI (P for interaction: 0.031; 0.043). When analyzed stratified by diabetes status, the positive correlation between CMI and total femur BMD, trochanter BMD, and intertrochanter BMD was predominantly observed in individuals with diabetes ($p < 0.01$). Moreover, the impact of CMI on trochanter BMD was significantly modified by diabetes status (P for interaction: 0.044). In the analysis stratified by hypertension status, the positive association of CMI with total femur BMD, trochanter BMD, and intertrochanter BMD was primarily

TABLE 1 Weighted characteristics of the study population based on CMI.

Characteristic	Q1: 0.041–0.283	Q2: 0.284–0.485	Q3: 0.486–0.831	Q4: 0.832–24.483	*p*-value
Age (year)	63.2 ± 9.1	63.4 ± 8.3	63.1 ± 8.7	62.5 ± 8.2	0.466
Gender (%)					<0.001
Male	39.3	46.5	47.6	61.1	
Female	60.7	53.5	52.4	38.9	
Race (%)					<0.001
Mexican American	2.3	5.0	6.8	6.7	
Other Hispanic	5.1	7.2	7.5	7.4	
Non-Hispanic White	69.3	69.3	64.8	75.0	
Non-Hispanic Black	13.1	10.6	8.7	4.6	
Non-Hispanic Asian	6.1	5.5	7.8	3.9	
Other Race-Including Multi-Racial	4.2	2.4	4.3	2.3	
BMI	25.9 ± 4.6	27.8 ± 4.8	30.5 ± 5.6	32.4 + 6.3	<0.001
Hip Circumference (cm)	101.3 ± 9.6	104.5 ± 11.0	108.9 ± 12.5	111.4 ± 14.0	<0.001
Poverty income ratio	3.4 ± 1.6	3.5 ± 1.6	3.3 ± 1.7	3.2 ± 1.6	0.046
Alcohol drinking in the past 12 months (%)					0.368
Yes	92.4	89.1	91.9	91.3	
No	7.4	10.9	8.1	8.7	
Smoke ≥100 cigarettes in life					0.001
Yes	43.8	56.1	55.7	45.0	
No	56.2	43.9	44.3	55.0	
Hypertension (%)					0.890
Yes	29.4	29.9	31.8	30.4	
No	70.6	70.1	68.2	69.6	
Diabetes (%)					<0.001
Yes	4.3	11.8	21.2	33.6	
No	95.7	88.2	78.8	66.4	
Blood Urea Nitrogen (mmol/L)	5.784 ± 1.955	5.722 ± 2.040	5.638 ± 1.814	6.329 ± 2.278	<0.001
Blood Creatinine (mg/dl)	0.878 ± 0.298	0.912 ± 0.354	0.884 ± 0.221	0.939 ± 0.457	0.045
Globulin (g/dL)	2.918 ± 0.423	2.997 ± 0.438	3.025 ± 0.428	3.056 ± 0.393	<0.001
Blood Total Protein (g/dl)	69.821 ± 4.708	70.122 ± 4.079	70.472 ± 4.419	70.512 ± 4.120	0.0741
Uric Acid (mg/dl)	4.846 ± 1.222	5.331 ± 1.352	5.847 ± 1.379	6.029 ± 1.411	<0.001
Glycohemoglobin (%)	5.575 ± 0.600	5.775 ± 0.677	6.004 ± 1.013	6.322 ± 1.292	<0.001
Serum phosphorus (mmol/dl)	1.147 ± 0.156	1.118 ± 0.171	1.129 ± 0.167	1.118 ± 0.165	0.032

(Continued)

10.3389/fpubh.2024.1403450

10.3389/fpubh.2024.1403450

TABLE 1 (Continued)

Characteristic	Q1: 0.041–0.283	Q2: 0.284–0.485	Q3: 0.486–0.831	Q4: 0.832–24.483	*p*-value
Serum calcium (mmol/l)	2.319 ± 0.086	2.317 ± 0.084	2.326 ± 0.104	2.315 ± 0.090	0.336
Serum iron (ug/dl)	16.655 ± 6.292	17.577 ± 5.807	17.816 ± 6.608	16.358 ± 4.893	<0.001
HDL-C (mmol/L)	1.878 ± 0.428	1.521 ± 0.281	1.302 ± 0.240	1.076 ± 0.187	<0.001
TC (mmol/L)	4.915 ± 0.934	4.952 ± 1.002	4.848 ± 1.135	5.088 ± 1.257	0.015
TG (mmol)	0.636 ± 0.178	0.989 ± 0.225	1.330 ± 0.288	2.293 ± 1.788	<0.001
LDL-C (mmol/L)	2.745 ± 0.800	2.979 ± 0.879	2.937 ± 1.019	3.021 ± 1.113	<0.001
WHtR	0.560 ± 0.071	0.591 ± 0.072	0.630 ± 0.081	0.660 ± 0.086	<0.001
Total femur BMD (g/cm^2)	0.867 ± 0.145	0.908 ± 0.156	0.945 ± 0.145	0.987 ± 0.144	<0.001
Femur neck BMD (g/cm2)	0.729 ± 0.145	0.751 ± 0.145	0.776 ± 0.133	0.803 ± 0.130	<0.001
Trochanter BMD (g/cm^2)	0.648 ± 0.118	0.690 ± 0.126	0.710 ± 0.122	0.747 ± 0.122	<0.001
Intertrochanter BMD (g/cm^2)	1.032 ± 0.175	1.078 ± 0.186	1.128 ± 0.168	1.174 ± 0.175	<0.001
CMI	0.196 ± 0.059	0.382 ± 0.056	0.642 ± 0.097	1.470 ± 1.517	<0.001

Mean ± SD for continuous variables: *p*-value was calculated by weighted linear regression model. (%) for categorical variables: *p*-value was calculated by weighted chi-square test. CMI: Cardiometabolic index; BMI: body mass index; TC: total cholesterol, TG: triglyceride; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; WHtR: waist circumference (cm)/height (cm); BMD: bone mineral density.

evident in those with hypertension ($p < 0.01$). Additionally, the influence of CMI on total femur BMD and intertrochanter BMD was significantly modulated by hypertension status (P for interaction: 0.005; 0.010).

Saturation effect analysis between CMI and BMD

As shown in Table 9 there was a saturation effect of CMI between total femoral BMD, trochanter BMD, and intertrochanter BMD with thresholds of 1.073, 1.431, and 1.073. There was a significant positive effect on BMD when CMI was below the threshold, and the regression coefficient decreased when CMI exceeded the threshold.

Discussion

A total of 1,650 subjects, enrolled from 2017 to March 2020 (pre-pandemic period), were included in this study to evaluate the effect of CMI index on femur BMD. Our findings indicated that CMI had a significant positive correlation with total femoral BMD, trochanter BMD and intertrochanter BMD. Additionally, factors such as age, BMI, gender, diabetes, and hypertension status significantly influenced this correlation. However, there was no significant correlation between CMI and Femur neck BMD. This study is the first to identify a relationship between CMI and BMD, further demonstrating that BMD is closely related to fat metabolism.

CMI is influenced by a combination of triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), height, and waist circumference. Specifically, an increase in TG levels, a decrease in HDL-C levels, an increase in height, and a decrease in waist circumference all contribute to an increase in CMI. While many previous studies have examined these variables individually, the relationship between HDL-C and BMD has been particularly controversial. For example, In a screening of 1,304 women, Zolfaroli et al. identified a positive correlation between HDL-C and bone mineral density in the lumbar spine and femoral neck (20). Conversely, Han et al. found in a case–control study of 710 people that those with osteoporosis had higher HDL-C (21). Similarly, Kim et al. found a negative correlation between HDL-C and BMD and the correlation was not affected by gender in a cross-sectional study of a Korean population (9). Furthermore, Cui's study of 1,035 male and 3,953 female healthy volunteers found that Subjects have a significant reduction in bone mass when HDL-C is greater than 1.56 mmol/L (22). In a cross-sectional study of a larger population, Xie et al. found a U-shaped relationship between HDL-C and lumbar spine BMD, with a negative correlation between HDL-C and lumbar spine BMD when HDL-C was <0.98 (mmol/L), and a positive correlation when this value was exceeded (23). Supporting these findings, cellular studies have also confirmed this relationship. Huang et al. found that HDL-C promotes cholesterol efflux from osteoblasts by upregulating ABCG1 expression, which disrupts the dynamic balance of cholesterol in osteoblasts, thereby inducing apoptosis and impairing osteoblast formation (24). Kha et al. found that high levels of HDL-C inhibited bone differentiation, which is mainly related to the fact that HDL-C removes oxidized sterols from the peripheral circulation which play an important role in osteogenic

10.3389/fpubh.2024.1403450

TABLE 2 Associations between cardiometabolic index and BMD.

	Exposure	Model 1 β (95% CI), *p* value	Model 2 β (95% CI), *p* value	Model 3 β (95% CI), *p* value
Total femur BMD	CMI	0.028 (0.020, 0.036) <0.001	0.019 (0.012, 0.025) <0.001	0.026 (0.010, 0.041) 0.0012
	CMI Q1	Reference	Reference	Reference
	CMI Q2	0.041 (0.021, 0.061) <0.001	0.033 (0.016, 0.050)<0.001	0.014 (−0.003, 0.032) 0.111
	CMI Q3	0.077 (0.057, 0.098) <0.001	0.068 (0.050, 0.086) <0.001	0.020 (0.000, 0.040) 0.045
	CMI Q4	0.120 (0.100, 0.140) <0.001	0.092 (0.075, 0.110) <0.001	0.034 (0.013, 0.055) 0.001
	P for trend	<0.001	<0.001	0.002
Femur neck BMD	CMI	0.015 (0.008, 0.022) <0.001	0.009 (0.003, 0.016) 0.006	0.001 (−0.014, 0.016) 0.904
	CMI Q1	Reference	Reference	Reference
	CMI Q2	0.023 (0.004, 0.041) 0.01481	0.019 (0.003, 0.035) 0.023	0.002 (−0.015, 0.019) 0.799
	CMI Q3	0.047 (0.028, 0.067) <0.001	0.044 (0.027, 0.061) <0.001	0.003 (−0.016, 0.023) 0.742
	CMI Q4	0.074(0.056, 0.092) <0.001	0.059 (0.042, 0.075) <0.001	0.007 (−0.013, 0.028) 0.493
	P for trend	<0.001	<0.001	0.501
Trochanter BMD	CMI	0.023 (0.016, 0.029) <0.001	0.015 (0.009, 0.021) <0.001	0.022 (0.008, 0.035) 0.002
	CMI Q1	Reference	Reference	Reference
	CMI Q2	0.042 (0.026, 0.058) <0.001	0.036(0.021, 0.051) <0.001	0.026 (0.011, 0.041) <0.001
	CMI Q3	0.062 (0.045, 0.080) <0.001	0.055(0.040, 0.071) <0.001	0.020 (0.003, 0.038) 0.022
	CMI Q4	0.100 (0.083, 0.116) <0.001	0.078(0.063, 0.093) <0.001	0.035(0.017, 0.054) <0.001
	P for trend	<0.001	<0.001	<0.001
Intertrochanter BMD	CMI	0.034 (0.024, 0.043) <0.001	0.022(0.014, 0.030) <0.001	0.034(0.015, 0.053) <0.001
	CMI Q1	Reference	Reference	Reference
	CMI Q2	0.046 (0.022, 0.070) <0.001	0.036 (0.016, 0.057) 0.001	0.011 (−0.011, 0.032) 0.325
	CMI Q3	0.096 (0.072, 0.121) <0.001	0.084 (0.063, 0.106) <0.001	0.027 (0.002, 0.051) 0.033
	CMI Q4	0.142 (0.118, 0.165) <0.001	0.109 (0.088, 0.130) <0.001	0.039 (0.014, 0.065) 0.003
	P for trend	<0.001	<0.001	0.002

Model 1: no covariates were adjusted.
Model 2: age, gender and race were adjusted.
Model 3: age, gender, race, BMI, hip circumference, poverty income ratio, smoking status, alcohol status, hypertension status, diabetes status, blood urea nitrogen, blood creatinine, globulin, blood total protein, uric acid, glycohemoglobin, serum phosphorus, serum calcium, serum iron, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) were adjusted.

differentiation (25). In this study, the conversion of high HDL-C to CMI is reflected as low CMI, and the population in the low CMI group (Q1) in this study had lower BMD than the high CMI population, which briefly demonstrates the negative correlation between HDL-C and BMD.

I Furthermore, numerous studies have also explored the relationship between TG and BMD. Xu et al. found that TG can be used as a diagnostic indicator to assist in the diagnosis of osteoporosis in older women, and that TG levels were higher in the osteoporosis group than in the normal population (26). Similarly, Wang et al. analyzed NHANES data from 2017–2020 and found a positive correlation between TG and lumbar spine BMD at TG > 2.597 mmoL/L in the older age group of 50 years or older (18). These findings suggest that TG plays a significant role in bone health, and when TG was included in the calculation of CMI, it demonstrated a significant positive correlation between CMI and BMD.

Other indicators of lipid metabolism are also strongly associated with BMD. For example, there is a negative correlation between low-density lipoprotein cholesterol (LDL-C) and BMD, which is likely due to the fact that high levels of LDL-C promote osteoclastogenesis. Elevated LDL-C levels are believed to contribute to the loss of bone mineral density by enhancing osteoclast activity (27). This process is closely linked to key enzymes in the cholesterol metabolic pathway, such as HMG-CoA reductase.

The primary mechanisms underlying these effects include the removal of oxidized sterols from peripheral tissues by HDL-C and the inhibition of osteoblast differentiation by oxidation products of LDL-C. Cholesterol, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) induced progenitor MSCs (mesenchymal stem cells) to undergo lipogenic, rather than osteogenic differentiation and induced RANKL—(nuclear factor receptor activator of κB ligand-) dependent osteoclast differentiation (25, 28). Trimpou et al. further observed necrosis of the femoral head under electron microscopy, noting a significant increase in both the number and size of adipocytes, which suggests that lipid metabolism may play a crucial role in the formation of bone geometry (29). Meanwhile, fatty acids, phospholipids and several endogenous metabolites have been reported to play a key role in the homeostatic level of bone. These molecules influence the survival and function of osteoblasts, participate in the bone mineralization process, and even regulate various critical signaling pathways (30).

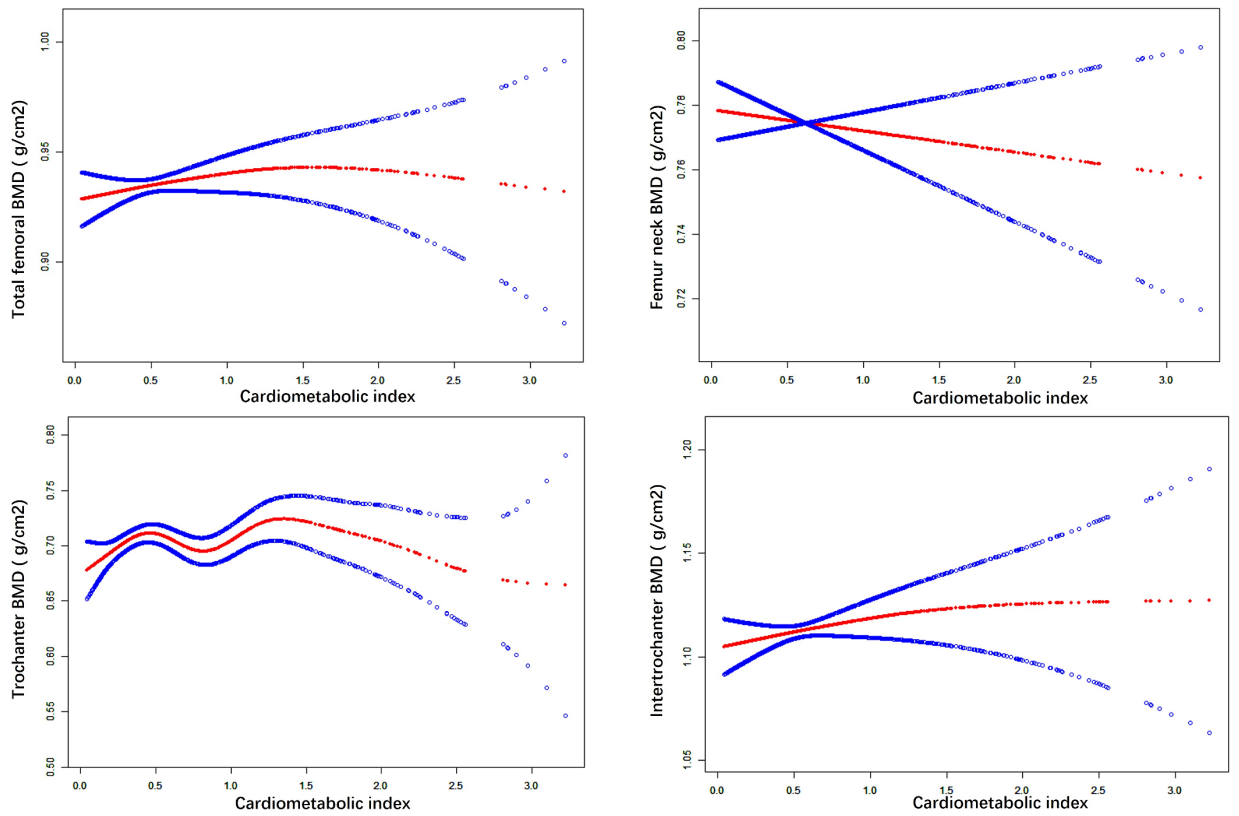


FIGURE 1
The nonlinear associations between CMI and BMD. The solid red line represents the smooth curve fit between variables. Blue bands represent the 95% of confidence interval from the fit.

TABLE 3 Subgroup analysis of the association between CMI and BMD (stratified by gender).

	Stratified by gender	Adjust model β (95% CI), *p* value
Total femur BMD	Male	0.011 (−0.008, 0.031) 0.250
	Female	0.040 (0.014, 0.067) 0.003
	P for interaction	0.614
Femur neck BMD	Male	−0.022 (−0.042, −0.002) 0.028
	Female	0.029 (0.003, 0.055) 0.030
	P for interaction	0.101
Trochanter BMD	Male	0.015 (−0.004, 0.034) 0.116
	Female	0.026 (0.005, 0.048) 0.018
	P for interaction	0.686
Intertrochanter BMD	Male	0.019 (−0.005, 0.042) 0.122
	Female	0.044 (0.012, 0.077) 0.008
	P for interaction	0.796

Age, race, BMI, hip circumference, poverty income ratio, smoking status, alcohol status, hypertension status, diabetes status, blood urea nitrogen, blood creatinine, globulin, blood total protein, uric acid, glycohemoglobin, serum phosphorus, serum calcium, serum iron, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) were adjusted.

Moreover, CMI is a new obesity index that reflects the distribution and functional status of visceral fat in the body. It represents both the degree of obesity and an individual's lipid levels (17). Abdominal obesity is characterized by an increase in visceral fat, mainly in the form of an increased BMI. The relationship between BMI and BMD is currently controversial, and Asuman found that BMD was significantly higher in overweight individuals than in normal weight individuals (31). A cross-sectional study by Ma et al., based on NHANES data from 2005–2018, observed that the relationship between BMI and BMD is not simply linear; instead,

10.3389/fpubh.2024.1403450

TABLE 4 Subgroup analysis of the association between CMI and BMD (stratified by race).

	Stratified by race	Adjust model β (95% CI), *p* value
Total femur BMD	Mexican American	0.039 (−0.004, 0.082) 0.075
	Other Hispanic	−0.025 (−0.065, 0.014) 0.209
	Non-Hispanic White	0.036 (0.011, 0.062) 0.006
	Non-Hispanic Black	0.019 (−0.028, 0.065) 0.431
	Non-Hispanic Asian	0.076 (0.021, 0.131) 0.007
	Other Race—Including Multi-Racial	−0.071 (−0.188, 0.046) 0.247
	P for interaction	0.573
Femur neck BMD	Mexican American	0.015 (−0.028,0.058) 0.489
	Other Hispanic	−0.040 (−0.082, 0.002) 0.067
	Non-Hispanic White	0.007 (−0.018, 0.032) 0.591
	Non-Hispanic Black	−0.010(−0.055, 0.035) 0.666
	Non-Hispanic Asian	0.065 (0.009, 0.122) 0.024
	Other Race—Including Multi-Racial	−0.051(−0.188, 0.086) 0.470
	P for interaction	0.639
Trochanter BMD	Mexican American	0.023 (−0.016, 0.063) 0.253
	Other Hispanic	−0.020 (−0.056, 0.017) 0.292
	Non-Hispanic White	0.036 (0.014, 0.059) 0.002
	Non-Hispanic Black	0.006 (−0.035, 0.047) 0.770
	Non-Hispanic Asian	0.033 (−0.015, 0.080) 0.177
	Other Race—Including Multi-Racial	−0.096(−0.187, −0.004) 0.051
	P for interaction	0.310
Intertrochanter BMD	Mexican American	0.044 (−0.009, 0.098) 0.1058
	Other Hispanic	−0.026(−0.070, 0.018) 0.251
	Non-Hispanic White	0.043 (0.012, 0.075) 0.007
	Non-Hispanic Black	0.022 (−0.035, 0.078) 0.449
	Non-Hispanic Asian	0.116 (0.050, 0.182) 0.001
	Other Race—Including Multi-Racial	−0.070 (−0.214, 0.074) 0.353
	P for interaction	0.601

Age, gender, BMI, hip circumference, poverty income ratio, smoking status, alcohol status, hypertension status, diabetes status, blood urea nitrogen, blood creatinine, globulin, blood total protein, uric acid, glycohemoglobin, serum phosphorus, serum calcium, serum iron, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) were adjusted.

TABLE 5 Subgroup analysis of the association between CMI and BMD (stratified by age).

	Stratified by age	Adjust model β (95% CI), *p* value
Total femur BMD	<60 year	0.017 (−0.009, 0.043) 0.192
	≥60	0.030 (0.011, 0.050) 0.003
	P for interaction	0.176
Femur neck BMD	<60 year	−0.008 (−0.036, 0.019) 0.541
	≥60	0.008 (−0.011, 0.027) 0.402
	P for interaction	0.587
Trochanter BMD	<60 year	0.031 (0.009, 0.053) 0.007
	≥60	0.016 (−0.002, 0.033) 0.080
	P for interaction	0.876
Intertrochanter BMD	<60 year	0.012 (−0.018, 0.043) 0.429
	≥60	0.046 (0.022, 0.071) <0.001
	P for interaction	0.024

Gender, race, BMI, hip circumference, poverty income ratio, smoking status, alcohol status, hypertension status, diabetes status, blood urea nitrogen, blood creatinine, globulin, blood total protein, uric acid, glycohemoglobin, serum phosphorus, serum calcium, serum iron, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) were adjusted.

TABLE 6 Subgroup analysis of the association between CMI and BMD (stratified by BMI).

	Stratified by BMI	Adjust model β (95% CI), *p* value
Total femur BMD	<25	−0.006 (−0.046, 0.034) 0.775
	25–29.9	0.017 (−0.008, 0.042) 0.189
	≥30	0.055 (0.032, 0.078) <0.001
	P for interaction	0.031
Femur neck BMD	<25	−0.031(−0.069, 0.008) 0.117
	25–29.9	−0.006(−0.032, 0.019) 0.614
	≥30	0.024 (0.002, 0.047) 0.036
	P for interaction	0.137
Trochanter BMD	<25	−0.006 (−0.043, 0.031) 0.751
	25–29.9	0.018 (−0.004, 0.039) 0.109
	≥30	0.046 (0.026, 0.066) <0.001
	P for interaction	0.043
Intertrochanter BMD	<25	0.009 (−0.041, 0.059) 0.719
	25–29.9	0.022 (−0.009, 0.054) 0.161
	≥30	0.063 (0.036, 0.091) <0.001
	P for interaction	0.107

Age, gender, race, hip circumference, poverty income ratio, smoking status, alcohol status, hypertension status, diabetes status, blood urea nitrogen, blood creatinine, globulin, blood total protein, uric acid, glycohemoglobin, serum phosphorus, serum calcium, serum iron, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) were adjusted.

TABLE 7 Subgroup analysis of the association between CMI and BMD (stratified by diabetes status).

	Stratified by diabetes status	Adjust model β (95% CI), *p* value
Total femur BMD	Yes	0.031 (0.013, 0.050) <0.001
	No	0.007 (−0.023, 0.036) 0.664
	P for interaction	0.241
Femur neck BMD	Yes	0.016 (−0.002, 0.035) 0.078
	No	−0.039 (−0.068, −0.011) 0.008
	P for interaction	0.012
Trochanter BMD	Yes	0.028 (0.012, 0.044) <0.001
	No	0.005 (−0.023, 0.032) 0.735
	P for interaction	0.044
Intertrochanter BMD	Yes	0.033 (0.011, 0.056) 0.003
	No	0.028 (−0.009, 0.066) 0.143
	P for interaction	0.803

Age, gender, race, hip circumference, poverty income ratio, smoking status, alcohol status, hypertension status, BMI, blood urea nitrogen, blood creatinine, globulin, blood total protein, uric acid, glycohemoglobin, serum phosphorus, serum calcium, serum iron, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) were adjusted.

there are saturation points where optimal BMD can be achieved by maintaining a slightly higher BMI (32). JIA et al. found that the lower the BMI, the greater the BMD loss in 128 postmenopausal women with osteoporotic fractures (33). However, Auslader et al. found no significant correlation between BMI and BMD in young women (34). The susceptibility of the female population to BMD is closely related to the decrease in oestrogen levels and the increase in osteoclast activity in postmenopausal women, resulting in a disruption of the balance between accelerated bone resorption and bone remodeling in favour of bone resorption (5, 35). This study also confirmed the significant effect of CMI on total femur BMD and trochanter BMD, with BMI playing a role in these outcomes. Additionally, our stratified analysis revealed that female BMD is more susceptible to the influence of CMI.

Furthermore, recent studies have demonstrated that the cardiometabolic index (CMI) is strongly associated with metabolic

TABLE 8 Subgroup analysis of the association between CMI and BMD (stratified by hypertension status).

	Stratified by hypertension status	Adjust model β (95% CI), *p* value
Total femur BMD	Yes	0.057 (0.033, 0.081) <0.001
	No	0.015 (−0.005, 0.034) 0.151
	P for interaction	0.005
Femur neck BMD	Yes	−0.002 (−0.020, 0.019) 0.941
	No	0.010 (−0.014, 0.033) 0.434
	P for interaction	0.210
Trochanter BMD	Yes	0.038 (0.017, 0.059) <0.001
	No	0.018 (0.002, 0.036) 0.044
	P for interaction	0.167
Intertrochanter BMD	Yes	0.071 (0.041, 0.101) <0.001
	No	0.020 (−0.004, 0.044) 0.107
	P for interaction	0.010

Age, gender, race, hip circumference, poverty income ratio, smoking status, alcohol status, BMI, diabetes status, blood urea nitrogen, blood creatinine, globulin, blood total protein, uric acid, glycohemoglobin, serum phosphorus, serum calcium, serum iron, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) were adjusted.

TABLE 9 Saturation effect analysis of CMI on BMD.

	Total femur BMD	Femur neck BMD	Trochanter BMD	Intertrochanter BMD
Fitting by the standard linear model	0.028 (0.020, 0.036) <0.001	0.001 (−0.014, 0.016) 0.9036	0.023 (0.016, 0.029) <0.001	0.034 (0.024, 0.043) <0.001
Fitting by the two-piecewise linear model				
Inflection point (k)	1.073	0.138	1.431	1.073
< K point effect 1	0.136 (0.113, 0.158) <0.001	1.093 (0.439, 1.747) 0.001	0.061 (0.032, 0.090) <0.001	0.163 (0.136, 0.190) <0.001
> K point effect 2	0.003 (−0.007, 0.012) 0.595	−0.004 (−0.019, 0.012) 0.623	0.001 (−0.007, 0.010) 0.725	0.002 (−0.009, 0.013) 0.686
Effect 2 minus effect1	−0.133 (−0.160, −0.107) <0.001	−1.097 (−1.754, −0.440) 0.001	−0.060 (−0.092, −0.027) <0.001	−0.161 (−0.193, −0.130) <0.001
Predicted value of the equation at the folding point	0.995 (0.981, 1.009)	0.746 (0.736, 0.757)	0.759 (0.742, 0.776)	1.186 (1.170, 1.203)
Log-likelihood ratio test	<0.001	<0.001	<0.001	<0.001

diseases such as cardiovascular disease, diabetes, and insulin resistance (36–38). Previous studies have shown that metabolic diseases such as diabetes mellitus, insulin resistance, and non-alcoholic fatty liver disease are strongly associated with BMD (13–15, 39). The haemodynamic changes in bone due to cardiovascular diseases such as hypertension and the hyperinsulinism associated with diabetes mellitus and insulin resistance will both promote osteoblast differentiation leading to increased BMD (40, 41). In addition, insulin resistance is often accompanied by changes in the secretion of adipokines, which may regulate bone metabolism through the RANKL/RANK/OPG system, promoting bone formation and leading to increased BMD (42) Consistent with these findings, a recent study demonstrated a positive relationship between insulin resistance, dysglycemia and BMD in young Indian women (39). This study also identified a positive correlation between CMI and BMD, particularly in hypertensive and diabetic populations, as revealed through stratified analyses.

In conclusion, osteoporosis and lipid metabolism are closely related. Therefore, the cardiometabolic index (CMI) can be used as a novel indicator of lipid metabolism levels in the body, which may aid in the diagnosis and prevention of osteoporosis. The strengths of this study include the use of a complex multi-stage probability sampling design, which enhances the reliability and representativeness of the findings. However, there are several limitations to consider. First, this study employed a primarily cross-sectional design, which limits the ability to establish a causal relationship between CMI, BMD, and osteoporosis. Additionally, bone microarchitecture and turnover were not evaluated, therefore limiting our ability to definitively determine the impact of increased CMI on bone health dynamics. Future research should include these parameters to provide a more comprehensive understanding of the relationship between CMI and bone health. Finally, the covariates included in this study were limited; however, the observed correlation between CMI and osteoporosis remains sufficiently robust, making it unlikely to be significantly affected by unmeasured factors.

Conclusion

This study revealed that total femur BMD, trochanter BMD, and intertrochanter BMD increase with higher CMI levels. This correlation was more pronounced in individuals aged 60 years and older, with a BMI of 30 or greater, and in those with diabetes or hypertension. However, further large-scale prospective studies are needed to validate these findings.

Data availability statement

Publicly available datasets were analyzed in this study. The data of this study are publicly available on the NHANES datasets. Specific data on this study is detailed at the following link: https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?Cycle=2017-2020.

Ethics statement

This study was based on publicly available datasets. Ethical review and approval was not required for the study, in accordance with the local legislation and institutional requirements.

Author contributions

XW: Conceptualization, Data curation, Formal analysis, Methodology, Software, Writing – original draft. XJ: Data curation, Formal analysis, Methodology, Software, Writing – original draft. WX: Funding acquisition, Project administration, Resources, Validation, Visualization, Writing – review & editing. CS: Funding acquisition, Project administration, Resources, Validation, Visualization, Writing – review & editing. LL: Funding acquisition, Resources, Visualization, Writing – review & editing. YM: Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. This research was funded by Gusu Talent Program (2020092), Suzhou Key Disciplines (no. SZXK202104), Open Project of the State Key Laboratory of Radiation Medicine and Radiation Protection Jointly Constructed by the Ministry and the Province (GZK1202215).

Acknowledgments

We thank the staff at the National Center for Health Statistics of the Centers for Disease Control for designing, collecting, and collating the NHANES data and creating the public database.

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

References

1. Lane JM, Russell L, Khan SN. Osteoporosis. *Clin Orthop Relat Res.* (2000) 372:139–50. doi: 10.1097/00003086-200003000-00016

2. Kushchayeva Y, Pestun I, Kushchayev S, Radzikhovska N, Lewiecki EM. Advancement in the treatment of osteoporosis and the effects on bone healing. *J Clin Med.* (2022) 11:7477. doi: 10.3390/jcm11247477

3. Looker ACI N, SarafraziFan B, Shepherd JA. Trends in osteoporosis and low bone mass in older US adults, 2005–2006 through 2013–2014. *Osteoporos Int.* (2017) 28:1979–88. doi: 10.1007/s00198-017-3996-1

4. Kanis JA, Cooper C, Rizzoli R, Reginster JY. Scientific advisory Board of the European Society for C, economic aspects of O, the committees of scientific a, National Societies of the international osteoporosis F: European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int.* (2019) 30:3–44. doi: 10.1007/s00198-018-4704-5

5. Qaseem A, Forciea MA, McLean RM, Denberg TD. Clinical guidelines Committee of the American College of P, Barry MJ, Cooke M, Fitterman N, Harris RP, Humphrey LL et al: treatment of low bone density or osteoporosis to prevent fractures in men and women: a clinical practice guideline update from the American College of Physicians. *Ann Intern Med.* (2017) 166:818–39. doi: 10.7326/M15-1361

6. Xue S, Kemal O, Lu M, Lix LM, Leslie WD, Yang S. Age at attainment of peak bone mineral density and its associated factors: the National Health and nutrition examination survey 2005–2014. *Bone.* (2020) 131:115163. doi: 10.1016/j.bone.2019.115163

7. Black DM, Rosen CJ. Clinical Practice. Postmenopausal Osteoporosis. *N Engl J Med.* (2016) 374:254–62. doi: 10.1056/NEJMcp1513724

8. Kline GA, Lix LM, Leslie WD. Patient outcomes in the years after a DXA-BMD treatment monitoring test: improved medication adherence in some, but too little too late. *J Bone Miner Res.* (2020) 36:1425–31. doi: 10.1002/jbmr.4333

9. Kim J, Ha J, Jeong C, Lee J, Lim Y, Jo K, et al. Bone mineral density and lipid profiles in older adults: a nationwide cross-sectional study. *Osteoporos Int.* (2023) 34:119–28. doi: 10.1007/s00198-022-06571-z

10. Bredella MA, Gill CM, Gerweck AV, Landa MG, Kumar V, Daley SM, et al. Ectopic and serum lipid levels are positively associated with bone marrow fat in obesity. *Radiology.* (2013) 269:534–41. doi: 10.1148/radiol.13130375

11. Khosla S, Oursler MJ, Monroe DG. Estrogen and the skeleton. *Trends Endocrinol Metabol.* (2012) 23:576–81. doi: 10.1016/j.tem.2012.03.008

12. Mahase E. NICE recommends new treatment option for osteoporosis after menopause. *British Med J Publish Group.* (2024) 386:q1769. doi: 10.1136/bmj.q1769

13. Goyal A, Kubihal S, Gupta Y. Shalimar, Kandasamy D, Kalaivani M, Tandon N: bone mass, microarchitecture and turnover among young Indian women with non-alcoholic fatty liver disease. *Endocrine.* (2024):1–10. doi: 10.1007/s12020-024-03934-w

14. Hygum K, Starup-Linde J, Langdahl BL. Diabetes and bone. *Osteoporos Sarcop.* (2019) 5:29–37. doi: 10.1016/j.afos.2019.05.001

15. Drapkina OM, Elkina AY, Sheptulina AF, Kiselev AR. Non-alcoholic fatty liver disease and bone tissue metabolism: current findings and future perspectives. *Int J Mol Sci.* (2023) 24:8445. doi: 10.3390/ijms24098445

16. Acosta-Garcia E, Concepcion-Paez M. Cardiometabolic index as a predictor of cardiovascular risk factors in adolescents. *Rev Salud Publica (Bogota)*. (2018) 20:340–5. doi: 10.15446/rsap.v20n3.61259

17. Wakabayashi I, Daimon T. The "cardiometabolic index" as a new marker determined by adiposity and blood lipids for discrimination of diabetes mellitus. *Clin Chim Acta*. (2015) 438:274–8. doi: 10.1016/j.cca.2014.08.042

18. Wang P, Chen C, Song C, Jia J, Wang Y, Mu W. High cholesterol and low triglycerides are associated with total lumbar bone mineral density among adults aged 50 years and over: the NHANES 2017-2020. *Front Med (Lausanne)*. (2022) 9:923730. doi: 10.3389/fmed.2022.923730

19. Tian N, Chen S, Han H, Jin J, Li Z. Association between triglyceride glucose index and total bone mineral density: a cross-sectional study from NHANES 2011-2018. *Sci Rep*. (2024) 14:4208. doi: 10.1038/s41598-024-54192-9

20. Zolfaroli I, Ortiz E, García-Pérez M-Á, Hidalgo-Mora JJ, Tarín JJ, Cano A. Positive association of high-density lipoprotein cholesterol with lumbar and femoral neck bone mineral density in postmenopausal women. *Maturitas*. (2021) 147:41–6. doi: 10.1016/j.maturitas.2021.03.001

21. Han H, Li R, Fu D, Zhou H, Zhan Z, Wu Y, et al. Correlation between bone density, bone metabolism markers with lipid metabolism markers and body mass index. *BMC Musculoskelet Disord*. (2024) 25:162. doi: 10.1186/s12891-024-07284-6

22. Cui R, Zhou L, Li Z, Li Q, Qi Z, Zhang J. Assessment risk of osteoporosis in Chinese people: relationship among body mass index, serum lipid profiles, blood glucose, and bone mineral density. *Clin Interv Aging*. (2016) 11:887–95. doi: 10.2147/CIA.S103845

23. Xie R, Huang X, Liu Q, Liu M. Positive association between high-density lipoprotein cholesterol and bone mineral density in US adults: the NHANES 2011–2018. *J Orthop Surg Res*. (2022) 17:92. doi: 10.1186/s13018-022-02986-w

24. Huang X, Lv Y, He P, Wang Z, Xiong F, He L, et al. HDL impairs osteoclastogenesis and induces osteoclast apoptosis via upregulation of ABCG1 expression. *Acta Biochim Biophys Sin Shanghai*. (2018) 50:853–61. doi: 10.1093/abbs/gmy081

25. Kha HT, Basseri B, Shouhed D, Richardson J, Tetradis S, Hahn TJ, et al. Oxysterols regulate differentiation of mesenchymal stem cells: pro-bone and anti-fat. *J Bone Miner Res*. (2004) 19:830–40. doi: 10.1359/JBMR.040115

26. Xu D, di Wang K, Yang J. Triglyceride can predict the discordance between QCT and DXA screening for BMD in old female patients. *Dis Markers*. (2020) 2020:1–5. doi: 10.1155/2020/8898888

27. Xie R, Huang X, Zhang Y, Liu Q, Liu M. High low-density lipoprotein cholesterol levels are associated with osteoporosis among adults 20–59 years of age. *Int J Gen Med*. (2022) 15:2261–70. doi: 10.2147/IJGM.S353531

28. Yang Y, Liu G, Zhang Y, Xu G, Yi X, Liang J, et al. Association between bone mineral density, bone turnover markers, and serum cholesterol levels in type 2 diabetes. *Front Endocrinol (Lausanne)*. (2018) 9:646. doi: 10.3389/fendo.2018.00646

29. Trimpou P, Oden A, Simonsson T, Wilhelmsen L, Landin-Wilhelmsen K. High serum total cholesterol is a long-term cause of osteoporotic fracture. *Osteoporos Int*. (2011) 22:1615–20. doi: 10.1007/s00198-010-1367-2

30. During A, Penel G, Hardouin P. Understanding the local actions of lipids in bone physiology. *Prog Lipid Res*. (2015) 59:126–46. doi: 10.1016/j.plipres.2015.06.002

31. Dogan A, Nakipoglu-Yuzer GF, Yildizgoren MT, Ozgirgin N. Is age or the body mass index (BMI) more determinant of the bone mineral density (BMD) in geriatric women and men? *Arch Gerontol Geriatr*. (2010) 51:338–41. doi: 10.1016/j.archger.2010.01.015

32. Ma M, Feng Z, Liu X, Jia G, Geng B, Xia Y. The saturation effect of body mass index on bone mineral density for people over 50 years old: a cross-sectional study of the US population. *Front Nutr*. (2021) 8:763677. doi: 10.3389/fnut.2021.763677

33. Jia L, Cheng M. Correlation analysis between risk factors, BMD and serum osteocalcin, CatheK, PINP, beta-crosslaps, TRAP, lipid metabolism and BMI in 128 patients with postmenopausal osteoporotic fractures. *Eur Rev Med Pharmacol Sci*. (2022) 26:7955–9. doi: 10.26355/eurrev_202211_30147

34. Auslander A, Liang MTC, Gavin J, Jo E, Rocha-Rangel J, Lin JH, et al. Association between body mass index, bone bending strength, and BMD in young sedentary women. *Osteoporos Int*. (2022) 33:673–83. doi: 10.1007/s00198-021-06201-0

35. Cauley JA. Estrogen and bone health in men and women. *Steroids*. (2015) 99:11–5. doi: 10.1016/j.steroids.2014.12.010

36. Wu L, Xu J. Relationship between Cardiometabolic index and insulin resistance in patients with type 2 diabetes. *Diab Metab Syndr Obes*. (2024) 17:305–15. doi: 10.2147/DMSO.S449374

37. Yannas D, Sansone A, Jannini EA. The canary in the coal mine. Comment on "association between cardiometabolic index and erectile dysfunction among US adults: a cross-sectional analysis of the National Health and nutrition examination survey 2001–2004". *Int J Impot Res*. (2024) 36:452–3. doi: 10.1038/s41443-024-00847-0

38. Gu D, Lu Y, Xu B, Tang X. Sex-specific contribution of Cardiometabolic index in predicting metabolic dysfunction-associated fatty liver disease: insights from a general population. *Diab Metab Synd Obesity*. (2023) 16:3871–83. doi: 10.2147/DMSO.S437413

39. Kubihal S, Gupta Y, Goyal A, Kalaivani M, Tandon N. Bone microarchitecture, bone mineral density and bone turnover in association with glycemia and insulin action in women with prior gestational diabetes. *Clin Endocrinol*. (2022) 96:531–8. doi: 10.1111/cen.14641

40. Su Y, Ding N, Zhou Y, Yang G, Chai X. The relationship between uric acid and total femur bone mineral density in hypertensive and non-hypertensive populations. *Front Endocrinol*. (2022) 13:1022031. doi: 10.3389/fendo.2022.1022031

41. Walsh JS, Vilaca T. Obesity, type 2 diabetes and bone in adults. *Calcif Tissue Int*. (2017) 100:528–35. doi: 10.1007/s00223-016-0229-0

42. Cao JJ. Effects of obesity on bone metabolism. *J Orthop Surg Res*. (2011) 6:30–7. doi: 10.1186/1749-799X-6-30

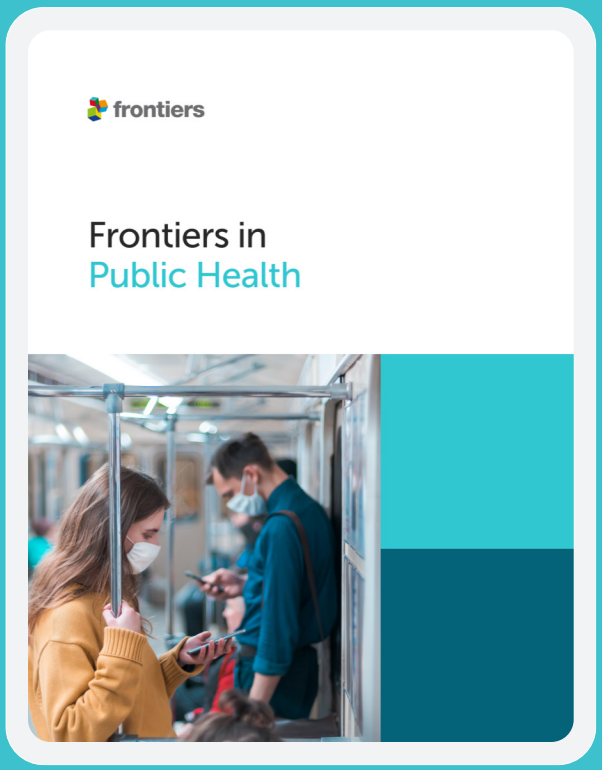
Frontiers in Public Health

Explores and addresses today's fast-moving healthcare challenges

One of the most cited journals in its field, which promotes discussion around inter-sectoral public health challenges spanning health promotion to climate change, transportation, environmental change and even species diversity.

Discover the latest Research Topics

See more →



Frontiers

Avenue du Tribunal-Fédéral 34
1005 Lausanne, Switzerland
frontiersin.org

Contact us

+41 (0)21 510 17 00
frontiersin.org/about/contact