Research Topics

Physical activity as a natural cure for non-communicable diseases

Edited by
Bojan Masanovic, Stevo Popovic, Selcuk Akpinar, Szabolcs Halasi and Dušan Stupar

Published in
Frontiers in Public Health
Frontiers in Pediatrics

ISSN 1664-8714
ISBN 978-2-8325-2699-6
DOI 10.3389/978-2-8325-2699-6

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

Physical activity as a natural cure for non-communicable diseases

Topic editors
Bojan Masanovic — University of Montenegro, Montenegro
Stevo Popovic — University of Montenegro, Montenegro
Selcuk Akpinar — Nevşehir Hacı Bektaş Veli University, Türkiye
Szabolcs Halasi — University of Novi Sad, Serbia
Dušan Stupar — Novi Sad, Serbia

Citation
Masanovic, B., Popovic, S., Akpinar, S., Halasi, S., Stupar, D., eds. (2023). *Physical activity as a natural cure for non-communicable diseases*.
Lausanne: Frontiers Media SA. doi: 10.3389/978-2-8325-2699-6

Table of contents

05 Editorial: Physical activity as a natural cure for non-communicable diseases
Bojan Masanovic, Selcuk Akpinar, Szabolcs Halasi, Dušan Stupar and Stevo Popovic

08 Physical Activity Reduces the Effect of High Body Mass Index on Kidney Stones in Diabetes Participants From the 2007–2018 NHANES Cycles: A Cross-Sectional Study
Weipu Mao, Lei Zhang, Si Sun, Jianping Wu, Xiangyu Zou, Guangyuan Zhang and Ming Chen

18 Functional Training Focused on Motor Development Enhances Gross Motor, Physical Fitness, and Sensory Integration in 5–6-Year-Old Healthy Chinese Children
Tao Fu, Diruo Zhang, Wei Wang, Hui Geng, Yao Lv, Ruiheng Shen and Te Bu

26 Effect of mass sports activity on prosocial behavior: A sequential mediation model of flow trait and subjective wellbeing
Xiyan Duan, Xiaohua Wang, Xiaogang Li, Shichen Li, Yiping Zhong and Te Bu

34 Effect of physical activity combined with extra ciliary-muscle training on visual acuity of children aged 10–11
Rongbin Yin, Jianrong Xu, Hongyun Wang, Sheng Zhou, Meng Zhang and Geng Cai

44 The role of school physical education on adolescents' fitness levels during the pandemic period from COVID-19: An observational study of the Italian scientific high school—section sport and physical activity
Antonino Patti, Valerio Giustino, Flavia Figlioli, Matteo Miceli, Martina Barca, Patrik Drid, Antonio Palma and Antonino Bianco

52 Association between physical activity dimensions and the risk of hypertension among middle and older adults: A cross-sectional study in China
Linlin Zhou, Wei Feng, Na Xiang, Yue Cheng, Xudong Ya, Mingxia Wang, Xingqi Wang and Yujia Liu

62 Joint association of smoking and physical activity with mortality in elderly hypertensive patients: A Chinese population-based cohort study in 2007–2018
Yating Yang, Huilin Xu, Xiaoqin Liu, Jiong Li, Zeyan Liew, Xing Liu, Chen Huang, Jingjing Zhu, Jinling Zhang, Linli Chen, Yuantao Hao, Guoyou Qin and Yongfu Yu

74 Physical exercise and cognitive training interventions to improve cognition in hemodialysis patients: A systematic review
Špela Bogataj, Katja Kurnik Mesarič, Maja Pajek, Tanja Petrušič and Jernej Pajek

85 **Association between sedentary behavior, physical activity, and cardiovascular disease-related outcomes in adults—A meta-analysis and systematic review**
Zhi-de Liang, Meng Zhang, Chuan-zhi Wang, Yang Yuan and Jing-hong Liang

100 **Non-exercise activity thermogenesis in the workplace: The office is on fire**
Alex Rizzato, Giuseppe Marcolin and Antonio Paoli

frontiers | Frontiers in Public Health

TYPE Editorial
PUBLISHED 31 May 2023
DOI 10.3389/fpubh.2023.1209569

Check for updates

OPEN ACCESS

EDITED AND REVIEWED BY
Michelle Plusquin,
University of Hasselt, Belgium

*CORRESPONDENCE
Bojan Masanovic
✉ bojanma@ucg.ac.me

RECEIVED 20 April 2023
ACCEPTED 12 May 2023
PUBLISHED 31 May 2023

CITATION
Masanovic B, Akpinar S, Halasi S, Stupar D and Popovic S (2023) Editorial: Physical activity as a natural cure for non-communicable diseases. *Front. Public Health* 11:1209569.
doi: 10.3389/fpubh.2023.1209569

Editorial: Physical activity as a natural cure for non-communicable diseases

Bojan Masanovic[1,2]*, Selcuk Akpinar[3], Szabolcs Halasi[4], Dušan Stupar[5] and Stevo Popovic[1,2]

[1]Faculty for Sport and Physical Education, University of Montenegro, Niksic, Montenegro, [2]Western Balkan Sport Innovation Lab, Podgorica, Montenegro, [3]Faculty of Sports Science, Nevşehir Haci Bektaş Veli University, Nevşehir, Türkiye, [4]Hungarian Language Teacher Training Faculty, University of Novi Sad, Subotica, Serbia, [5]Faculty of Sport and Psychology, Educons University, TIMS, Novi Sad, Serbia

KEYWORDS

exercise, healthy lifestyle, children, adults, older adult, chronic diseases

Editorial on the Research Topic
Physical activity as a natural cure for non-communicable diseases

1. Introduction

Despite the numerous epidemiological studies demonstrating the health benefits of physical activity and the increased risk of chronic diseases associated with physical inactivity, a significant portion of the global population remains physically inactive (1–4). The modern era of industrialization and communication has resulted in a lifestyle shift and reduced physical activity across all age groups (5, 6). Physical activity and physical fitness are recognized determinants of health, and thus the negative health consequences resulting from physical inactivity are not surprising (7). The global burden of non-communicable diseases (NCDs), responsible for over 40 million deaths annually (8), is alarming, particularly in individuals aged 30–69 years (15 million deaths per year). This highlights the need to focus on the significant social issue of physical inactivity as part of the United Nations 2030 agenda. Given the negative trends of modern lifestyles, it is essential to develop strategies to promote physical activity behavior and understand the genetic, physiological, environmental, and behavioral factors related to major NCDs. Consequently, the objective of this Research Topic is to further develop knowledge on the effects of physical (in)activity on major NCDs and improve our understanding of the factors involved. In conclusion, physical inactivity is a significant public health issue that requires urgent attention. The development of effective strategies to promote physical activity and reduce the incidence of NCDs is essential. A deeper understanding of the underlying mechanisms and risk factors involved in NCDs will enable the identification of new therapeutic and preventative approaches and contribute to the development of effective public health strategies.

2. Contribution to the field

The aim of this Research Topic is to gather and disseminate new knowledge pertaining to the impact of physical (in) activity on major non-communicable diseases across all age groups, ranging from childhood to old age. The 10 studies that have emerged as a result of this Research Topic, comprising six cross-sectional studies, one case-control study, and three review articles, offer readers a unique opportunity to expand their knowledge in this field. The findings presented in these studies are expected to advance our understanding of the relationship between physical activity and non-communicable diseases, thus contributing to the development of effective strategies to prevent and manage these diseases. By focusing on a range of age groups, these studies provide a comprehensive view of the impact of physical activity on health outcomes across the lifespan, offering valuable insights into the potential benefits of physical activity promotion programs for individuals of all ages.

The majority of the studies conducted in this Research Topic primarily focused on adults. However, to establish a comprehensive understanding of the impact of physical (in)activity on non-communicable diseases, it is crucial to also investigate its effects on the youngest population, i.e., children. This Research Topic included three studies that examined the effects of physical activity on children aged 5–17 years. These studies, consisting of two cross-sectional studies and one case-control study, evaluated the benefits of physical activity on gross motor skills, physical fitness, sensory integration, kinetic visual acuity, uncorrected distance visual acuity, and strength performance. The first study by Fu et al. investigated the effects of functional training, lasting 12 weeks, on children's gross motor skills, physical fitness, and sensory integration. The results of this study showed a significant improvement in all three areas, highlighting the benefits of functional training for children's physical development. The second study by Yin et al. examined the effects of physical activity combined with extra ciliary-muscle training, lasting 16 weeks, on children's kinetic visual acuity and uncorrected distance visual acuity. The results showed that the combination of physical activity and extra ciliary-muscle training improved both visual acuity measures, indicating the potential benefits of this intervention for children's vision. The third study by Patti et al. assessed the effects of physical exercise continuity during the COVID-19 pandemic on strength performance in children. The results indicated that consistent physical exercise during the pandemic period resulted in higher strength performance in both the Handgrip test and the Countermovement Jump test. Overall, these studies provide important insights into the benefits of physical activity for children's physical development, particularly in the areas of gross motor skills, physical fitness, sensory integration, vision, and strength performance.

The following five studies investigated the effect of physical activity on a sample of adults aged 18–60 years. The first three studies, which were cross-sectional in design, examined the impact of physical activity on various health outcomes, all concluding that physical activity has a positive effect. One study found that physical activity could reduce the incidence of kidney stones in diabetes patients with a high body mass index (BMI), despite high BMI being a risk factor for kidney stones (Mao et al.). Another study reported that greater participation in mass sports increased the likelihood of prosocial behavior (Duan et al.), while a third study found that increased physical activity could prevent hypertension (Zhou et al.). The remaining two studies, which were review articles, aimed to determine the potential of physical activity in suppressing the negative effects of sedentary behavior on cardiovascular disease and obesity epidemics (Liang et al.; Rizzato et al.). The results of these studies suggest that physical activity can reduce the risk of cardiovascular disease and improve indicators associated with it. Furthermore, alternative workstations, such as standing or walking workstations, seated pedals, and gymnastic balls, may be useful in combating the obesity epidemic.

An additional study in this Research Topic focused on both adults and older adult individuals. It was a systematic review study that examined a clinical population with participants ranging from 48 to 75 years of age. The study concluded that physical exercise interventions may improve, or at least not worsen, cognitive performance in patients undergoing hemodialysis (Bogataj et al.).

The last study was a cross-sectional study that examined individuals in the older adult age group (65–85 years). The study aimed to investigate the combined impact of smoking and physical activity on mortality rates in older adult patients diagnosed with hypertension. The study's results suggest that the combination of smoking and physical inactivity may have a synergistic effect on the risk of premature death, emphasizing the critical need to enhance behavioral factors and advocate for a comprehensive healthy lifestyle in older adult patients with hypertension (Yang et al.).

3. Conclusion

This particular Research Topic contains 10 articles that support well-established evidence regarding the positive effects of regular physical activity on health outcomes (9). In addition, the Research Topic provides specific recommendations in the form of prepared physical exercise programs, which can be found in the published articles. These programs have undergone verification and can be implemented, either in full or in part, by practitioners to prevent, treat, or alleviate certain health conditions. Moreover, there is a high likelihood that these programs will lead to a predicted transformation or output state. It is highly probable that the information and practical suggestions presented in this Research Topic will inspire researchers to develop even better solutions to combat Non-communicable Diseases.

Author contributions

BM and SA drafted the Editorial. SP, SH, and DS revised and approved the final version. All authors contributed to the article and approved the submitted version.

Acknowledgments

The authors gratefully acknowledges the assistance of Frontiers in Public Health Journal Specialists.

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. Sember V, Jurak G, Kovac M, Morrison SA, Starc G. Children's physical activity, academic performance, and cognitive functioning: A systematic review and meta-analysis. *Front Public Health.* (2020) 8:307. doi: 10.3389/fpubh.2020.00307

2. Masanovic B, Gardasevic J, Marques A, Peralta M, Demetriou Y, Sturm DJ, et al. Trends in physical fitness among school-aged children and adolescents: A systematic review. *Front Pediatr.* (2020) 8:627529. doi: 10.3389/fped.2020.627529

3. Liu W, Dostdar-Rozbahani A, Tadayon-Zadehm F, Akbarpour-Benim M, Pourkianim M, Sadat-Razavim F, et al. Insufficient level of physical activity and its effect on health costs in low- and middle-income countries. *Front Public Health.* (2022) 10:937196. doi: 10.3389/fpubh.2022.937196

4. Renninger D, Sturm DJ, Marques A, Peralta M, Popovic S, Gardasevic J, et al. Physical activity and body-mass-index: Do family, friends and teachers restrain the risk for physical inactivity in adolescents? *Sustainability.* (2021) 13:6992. doi: 10.3390/su13136992

5. Kohl HW 3rd, Craig CL, Lambert EV, Inoue S, Alkandari JR, Leetongin G, et al. The pandemic of physical inactivity: Global action for public health. *Lancet.* (2012) 380:294–305. doi: 10.1016/S0140-6736(12)60898-8

6. Masanovic B, Popovic S, Jarani J, Matic RM. Editorial: Physical activity and lifestyle sustainability: From childhood to old age. *Front Public Health.* (2023) 10:1097451. doi: 10.3389/fpubh.2022.1097451

7. NCD Risk Factor Collaboration (NCD-RisC). Heterogeneous contributions of change in population distribution of body mass index to change in obesity and underweight. *eLife* (2021) 10:e60060. doi: 10.7554/eLife.60060

8. World Health Organization. *Noncommunicable Diseases.* (2021). Retrieved from: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases

9. Budreviciute A, Damiati S, Sabir DK, Onder K, Schuller-Goetzburg P, Plakys G, et al. Management and prevention strategies for non-communicable diseases (NCDs) and their risk factors. *Front Public Health.* (2020) 8:574111. doi: 10.3389/fpubh.2020.574111

frontiers | Frontiers in Public Health

ORIGINAL RESEARCH
published: 01 July 2022
doi: 10.3389/fpubh.2022.936552

Check for updates

Physical Activity Reduces the Effect of High Body Mass Index on Kidney Stones in Diabetes Participants From the 2007–2018 NHANES Cycles: A Cross-Sectional Study

Weipu Mao[1,2†], *Lei Zhang*[2†], *Si Sun*[2†], *Jianping Wu*[2], *Xiangyu Zou*[3*], *Guangyuan Zhang*[2*] *and Ming Chen*[2*]

[1] People's Hospital of Putuo District, Shanghai, China, [2] Affiliated Zhongda Hospital of Southeast University, Nanjing, China, [3] School of Basic Medical Sciences, Weifang Medical University, Weifang, China

OPEN ACCESS

Edited by:
Stevo Popovic,
University of Montenegro, Montenegro

Reviewed by:
Radenko M. Matic,
University of Novi Sad, Serbia
Seyed Morteza Tayebi,
Allameh Tabataba'i University, Iran

***Correspondence:**
Xiangyu Zou
zouxiangyudy@126.com
Guangyuan Zhang
zgy0879@qq.com
Ming Chen
mingchenseu@126.com

† These authors have contributed equally to this work

Specialty section:
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

Received: 05 May 2022
Accepted: 09 June 2022
Published: 01 July 2022

Citation:
Mao W, Zhang L, Sun S, Wu J, Zou X, Zhang G and Chen M (2022) Physical Activity Reduces the Effect of High Body Mass Index on Kidney Stones in Diabetes Participants From the 2007–2018 NHANES Cycles: A Cross-Sectional Study. Front. Public Health 10:936552. doi: 10.3389/fpubh.2022.936552

Background: Body mass index (BMI) is a vital risk factor for kidney stones, but physical activity may reduce the incidence of kidney stones. However, it remains unknown whether physical activity reduces the effect of high BMI on kidney stones in diabetes participants.

Methods: We included clinical information from 4,008 adult participants with diabetes from the National Health and Nutrition Examination Survey (NHANES) database from 2007 to 2018. Univariate and multivariate logistic regression analyses were used to analyze the relationship between BMI and kidney stones, as well as the risk of BMI and kidney stones in different physical activity subgroups.

Results: A total of 4,008 diabetic participants were included in this study, of whom 652 (16.3%) self-reported a history of kidney stones. Logistic regression analysis showed a positive association between BMI and kidney stones. After adjusting for other confounders, the adjusted ORs for the risk of kidney stones was 1.514 (95% CI, 1.134–2.022, $p = 0.005$) for participants with BMI $\geq$30 kg/m^2 among all participants; the risk of kidney stones was elevated (OR = 1.572, 95% CI, 1.134–2.022, $p = 0.005$) in group without physical activity, and a reduced risk (OR = 1.421, 95% CI, 0.847–2.382, $p = 0.183$) in the group with physical activity. Furthermore, similar results were found in most subgroups.

Conclusion: Our study suggests that high BMI is a risk factor for diabetes kidney stone participants and that physical activity may moderate this relationship to some extent.

Keywords: kidney stones, body mass index, physical activity, diabetes, NHANES database

BACKGROUND

Kidney stones are stones in the junction of renal calyces, renal pelvis or pelvic ureter and are one of the most common urological diseases, accounting for 40–50% of all urinary stone diseases (1, 2). Hematuria and back pain are the main clinical manifestations, which can cause urological infection, urinary tract obstruction and even uremia (3, 4). Kidney stones are a complex disease caused by environmental, dietary and genetic factors, with an incidence of over 6–12% and a 5-year recurrence rate of up to 50%, seriously affecting human health (5).

There are many risk factors for kidney stones, such as metabolic, dietary, pharmacological and environmental (6, 7). Metabolic syndrome is a group of clinical symptoms of metabolic disorders characterized by abdominal obesity, hyperglycemia, hypertension, high triglycerides, and abnormal HDL cholesterol (8). Related studies have found that the development of kidney stones is closely related to lifestyle-related diseases such as hyperglycemia, obesity, hypertension and dyslipidemia components of the metabolic syndrome, and that the metabolic syndrome and its components can significantly increase the prevalence of kidney stones (9, 10).

Diabetes is a common metabolic disease, and previous studies have shown a positive association between diabetes and kidney stone risk (11). Taylor et al. (12) found that diabetic patients are more likely to develop kidney stones than the general population. Domingos et al. (13) found a higher prevalence of diabetes in patients with kidney stones compared to normal subjects through a survey analysis of 23,349 individuals. Patients with diabetic kidney stones have a worse prognosis and poorer quality of life than patients with general kidney stones (14).

Obesity is a common disease worldwide and is often defined by body mass index (BMI). One study found a correlation between the incidence of kidney stones and human BMI, with both overweight (BMI 25.0–29.9 kg/m^2) and obesity (BMI $\geq$30 kg/m^2) increasing the risk of kidney stones to some extent (15). Obesity is not only associated with the formation of kidney stones but also with their recurrence. Lee et al. (16) analyzed more than 700 patients with primary kidney stones and found that the proportion of stone recurrence within 5 years was significantly higher in patients with BMI $\geq$30 kg/m2 than in those with BMI <25 kg/m2 (42 vs. 14.9%, $p = 0.0012$), and multiple logistic regression analysis showed obesity was the only predictor of stone recurrence.

A healthy lifestyle can improve quality of life and reduce the incidence of disease, and physical activity is an integral aspect of this (17). However, studies on the relationship between physical activity and kidney stones are relatively few and the results are inconsistent. Feng et al. (18) found that physical activity was inversely associated with the prevalence of kidney stones through a survey of 8,931 US participants, and that physical activity reduced the incidence of kidney stones. In contrast, in a large prospective cohort, no independent association between physical activity and kidney stones was found (19). The specific relationship between physical activity levels and kidney stones is not known.

Since most of the current study population is general kidney stone patients, fewer studies have been conducted on diabetes kidney stone patients. In addition, since both BMI and physical activity may have an effect on kidney stones, it is unclear whether they have a combined effect in modulating diabetes kidney stones. In this study, we used data from the National Health and Nutrition Examination Survey (NHANES) database to explore the relationship between BMI and patients with diabetes kidney stones and to provide insight into whether physical activity may reduce the risk of kidney stones caused by high BMI.

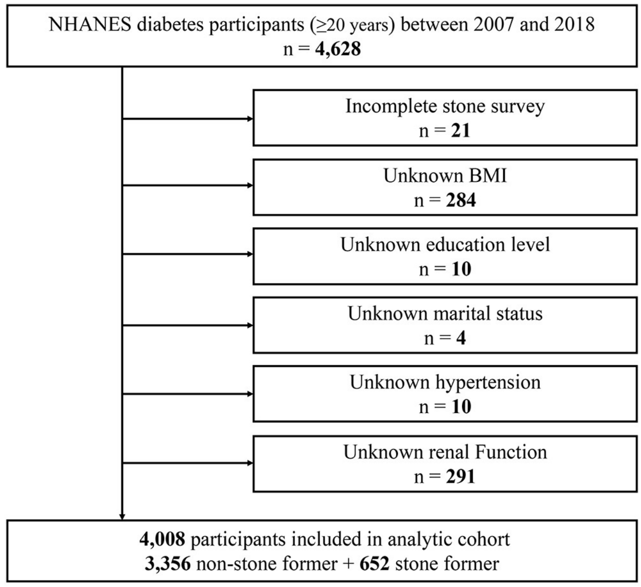

FIGURE 1 | Schematic overview for patient identification.

MATERIALS AND METHODS

Data Sources and Preparation

The NHANES database is a cross-sectional survey conducted by the National Center for Health Statistics (NCHS) to assess the health and nutritional status of adults and children in the U.S. The NHANES database includes demographic information, socioeconomic information, dietary status, health-related issues, and medical health-related physical examinations and laboratory tests (20). The NHANES database is a publicly available database that the database has published data files from the survey online on a 2-year cycle since 1999.

The current study included publicly available data from NHANES for six cycles between 2007 and 2018. We first identified 4,628 adult participants with diabetes and subsequently developed the following exclusion criteria: a) incomplete stone survey ($n = 21$); b) unknown BMI ($n = 284$); c) unknown education level ($n = 10$); d) unknown marital status ($n = 4$); e) unknown hypertension status ($n = 10$); f) unknown renal function indicators ($n = 291$). A total of 4,008 study subjects were eventually enrolled in this study (**Figure 1**).

Study Variables and Other Variables

Kidney stones were determined based on the KIQ026 question from the Kidney Conditions - Urology survey in the questionnaire data. Questions on kidney stones was asked in the home, by trained interviewers, using the Computer-Assisted Personal Interview (CAPI) system (21). In the questionnaire, participants were asked by a trained professional, "Have you ever had a kidney stone" and if the participant answered "Yes," they were considered to have a history of kidney stones.

In addition, some other variables such as gender (female and male), age (<60 years and ≥60 years), race (Non-Hispanic white, Non-Hispanic black, Mexican American, other Hispanic, and other race), education level (less than high school, high school or equivalent, and college or above), marital status (married and unmarried), BMI (<25.0 kg/m^2 25.0–29.9 kg/m^2 and ≥30.0 kg/m^2), hypertension (yes and no), smoking status (never, former and current), physical activities status (yes and no), and blood urea nitrogen, creatinine, uric acid, and estimated glomerular filtration rate (eGFR) were also included in this study. BMI was calculated by the formula: weight(kg)/(height(m^2)*height(m^2)). Physical activity was determined according to "Physical Activity" in the questionnaire data. Hypertension and diabetes were diagnosed by

TABLE 1 | Baseline characteristics of diabetes participants between 2007 and 2018.

Characteristic	Total No. (%)	None-stone formers No. (%)	Stone formers No. (%)	P-value
Total patients	4,008	3,356 (83.7)	652 (16.3)	
Gender				<0.001
Male	2,081 (51.9)	1,684 (50.2)	397 (60.9)	
Female	1,927 (48.1)	1,672 (49.8)	255 (39.1)	
Age				0.027
<60 years	1,487 (37.1)	1,270 (37.8)	217 (33.3)	
≥60 years	2,521 (62.9)	2,086 (62.2)	435 (66.7)	
Race				<0.001
Non-Hispanic white	1,382 (34.5)	1,072 (31.9)	310 (47.5)	
Non-Hispanic black	1,021 (25.5)	924 (27.5)	97 (14.9)	
Mexican American	711 (17.7)	607 (18.1)	104 (16.0)	
Other Hispanic	433 (10.8)	361 (10.8)	72 (11.0)	
Other	461 (11.5)	392 (11.7)	69 (10.6)	
Education level				0.448
Less than high school	1,393 (34.8)	1,179 (35.1)	214 (32.8)	
High school or equivalent	890 (22.2)	746 (22.2)	144 (22.1)	
College or above	1,725 (43.0)	1,431 (42.6)	294 (45.1)	
Marital status				0.007
Married	2223 (55.5)	1830 (54.5)	393 (60.3)	
Unmarried	1785 (44.5)	1526 (45.5)	259 (39.7)	
BMI (kg/m^2)				0.017
<25.0	536 (13.4)	464 (13.8)	72 (11.0)	
25.0–29.9	1,154 (28.8)	983 (29.3)	171 (26.2)	
≥30.0	2,318 (57.8)	1,909 (56.9)	409 (62.7)	
Hypertension				0.544
Yes	2800 (69.9)	2338 (69.7)	462 (70.9)	
No	1208 (30.1)	1018 (30.3)	190 (29.1)	
Smoking status				0.099
Never	2,004 (50.0)	1,699 (50.6)	305 (46.8)	
Former	1,380 (34.4)	1,132 (33.7)	248 (38.0)	
Current	624 (15.6)	525 (15.6)	99 (15.2)	
Physical activities				0.160
No	2,671 (66.6)	2,221 (66.2)	450 (69.0)	
Yes	1,337 (33.4)	1,135 (33.8)	202 (31.0)	
Blood urea nitrogen (mg/dL)	17.13, 8.82	16.93, 8.60	18.17, 9.78	0.001
Creatinine (mg/dL)	1.05, 0.77	1.03, 0.73	1.11, 0.98	0.024
Uric acid (mg/dL)	5.74, 1.60	5.73, 1.58	5.80, 1.68	0.363
eGFR [mL/(min·1.73 m^2)]	80.64, 26.26	81.21, 26.39	77.69, 25.40	0.002

For categorical variables, P-values were analyzed by chi-square tests. For continuous variables, the t-test was used.
BMI, body mass index; eGFR, estimated glomerular filtration rate.

a physician or other health professional. The eGFR was calculated by the following Equation (4):

$$\begin{aligned} eGFR &= 141 \times min(Scr/\alpha, 1)^{\beta} \times max(Scr/\alpha, 1)^{-1.209} \times 0.993^{age} \\ &\quad \times \gamma \times 1.159(ifblack). \\ Male: &\quad \alpha = 0.9, \beta = -0.411, \gamma = 1, \\ Female: &\quad \alpha = 0.7, \beta = -0.329, \gamma = 1.018. \end{aligned}$$

Statistical Analysis

Continuous data were presented as mean ± standard deviation (SD) and categorical data were described as number (n) and percentage (%). T-tests were used to assess continuous variables and chi-square tests were used to assess categorical demographic differences. In processing the data, weights were analyzed for the data in different cycles. Logistic regression models and dose-response curves with restricted cubic spline (RCS) were used to assess the association between BMI and kidney stones in different physical activity groups, and results are presented as adjusted odds ratios (aORs) and 95% confidence intervals (CIs). We constructed four models for the logistic regression analysis. Model 1 was univariate analysis. In model 2, we adjusted for gender, age, and race because demographic factors were associated with physical activity. Subsequently, we further

TABLE 2 | Baseline characteristics of diabetes participants between 2007 and 2018 based on physical activity status.

Characteristic	Total No. (%)	No physical activity No. (%)	Physical activity No. (%)	P-value
Total patients	4,008	2,671 (66.6)	1,337 (33.4)	
Gender				<0.001
Male	2,081 (51.9)	1,311 (49.1)	770 (57.6)	
Female	1,927 (48.1)	1,360 (50.9)	567 (42.4)	
Age				<0.001
<60 years	1,487 (37.1)	904 (33.8)	583 (43.6)	
≥60 years	2,521 (62.9)	1,767 (66.2)	754 (56.4)	
Race				<0.001
Non-Hispanic white	1,382 (34.5)	951 (35.6)	431 (32.2)	
Non-Hispanic black	1,021 (25.5)	651 (24.4)	370 (27.7)	
Mexican American	711 (17.7)	495 (18.5)	216 (16.2)	
Other Hispanic	433 (10.8)	309 (11.6)	124 (9.3)	
Other	461 (11.5)	265 (9.9)	196 (14.7)	
Education level				<0.001
Less than high school	1,393 (34.8)	1,099 (41.1)	294 (22.0)	
High school or equivalent	890 (22.2)	616 (23.1)	274 (20.5)	
College or above	1,725 (43.0)	956 (35.8)	769 (57.5)	
Marital status				0.214
Married	2,223 (55.5)	1,463 (54.8)	760 (56.8)	
Unmarried	1,785 (44.5)	1,208 (45.2)	577 (43.2)	
BMI (kg/m^2)				0.010
<25.0	536 (13.4)	347 (13.0)	189 (14.1)	
25.0-29.9	1,154 (28.8)	735 (27.5)	419 (31.3)	
≥30.0	2,318 (57.8)	1,589 (59.5)	729 (54.5)	
Hypertension				<0.001
Yes	2,800 (69.9)	1,926 (72.1)	874 (65.4)	
No	1208 (30.1)	745 (27.9)	463 (34.6)	
Smoking status				<0.001
Never	2,004 (50.0)	1,284 (48.1)	720 (53.9)	
Former	1,380 (34.4)	928 (34.7)	452 (33.8)	
Current	624 (15.6)	459 (17.2)	165 (15.6)	
Blood urea nitrogen (mg/dL)	17.13, 8.82	17.59, 9.46	16.22, 7.29	<0.001
Creatinine (mg/dL)	1.05, 0.77	1.07, 0.80	1.00, 0.72	0.010
Uric acid (mg/dL)	5.74, 1.60	5.76, 1.65	5.70, 1.50	0.260
eGFR [mL/(min·1.73 m^2)]	80.64, 26.26	78.52, 26.74	84.86, 24.75	<0.001

For categorical variables, P-values were analyzed by chi-square tests. For continuous variables, the t-test was used.
BMI, body mass index; eGFR, estimated glomerular filtration rate.

TABLE 3 | Logistic regression analyzed the relationship between BMI and the presence of kidney stone in different physical activity groups.

BMI	Model 1		Model 2		Model 3		Model 4	
	aOR (95% CI)	P	aOR (95% CI)	P	aOR (95% CI)	P	aOR (95% CI)	P
All participants		0.017		0.001		0.003		0.001
<25.0 kg/m^2	Reference		Reference		Reference		Reference	
25.0–30.0 kg/m^2	1.121 (0.833–1.508)	0.490	1.090 (0.806–1.474)	0.577	1.081 (0.798–1.464)	0.614	1.111 (0.820–1.507)	0.497
≥30.0 kg/m^2	1.381 (1.054–1.809)	0.019	1.483 (1.119–1.963)	0.006	1.457 (1.096–1.938)	0.010	1.514 (1.134–2.022)	0.005
No physical activity		0.015		0.004		0.009		0.004
<25.0 kg/m^2	Reference		Reference		Reference		Reference	
25.0–30.0 kg/m^2	1.099 (0.760-1.590)	0.615	1.078–(0.741–1.568)	0.696	1.072 (0.735–1.562)	0.718	1.104 (0.756–1.612)	0.608
≥30.0 kg/m^2	1.455 (1.044–2.029)	0.027	1.531 (1.087–2.157)	0.015	1.491 (1.053–2.111)	0.025	1.572 (1.103–2.240)	0.012
Physical activity		0.711		0.315		0.372		0.342
<25.0 kg/m^2	Reference		Reference		Reference		Reference	
25.0–30.0 kg/m^2	1.161 (0.705–1.912)	0.558	1.116 (0.669–1.860)	0.675	1.112 (0.663–1.864)	0.688	1.176 (0.697–1.983)	0.544
≥30.0 kg/m^2	1.216 (0.763–1.938)	0.411	1.379 (0.841–2.259)	0.202	1.361 (0.819–2.261)	0.234	1.421 (0.847–2.382)	0.183

Adjusted covariates: model 1: univariate analysis; model 2: gender, age and race; model 3: model 1 plus education level, marital status, hypertension and smoking status; model 4: model 3 plus blood urea nitrogen, creatinine, uric acid and eGFR.
PA, physical activities; BMI, body mass index; eGFR, estimated glomerular filtration rate; CI, confidence interval; aOR, adjusted odds ratio.

adjusted for variables related to participants' living conditions, such as education, marital status, hypertension, and smoking status in model 3. Finally, we included renal function-related indicators (blood urea nitrogen, creatinine, uric acid and eGFR) in model 4. R software (version 3.5.3) and SPSS software (version 24.0) were applied in the present study, and *P*-values calculated at <0.05 were considered statistically significant.

RESULTS

Table 1 demonstrates the clinicopathological characteristics of all participants. A total of 4,008 diabetes participants were enrolled in the study between 2007 and 2018, of whom 652 (16.3%) self-reported a history of kidney stones and 3,356 (83.7%) had no history of kidney stones. Chi-square test revealed significant differences between stone formers and non-stone formers groups on the variables of gender, age, race, marital status and BMI. The proportion of stone formers who were male, ≥60 years, Non-Hispanic white, married, and BMI ≥30.0 kg/m^2 were higher in stone formers than in non-stone formers groups. Stone formers group had higher blood urea nitrogen and creatinine levels and lower eGFR compared to non-stone formers. In addition, among the total participants, 2,671 (66.6%) did not engage in physical activity and 1,337 (33.4%) did not engage in physical activity, with a slightly higher proportion of no physical activity in the stone formers group ($p = 0.160$).

We also studied the clinicopathological characteristics of the total population according to physical activity (**Table 2**). The results showed significant differences between the physical activity and no physical activity groups in the variables of gender, age, race, education, BMI, hypertension, smoking status, blood urea nitrogen, creatinine and eGFR. The proportion of <60 years, college or above, BMI <30 kg/m^2, no hypertension, and never smoking was significantly higher in the physical activity group than in the no physical activity group. In addition, participants in the physical activity group had lower levels of blood urea nitrogen, creatinine and higher levels of eGFR compared to the no physical activity group.

Participants were divided into three groups according to BMI criteria: BMI <25 kg/m^2, BMI 25.0–29.9 kg/m^2 and BMI ≥30 kg/m^2 groups. Among all diabetes participants, univariate logistic regression analysis showed that the risk of kidney stones was 12.1% higher (95% CI, 0.833–1.508, $p = 0.490$) in the BMI 25.0–29.9 kg/m^2 group and 38.1% higher (95% CI, 1.054–1.809, $p = 0.019$) in the BMI ≥30 kg/m^2 group compared with the BMI <25 kg/m^2 group. After adjusting for all other variables, BMI ≥30 kg/m^2 remained an independent risk factor for kidney stones, with a risk of 1.514 (95% CI, 1.134–2.022, $p = 0.005$) in the BMI ≥30 kg/m2 group compared to the BMI <25 kg/m2 group (**Table 3**).

In addition, we evaluated the effect of physical activity on the relationship between BMI and kidney stones. We found a positive association between BMI and kidney stones in all participants ($p = 0.017$), with a prevalence of kidney stones in the three BMI groups being 13.4, 14.8, and 17.6%, respectively, and the highest prevalence of kidney stones in the BMI ≥30 kg/m^2 group (**Figure 2**). However, in the no physical activity group, the prevalence of kidney stones increased to 18.6% in the BMI ≥30 kg/m^2 group ($p = 0.017$) and decreased to 15.6% in the BMI ≥30 kg/m^2 group with physical activity ($p = 0.711$). Moreover, dose-response curves showed a correlation between BMI and kidney stones in all participants ($p = 0.036$) and no physical activity group ($p = 0.011$), while no correlation in the physical activity group ($p = 0.640$) (**Figure 3**).

Table 3 shows the relationship between BMI and kidney stones in different physical activity groups. We found that BMI was an independent risk factor for kidney stones in the no physical activity group, with a risk of 1.572 (95% CI, 1.103–2.240, $p = 0.012$) for kidney stones in the BMI ≥30 kg/m^2 group

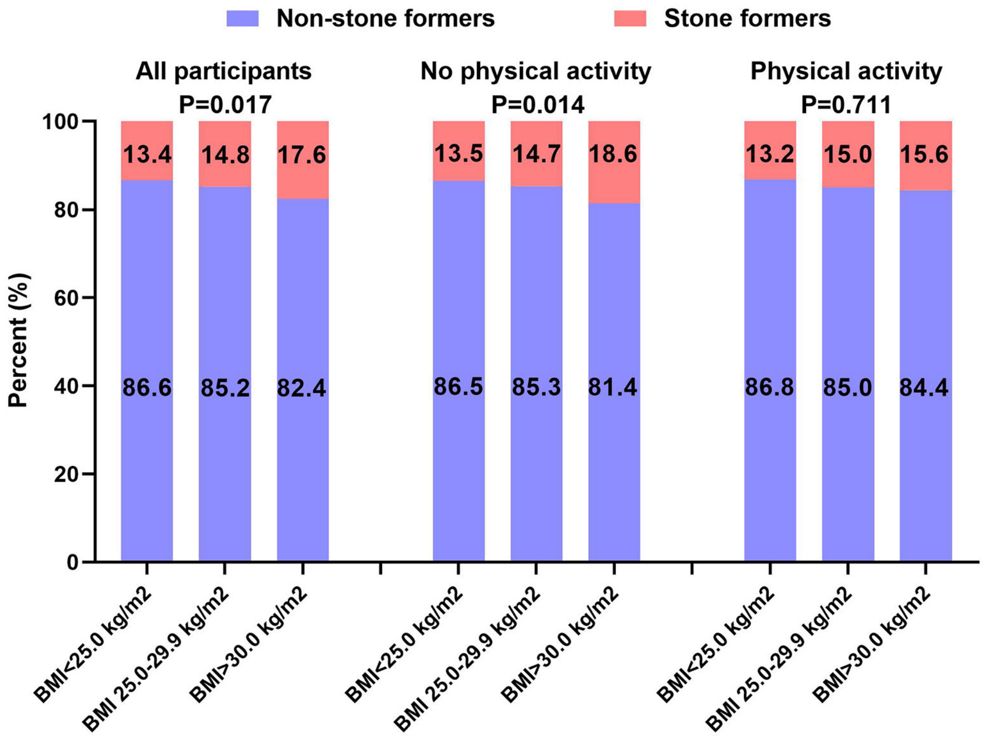

FIGURE 2 | Prevalence of kidney stones in different BMI groups among different physical activity groups.

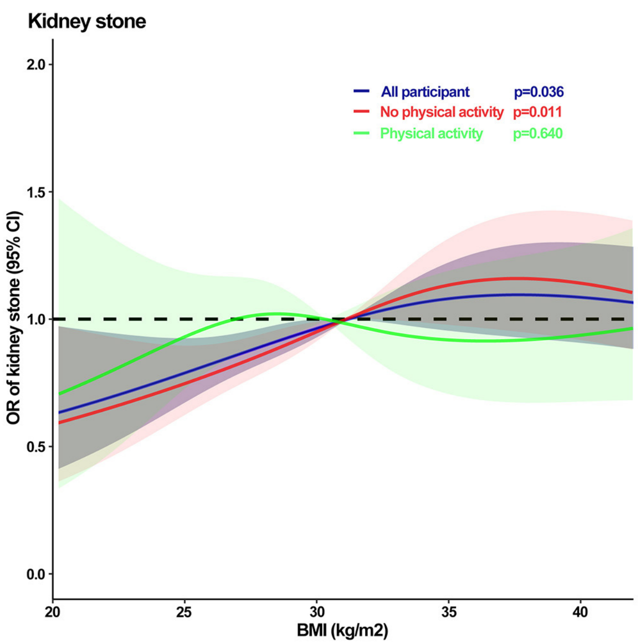

FIGURE 3 | The dose–response analysis of kidney stones with BMI by physical activity type. OR, Odds ratio; CI, Confidence interval.

compared to the BMI <25 kg/m^2 group. In contrast, in the physical activity group, BMI was not an independent risk factor for kidney stones ($p = 0.342$), and the risk of kidney stones in the BMI ≥30 kg/m^2 group was 1.421 compared to the BMI <25 kg/m^2 group ($p = 0.183$, no statistically significant). In addition, the risk of kidney stones in the BMI ≥30 kg/m2 group was also found to be lower in the physical activity group than in the no physical activity group in most subgroup analyses (**Table 4**).

DISCUSSION

In the current study, we explored the relationship between physical activity, BMI and kidney stones using clinical data from the NHANES database of participants with diabetes kidney stones during 2007–2018. We first investigated the relationship between BMI and kidney stones: multivariate logistic regression revealed that the risk of kidney stones increased with increasing BMI and that BMI was an independent risk factor for kidney stones. Subsequently, we explored the effect of physical activity and found that physical activity reduced the effect of high BMI on kidney stones in participants with diabetes. We demonstrated for the first time that physical activity exerts a beneficial effect on diabetes kidney stone participants at high BMI. This result may provide new insights into the impact of reducing BMI on kidney stones and provide new ways to prevent kidney stones.

Kidney stones are one of the most frequent and common diseases in urology, with complex causes and high recurrence rates. With the in-depth research on the etiology of kidney stones, the role of metabolic syndrome in the pathogenesis of

TABLE 4 | Subgroup analyses between BMI and the presence of kidney stone in NHANES 2007–2018.

Subgroups	BMI (kg/m^2) [aOR (95% CI)]			*P*
	<25.0	25.0–29.9	≥30.0	
Gender				
Male				
All patients	1.000	1.216 (0.834–1.774)	1.493 (1.030–2.163)	0.068
No physical activity	1.000	1.271 (0.779–2.073)	1.661 (1.032–2.673)	0.066
Physical activity	1.000	1.258 (0.681–2.323)	1.383 (0.743–2.574)	0.591
Female				
All patients	1.000	0.919 (0.540–1.561)	1.477 (0.922–2.365)	0.019
No physical activity	1.000	0.889 (0.481–1.643)	1.490 (0.867–2.562)	0.034
Physical activity	1.000	0.996 (0.336–2.951)	1.472 (0.542–3.998)	0.504
Age				
<60 years				
All patients	1.000	0.921 (0.513–1.652)	1.434 (0.847–2.427)	0.060
No physical activity	1.000	1.147 (0.434–3.033)	1.971 (0.792–4.901)	0.143
Physical activity	1.000	0.827 (0.392–1.748)	1.209 (0.624–2.342)	0.342
≥60 years				
All patients	1.000	1.192 (0.831–1.708)	1.517 (1.069–2.151)	0.028
No physical activity	1.000	1.213 (0.779–1.889)	1.692 (1.109–2.581)	0.014
Physical activity	1.000	1.248 (0.655–2.378)	1.241 (0.643–2.399)	0.780
Race				
Non-Hispanic White				
All patients	1.000	0.775 (0.484–1.240)	1.166 (0.757–1.796)	0.044
No physical activity	1.000	0.736 (0.416–1.302)	1.221 (0.727–2.050)	0.045
Physical activity	1.000	0.906 (0.376–2.181)	1.213 (0.527–2.793)	0.593
Non-Hispanic Black				
All patients	1.000	1.368 (0.544–3.440)	2.251 (0.980–5.170)	0.059
No physical activity	1.000	3.572 (0.763–16.728)	6.401 (1.492–27.454)	0.017
Physical activity	1.000	0.649 (0.163–2.573)	0.880 (0.257–3.011)	0.789
Others				
All patients	1.000	1.435 (0.908–2.266)	1.633 (1.034–2.577)	0.109
No physical activity	1.000	1.817 (0.816–4.044)	1.840 (0.802–4.221)	0.303
Physical activity	1.000	1.276 (0.722–2.257)	1.414 (0.808–2.474)	0.474
Education				
Less than high school				
All patients	1.000	1.061 (0.637–1.767)	1.572 (0.975–2.535)	0.041
No physical activity	1.000	1.106 (0.621–1.969)	1.647 (0.965–2.813)	0.056
Physical activity	1.000	0.771 (0.244–2.430)	1.127 (0.360–3.524)	0.706
High school or equivalent				
All patients	1.000	0.908 (0.492–1.677)	1.092 (0.607–1.967)	0.695
No physical activity	1.000	0.725 (0.337–1.560)	1.090 (0.532–2.234)	0.320
Physical activity	1.000	1.186 (0.396–3.550)	0.906 (0.299–2.746)	0.782
College or above				
All patients	1.000	1.297 (0.792–2.124)	1.728 (1.078–2.769)	0.036
No physical activity	1.000	1.496 (0.747–2.995)	1.976 (1.022–3.819)	0.093
Physical activity	1.000	1.346 (0.642–2.820)	1.934 (0.939–3.983)	0.132
Marital status				
Married				
All patients	1.000	1.095 (0.736–1.630)	1.446 (0.980–2.134)	0.052
No physical activity	1.000	1.234 (0.737–2.066)	1.683 (1.021–2.773)	0.051
Physical activity	1.000	0.960 (0.506–1.821)	1.171 (0.615–2.232)	0.686

(Continued)

TABLE 4 | Continued

Subgroups	BMI (kg/m²) [aOR (95% CI)]			*P*
	<25.0	25.0–29.9	≥30.0	
Unmarried				
All patients	1.000	1.139 (0.703–1.846)	1.652 (1.062–2.571)	0.020
No physical activity	1.000	1.863 (0.702–4.944)	2.224 (0.858–5.763)	0.258
Physical activity	1.000	0.979 (0.554–1.730)	1.508 (0.906–2.513)	0.058
Hypertension				
Yes				
All patients	1.000	0.951 (0.648–1.394)	1.308 (0.917–1.865)	0.028
No physical activity	1.000	1.029 (0.515–2.057)	1.315 (0.681–2.537)	0.493
Physical activity	1.000	0.916 (0.575–1.460)	1.282 (0.834–1.972)	0.073
No				
All patients	1.000	1.395 (0.838–2.322)	1.900 (1.147–3.146)	0.032
No physical activity	1.000	1.561 (0.807–3.022)	2.370 (1.254–4.478)	0.019
Physical activity	1.000	1.202 (0.527–2.743)	1.404 (0.590–3.343)	0.735
Smoking status				
Never				
All patients	1.000	1.137 (0.717–1.804)	1.709 (1.102–2.651)	0.007
No physical activity	1.000	1.208 (0.674–2.164)	1.728 (0.997–2.996)	0.056
Physical activity	1.000	1.117 (0.516–2.417)	1.804 (0.853–3.814)	0.112
Former				
All patients	1.000	1.023 (0.620–1.689)	1.244 (0.771–2.006)	0.432
No physical activity	1.000	0.922 (0.503–1.692)	1.241 (0.704–2.186)	0.329
Physical activity	1.000	1.469 (0.564–3.827)	1.247 (0.474–3.282)	0.708
Current				
All patients	1.000	1.148 (0.555–2.376)	1.540 (0.776–3.055)	0.363
No physical activity	1.000	1.262 (0.491–3.241)	2.120 (0.88–5.057)	0.132
Physical activity	1.000	0.725 (0.208–2.531)	0.704 (0.193–2.573)	0.850

Adjusted covariates: gender, age, race, education levels, marital status, hypertension, smoking status, blood urea nitrogen, creatinine, uric acid, and estimated glomerular filtration rate (eGFR). aOR, adjusted odds ratio; CI, confidence interval.

kidney stones has also received increasing attention. Related studies have found that the occurrence of kidney stones is closely related to lifestyle-related diseases such as obesity, hypertension, dyslipidemia and hyperglycemia (22, 23). It has been reported in the literature that 48.7% of kidney stone patients have metabolic syndrome and the prevalence of kidney stones in patients with metabolic syndrome is 7.5 to 8.8% (24, 25).

Diabetes mellitus is a common metabolic disease, and some studies have found that there may be a common pathophysiological mechanism between the formation of kidney stones and the development of diabetes mellitus (26). The interconnection between diabetes mellitus and kidney stones is mainly due to the effect of insulin resistance on urinary pH and and the transport of ammonia and calcium in the kidney, which affects the production and transport of ammonium, causing a decrease in urinary pH (27, 28). The decrease in dissociation of uric acid in an acidic environment leads to increased precipitation and the formation of stones. Domingos et al. (13) found a higher prevalence of diabetes mellitus in patients with kidney stones compared to normal population (OR = 1.475, 95% CI, 1.283–1.696, $p < 0.001$) through questionnaire analysis of 23,349 individuals. The prevalence of kidney stones in diabetes patients was found to be 16.3% in this study, which is much higher than the prevalence of kidney stones in the normal population (9.3%) (4). This result is consistent with the findings of Taylor et al. (12) who found that diabetes patients are more likely to develop kidney stones than the general population.

Obesity and kidney stones obesity is a public health problem in many countries. Recent studies have shown that 34.8 to 41% of patients with kidney stones are also obese and that obesity is associated with an increased prevalence and recurrence of kidney stones (29, 30). Meanwhile, BMI is a common indicator used to define obesity. It has been found that BMI is positively correlated with calcium, oxalate, citrate, uric acid, sodium, potassium and phosphate in the urine, and the pH of the urine decreases with increasing BMI (31). Furthermore, even in patients with BMI <30 kg/m^2, the higher the BMI, the greater the chance of kidney stones. Similar results were found in our study, where the risk of kidney stones was 1.514 (95% CI, 1.134–2.022, $p = 0.005$) for participants in the BMI ≥30.0 kg/m^2 group compared to BMI <25.0 kg/m^2 group.

Expect for metabolic factors, lifestyle such as smoking, alcohol consumption and physical activity have an important impact on the prevalence of kidney stones. However, there are relatively few studies on the relationship between physical activity and kidney stones, and the results are inconsistent (32). Three groups of studies reported a statistically significant protective effect of physical activity on kidney stones (19, 33, 34), and conversely, three studies reported no effect of physical activity on the risk of kidney stones (18, 29, 35). Sorensen et al. (29) found that physical activity reduced the risk of stones in women by 16%-31%. In addition, Zhuo et al. (35) found that duration of physical activity was an independent risk factor for kidney stones (OR = 0.840; 95% CI, 0.808–0.973) in a survey of 1,519 people in Southern China.

To our knowledge, the present study is the first to explore the association between physical activity, BMI, and diabetes kidney stones. Combined with interaction analysis, we found an interaction between physical activity and BMI on the occurrence of kidney stones. The results of the interaction between BMI and kidney stones indicated that the risk of kidney stones increased with increasing BMI but decreased with participation in physical activity. We also found that the proportion of <60 years, college or above, BMI <30 kg/m2, no hypertension, and never smoking was significantly higher in the physical activity group than in the no physical activity group. In addition, participants in the physical activity group had lower levels of blood urea nitrogen, creatinine and higher levels of eGFR compared to the no physical activity group. The above results suggest that physical activity can bring beneficial physiological aspects. In addition, some studies have found that physical activity can reduce the incidence of diabetes, hypertension, and obesity, which may explain why physical activity can reduce the incidence of kidney stones (36–38).

Although we have found significant modifications of the effect of physical activity on the effect of high BMI on participants with diabetes kidney stones, the study still has some limitations. First, this is a cross-sectional study and causality is difficult to verify. In addition, the NHANES database is a retrospective study with its inherent limitations. Finally, we did not provide the type of kidney stones and physical activity may have different outcomes for different stone types.

CONCLUSION

Our study found that high BMI was a risk factor for participants with diabetes kidney stones and that physical activity moderated this relationship to some extent, with physical activity leading to beneficial physiological aspects. This result may provide new insights into the impact of reducing BMI on kidney stones and offer new approaches to kidney stone prevention.

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

This study was carried out in accordance with the recommendations of NHANES Committee with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the NHANES Committee. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

WM, XZ, GZ, and MC designed the research. WM, LZ, SS, and JW performed the research and analyzed results. WM, LZ, and SS wrote the paper. WM, LZ, XZ, GZ, and MC edited the manuscript and provided critical comments. All authors read and approved the final manuscript.

FUNDING

This work was supported by National Natural Science Foundation of China (81900618 and 82170703), Tai-Shan Scholar Program from Shandong Province (tsqn202103116), Jiangsu Provincial Key Research and Development Program (BE2019751), Innovative Team of Jiangsu Provincial (2017ZXKJQW07), and the National Key Research and Development Program of China (SQ2017YFSF090096).

REFERENCES

1. Singh P, Harris PC, Sas DJ, Lieske JC. The genetics of kidney stone disease and nephrocalcinosis. *Nat Rev Nephrol.* (2022) 18:224–40. doi: 10.1038/s41581-021-00513-4
2. Zisman AL, Coe FL, Cohen AJ, Riedinger CB, Worcester EM. Racial differences in risk factors for kidney stone formation. *Clin J Am Soc Nephrol.* (2020) 15:1166–73. doi: 10.2215/CJN.12671019
3. Denburg MR, Koepsell K, Lee JJ, Gerber J, Bittinger K, Tasian GE. Perturbations of the gut microbiome and metabolome in children with calcium oxalate kidney stone disease. *J Am Soc Nephrol.* (2020) 31:1358–69. doi: 10.1681/ASN.2019101131
4. Mao W, Hu Q, Chen S, Chen Y, Luo M, Zhang Z, et al. Polyfluoroalkyl chemicals and the risk of kidney stones in US adults: a population-based study. *Ecotoxicol Environ Saf.* (2021) 208:111497. doi: 10.1016/j.ecoenv.2020.111497
5. Islam AK, Holt S, Reisch J, Nwariaku F, Antonelli J, Maalouf NM. What predicts recurrent kidney stone after parathyroidectomy in patients with primary hyperparathyroidism? *J Am Coll Surg.* (2020) 231:74–82. doi: 10.1016/j.jamcollsurg.2020.04.015
6. Bartoletti R, Cai T, Mondaini N, Melone F, Travaglini F, Carini M, et al. Epidemiology and risk factors in urolithiasis. *Urol Int.* (2007) 79:3–7. doi: 10.1159/000104434
7. Ferraro PM, Bargagli M, Trinchieri A, Gambaro G. Risk of kidney stones: influence of dietary factors, dietary patterns, and vegetarian-vegan diets. *Nutrients.* (2020) 12:779. doi: 10.3390/nu12030779

8. Hoffman EL, VonWald T, Hansen K. The metabolic syndrome. *S D Med.* (2015) 24–8.
9. Sakhaee K. Recent advances in the pathophysiology of nephrolithiasis. *Kidney Int.* (2009) 75:585–95. doi: 10.1038/ki.2008.626
10. Uribarri J. Chronic kidney disease and kidney stones. *Curr Opin Nephrol Hypertens.* (2020) 29:237–42. doi: 10.1097/MNH.0000000000000582
11. Weinberg AE, Patel CJ, Chertow GM, Leppert JT. Diabetic severity and risk of kidney stone disease. *Eur Urol.* (2014) 65:242–7. doi: 10.1016/j.eururo.2013.03.026
12. Taylor EN, Stampfer MJ, Curhan GC. Diabetes mellitus and the risk of nephrolithiasis. *Kidney Int.* (2005) 68:1230–5. doi: 10.1111/j.1523-1755.2005.00516.x
13. Domingos F, Serra A. Nephrolithiasis is associated with an increased prevalence of cardiovascular disease. *Nephrol Dial Transplant.* (2011) 26:864–8. doi: 10.1093/ndt/gfq501
14. Eisner BH, Porten SP, Bechis SK, Stoller ML. Diabetic kidney stone formers excrete more oxalate and have lower urine pH than nondiabetic stone formers. *J Urol.* (2010) 183:2244–8. doi: 10.1016/j.juro.2010.02.007
15. Aune D, Mahamat-Saleh Y, Norat T, Riboli E. Body fatness, diabetes, physical activity and risk of kidney stones: a systematic review and meta-analysis of cohort studies. *Eur J Epidemiol.* (2018) 33:1033–47. doi: 10.1007/s10654-018-0426-4
16. Lee SC, Kim YJ, Kim TH, Yun SJ, Lee NK, Kim WJ. Impact of obesity in patients with urolithiasis and its prognostic usefulness in stone recurrence. *J Urol.* (2008) 179:570–4. doi: 10.1016/j.juro.2007.09.040
17. Lagestad P, Mikalsen H, Ingulfsvann LS, Lyngstad I, Sandvik C. Associations of participation in organized sport and self-organized physical activity in relation to physical activity level among adolescents. *Front Public Health.* (2019) 7:129. doi: 10.3389/fpubh.2019.00129
18. Feng X, Wu W, Zhao F, Xu F, Han D, Guo X, et al. Association between physical activity and kidney stones based on dose-response analyses using restricted cubic splines. *Eur J Public Health.* (2020) 30:1206–11. doi: 10.1093/eurpub/ckaa162
19. Ferraro PM, Curhan GC, Sorensen MD, Gambaro G, Taylor EN. Physical activity, energy intake and the risk of incident kidney stones. *J Urol.* (2015) 193:864–8. doi: 10.1016/j.juro.2014.09.010
20. Mao W, Wu J, Zhang Z, Xu Z, Xu B, Chen M. Neutrophil-lymphocyte ratio acts as a novel diagnostic biomarker for kidney stone prevalence and number of stones passed. *Transl Androl Urol.* (2021) 10:77–86. doi: 10.21037/tau-20-890
21. Sandvik H, Seim A, Vanvik A, Hunskaar S, A. severity index for epidemiological surveys of female urinary incontinence: comparison with 48-h pad-weighing tests. *Neurourol Urodyn.* (2000) doi: 10.1002/(SICI)1520-6777(2000)19:2<137::AID-NAU4>3.0.CO;2-G
22. Obligado SH, Goldfarb DS. The association of nephrolithiasis with hypertension and obesity: a review. *Am J Hypertens.* (2008) 21:257–64. doi: 10.1038/ajh.2007.62
23. Wong Y, Cook P, Roderick P, Somani BK. Metabolic syndrome and kidney stone disease: a systematic review of literature. *J Endourol.* (2016) 30:246–53. doi: 10.1089/end.2015.0567
24. Cho ST, Jung SI, Myung SC, Kim TH. Correlation of metabolic syndrome with urinary stone composition. *Int J Urol.* (2013) 20:208–13. doi: 10.1111/j.1442-2042.2012.03131.x
25. Tasca A. Metabolic syndrome and bariatric surgery in stone disease etiology. *Curr Opin Urol.* (2011) 21:129–33. doi: 10.1097/MOU.0b013e3283435cbc
26. Chung SD, Chen YK, Lin HC. Increased risk of diabetes in patients with urinary calculi: a 5-year followup study. *J Urol.* (2011) 186:1888–93. doi: 10.1016/j.juro.2011.07.011
27. Daudon M, Traxer O, Conort P, Lacour B, Jungers P. Type 2 diabetes increases the risk for uric acid stones. *J Am Soc Nephrol.* (2006) 17:2026–33. doi: 10.1681/ASN.2006030262
28. Zimmerer T, Weiss C, Hammes HP, Braun C, Hesse A, Alken P, et al. Evaluation of urolithiasis: a link between stone formation and diabetes mellitus? *Urol Int.* (2009) 82:350–5. doi: 10.1159/000209371
29. Sorensen MD, Chi T, Shara NM, Wang H, Hsi RS, Orchard T, et al. Activity, energy intake, obesity, and the risk of incident kidney stones in postmenopausal women: a report from the Women's health initiative. *J Am Soc Nephrol.* (2014) 25:362–9. doi: 10.1681/ASN.2013050548
30. Taylor EN, Stampfer MJ, Curhan GC. Obesity, weight gain, and the risk of kidney stones. *JAMA.* (2005) 293:455–62. doi: 10.1001/jama.293.4.455
31. Taylor EN, Curhan GC. Body size and 24-hour urine composition. *Am J Kidney Dis.* (2006) 48:905–15. doi: 10.1053/j.ajkd.2006.09.004
32. Jones P, Karim Sulaiman S, Gamage KN, Tokas T, Jamnadass E, Somani BK. Do lifestyle factors including smoking, alcohol, and exercise impact your risk of developing kidney stone disease? *Outcomes of a Systematic Review J Endourol.* (2021) 35:1–7. doi: 10.1089/end.2020.0378
33. Soueidan M, Bartlett SJ, Noureldin YA, Andersen RE, Andonian S. Leisure time physical activity, smoking and risk of recent symptomatic urolithiasis: Survey of stone clinic patients. *Can Urol Assoc J.* (2015) 9:257–62. doi: 10.5489/cuaj.2879
34. Maric I, Kizivat T, Smolic M, Smolic R, Opacak-Bernardi T, Solic K, et al. Lifestyle risk factors and bone mass in recurrent stone-forming patients: a cross-sectional study in 144 subjects. *Acta Clin Croat.* (2019) 58:439–45. doi: 10.20471/acc.2019.58.03.06
35. Zhuo D, Li M, Cheng L, Zhang J, Huang H, Yao Y, et al. Study of diet and lifestyle and the risk of urolithiasis in 1,519 patients in Southern China. *Med Sci Monit.* (2019) 25:4217–24. doi: 10.12659/MSM.916703
36. Palermi S, Iacono O, Sirico F, Modestino M, Ruosi C, Spera R, et al. The complex relationship between physical activity and diabetes: an overview. *J Basic Clin Physiol Pharmacol.* (2021). doi: 10.1515/jbcpp-2021-0279
37. Sternfeld B, Gabriel KP, Jiang SF, Whitaker KM, Jacobs DR Jr, Quesenberry CP Jr, et al. Risk estimates for diabetes and hypertension with different physical activity methods. *Med Sci Sports Exerc.* (2019) 51:2498–505. doi: 10.1249/MSS.0000000000002083
38. Kong S, So WY. Association between physical activity and obesity-related factors. *Minerva Med.* (2021) 112:418–20. doi: 10.23736/S0026-4806.19.06356-0

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.

frontiers | Frontiers in Pediatrics

ORIGINAL RESEARCH
published: 11 July 2022
doi: 10.3389/fped.2022.936799

Functional Training Focused on Motor Development Enhances Gross Motor, Physical Fitness, and Sensory Integration in 5–6-Year-Old Healthy Chinese Children

Tao Fu[1*†], *Diruo Zhang*[1*†], *Wei Wang*[1], *Hui Geng*[1], *Yao Lv*[1], *Ruiheng Shen*[1] *and Te Bu*[2]

[1] *College of Health and Exercise Science, Tianjin University of Sport, Tianjin, China,* [2] *College of Physical Education, Hunan Normal University, Changsha, China*

Objective: Physical inactivity and sensory integration dysfunction are public health concerns among Chinese preschool children. The purpose of this study was to determine the efficacy of a novel functional training program focused on motor development for healthy children aged 5 to 6 years.

Methods: A total of 101 healthy children aged 5 to 6 years in Tianjin were randomly assigned to the experimental group ($N = 51$), which received 12-week functional training featuring essential motor skills, whilst the control group ($N = 50$) continued with their kindergarten-based physical education curriculum. Test of Gross Motor Development-2, national physical fitness measurement, and sensory integration were evaluated before and after the intervention. Children's height, body weight, and the corresponding pre-intervention test scores were utilized as covariates to compare the post-intervention outcomes between the groups.

Results: After the intervention, the experimental group scored considerably higher ($P < 0.01$) on the locomotor composite score, object control composite score, and overall gross motor score than the control group; the experimental group scored higher ($P < 0.05$) on the run, gallop, leap, stationary dribble, kick, striking a stationary ball, overhand throw, and underhand roll motor skill tests than the control group; the experimental group performed considerably better ($P < 0.01$) on the balance beam walking test and sit-and-reach test than the control group; and, the experimental group performed considerably better ($P < 0.01$) on the vestibular function, tactile defensiveness, and proprioception than the control group.

Conclusion: A 12-week functional training focused on motor development effectively enhanced gross motor, physical fitness, and sensory integration in 5–6-year-old healthy Chinese children.

Keywords: TGMD-2, preschool, motor skill, physical activity, vestibular function

Edited by:
Dušan Stupar,
Sports Association Super Active, Serbia

Reviewed by:
Milenko Janković,
Preschool Teacher Training College in Novi Sad, Serbia
Damjan Jakšić,
University of Novi Sad, Serbia

****Correspondence:***
Tao Fu
futaobg007@hotmail.com
Diruo Zhang
nitta0417@163.com

† These authors have contributed equally to this work

Specialty section:
This article was submitted to Children and Health, a section of the journal Frontiers in Pediatrics

Received: *05 May 2022*
Accepted: *21 June 2022*
Published: *11 July 2022*

Citation:
Fu T, Zhang D, Wang W, Geng H, Lv Y, Shen R and Bu T (2022) Functional Training Focused on Motor Development Enhances Gross Motor, Physical Fitness, and Sensory Integration in 5–6-Year-Old Healthy Chinese Children. Front. Pediatr. 10:936799. doi: 10.3389/fped.2022.936799

INTRODUCTION

The health of preschool children is critical for healthy growth throughout their lifespan (1). Numerous researches have demonstrated that motor development is closely related to individual health, cognitive ability, emotional wellbeing, and social development, and is a necessary condition for young children to thrive academically (2). Motor development can be classified into a gross motor which involves primarily large muscle groups in the trunk or limbs (e.g., running, jumping), and a fine motor which involves mostly the wrists of the arms or small muscle groups (e.g., drawing, using chopsticks). Gross motor is necessary for the development of motor skills, physical fitness, cognitive, perceptual, and emotional capabilities in early childhood (3, 4). Gross motor is not measured in terms of speed or distance traveled, but rather based on how coordinated and smooth the movement is completed (5). Five to six-years of age in children is a vital developmental stage for preschool children about to join an elementary school, as well as the optimal age for motor development (6). If children's motor skills are fully and evenly developed during this time, it could have a significant impact on their subsequent learning of motor skills in school and even as adults. Otherwise, motor development delay has been shown to be a factor in the developmental delay in children (7).

Functional training originated in rehabilitation and aims to restore the body's fundamental functioning through targeted motor activities on the affected limb. Functional training has now evolved significantly, and its emphasis on the kinetic chain exercise, balance training, and multi-joint functional movements is congruent with fundamental principles of early childhood motor skill development. Generally, researches have proven that functional training (8) or motor development training (9) has a beneficial influence on motor skills in disadvantaged children. However, their combined effect on motor skills in healthy, preschool children is missing in the literature. Given the important role of motor development in early childhood, it is critical to address this research gap.

By the time children reach the age of seven, they should have acquired acceptable levels of competency in fundamental motor skills, as they begin to participate in increasingly specialized physical activities (10). This research integrated functional training and motor development patterns in young children to construct a novel 12-week functional training program focused on motor development for preschool children. The study aimed to establish an experimental basis for promoting motor development, physical activity, and sensory integration in early childhood.

METHODS

Participants

The research was approved by the Ethics Committee of Tianjin University of Sport and the protocol adhered strictly to the Declaration of Helsinki. Criteria for inclusion include guardians' informed consent and, children were able to collaborate and engage throughout the intervention. Criteria for exclusion include: children without full participation in the intervention, including one missing visit; children who did not participate completely in the pre- and post-intervention assessments of gross motor, physical fitness, and sensory integration; children enrolled in after-school sports or physical fitness classes during the duration of the study; or, children with physical developmental disorders or a history of congenital diseases. A total of 101 eligible children aged 5 to 6 years in Tianjin were randomly assigned to the control and experimental groups. **Table 1** summarizes the demographic characteristics of the participants.

Experimental Design

This research was conducted between October and December of 2021. In October and November, the control and experimental groups were primarily engaged in outdoor activities. Due to the cold winter weather in Tianjin, both groups were primarily engaged in indoor activities in December. Outcome tests were administered 1 week before to the first intervention session and 1 day following the last session.

The control group followed a kindergarten-based physical education curriculum, with each lesson lasting 40–50 min and focusing on group games, gymnastics, and free play as the primary modes of movement. **Table 2** summarizes the three primary components of the kindergarten self-designed curriculum, which include rhythmic exercise, games, and free activities for children. In brief, the curriculum covers a limited number of motor skills, the movements are simple, and there is no discernible division of difficulty levels. This curriculum is designed to promote children's interest in physical education and fulfill the Ministry of Education's requirement for physical activity. The control group received the lesson once a week during weeks 1–8 and twice a week during weeks 9–12.

The experimental group participated in a functional training program meant to promote motor development. In constructing the functional training program, existing guidelines (11) and published protocol (5) were reviewed, as well as the developmental characteristics (12), cognitive qualities (13), Chinese-specific movement patterns of 5–6-year-old children (14). The protocol and components of the functional training program were refined by consulting with experts and teachers in preschool education. The intervention period was replaced by the same time as the kindergarten-based physical education curriculum, and each training session lasted 40–50 min. **Table 3** summarizes the main activities in the functional training program. The program is centered on motor skills and is tailored to the child's cognitive and emotional needs, with mini-games such as tennis, football (soccer), and basketball used to interest young children in training. Each training session begins with a preparation phase, including warm-up, neuromuscular activation, dynamic stretching, and core muscle activation. The main training phase has consisted of two modules. This first module is devoted to motor skill development, with an emphasis on walking, jumping, crawling, throwing, pushing, and catching. The second module focuses on physical fitness, with an emphasis on balance, agility, and endurance. Each training session concludes with a phase of motor skill consolidation and static stretching. The experimental group received a 1–4 week

TABLE 1 | Children's demographic characteristics.

	Control group			Experimental group		
	Male ($n = 26$)	**Female ($n = 24$)**	**Overall ($N = 50$)**	**Male ($n = 25$)**	**Female ($n = 26$)**	**Overall ($N = 51$)**
Height (cm)	115.7 ± 4.2	114.4 ± 4.3	115.1 ± 4.2	113.6 ± 3.0	114.9 ± 4.4	114.2 ± 3.8
Body weight (kg)	20.6 ± 4.0	20.0 ± 2.6	20.3 ± 3.4	19.2 ± 2.2	20.1 ± 2.9	19.7 ± 2.6

Data are expressed as mean ± standard deviation.

TABLE 2 | Description of the kindergarten-based physical education curriculum.

Curriculum contents	Duration	Activities
Warm-up	3–5 min	Jogging, rotational movement
Rhythmic exercise	5–10 min	Standing rhythmic exercise, or stationary drill
Games	7–10 min	Slapping ball, relay race, single leg jump, cart pushing run
Free play	10–15 min	Unstructured free activities, playground slides
Relaxation	3–5 min	Body shaking exercise
Stretching	1–3 min	Low-impact upper and lower body stretching

TABLE 3 | Description of the functional training program.

Exercise modules	Duration	Themes	Activities
Warm-up phase			
Warm-up	1–3 min	Train on the move	Children stand in a line while moving forward together
		Plane takeoff	Lateral raise of both arms and jog forward
Neuromuscular activation	1–3 min	High knees	Lift one knee to the chest and then the other
Dynamic stretching	1–3 min	Stretch in motion	Walk lunge step, bring leg up high to chest on each step
Core muscle activation	1–3 min	Tunnel pass	Crawl through a play tunnel
		Flutter kicks	Alternately raise and lower legs from floor
Main training phase			
Motor skill development	10–15 min	Walk	Obstacle curved walk, reactive direction, squat walk etc.
Physical fitness	7–10 min	Run	Chasing and fleeing run, reactive speed, join hands run etc.
		Jump	Multi-directional jump, jumping rope, straddle jump, etc.
		Mini-ball games	Kick, throw, catch, slap, dribble, tap, small-sided games
		Coordination	Skip with a hula hoop, over and under relay, group hug etc.
Cool-down phase			
Motor skill consolidation	1–3 min	Whac-A-Mole	Children are told what color the barrel is, and they touch it
		Pass the parcel	Pass around a ball while music is playing
Static stretching	1–3 min	Animal imitation	Practice various static postures

period for basic skill acquisition with one training per week, a 5–8 week period for basic skill consolidation with one training per week, and a 9–12 week period for skill strengthening with two training per week.

During the intervention period, both groups received similar types and frequencies of general education in kindergarten, including music and arts curriculum.

Instrument

Gross motor was assessed using the Chinese children's validated Test of Gross Motor Development-2 (TGMD-2) (15). TGMD-2 is composed of locomotor and object control domains. Each domain contains six skill tests, for a total of 12 fundamental movement skills. Each skill comprises 3–5 scoring criteria: performed the standard or not performed the standard, which are assigned one or zero points. Two domains' scores are added together to provide a composite score for each domain. After that, the scores for two domains can be added together to obtain an overall gross motor score.

Between 9:00 and 10:30 a.m., the same group of testers administered the physical fitness test in the kindergarten gym and playground, according to the test criteria outlined in the National Physical Fitness Measurement Standards Manual (Preschool Children Version) (16). The test battery gauges

TABLE 4 | Results of gross motor.

Domain	Test battery	Control group (*N* = 50)		Experimental group (*N* = 51)	
		Pre-intervention	**Post-intervention**	**Pre-intervention**	**Post-intervention**
Locomotor	Run	6.86 ± 1.01	6.74 ± 1.07	6.76 ± 0.99	7.16 ± 0.97‡¶
	Horizontal jump	6.72 ± 1.21	6.74 ± 1.01	6.49 ± 0.76	7.06 ± 0.79§
	Hop	8.30 ± 1.06	8.56 ± 0.99	8.18 ± 0.74	8.75 ± 0.87§
	Gallop	3.58 ± 0.91	3.96 ± 0.88‡	3.71 ± 0.83	5.29 ± 0.97§‖
	Leap	6.16 ± 0.77	6.44 ± 0.97	6.06 ± 0.88	6.96 ± 0.87§‖
	Slide	7.16 ± 0.84	7.42 ± 0.95	7.08 ± 0.87	7.57 ± 1.29‡
Locomotor composite score		38.78 ± 2.31	39.86 ± 2.39‡	38.27 ± 2.69	42.78 ± 2.11§‖
Object control	Stationary dribble	5.20 ± 1.11	5.62 ± 0.89‡	5.04 ± 0.98	6.14 ± 0.75§¶
	Kick	7.00 ± 0.78	6.08 ± 0.83§	6.51 ± 0.88†	6.86 ± 0.72‡‖
	Catch	4.98 ± 0.65	5.00 ± 0.81	4.69 ± 0.86	5.31 ± 0.88§
	Striking a stationary ball	5.04 ± 1.41	5.12 ± 0.82	5.41 ± 0.90	6.98 ± 1.03§‖
	Overhand throw	5.44 ± 0.97	5.02 ± 0.71‡	5.20 ± 1.02	6.22 ± 0.92§‖
	Underhand roll	5.40 ± 0.95	5.12 ± 0.82	5.35 ± 0.96	6.22 ± 0.76§‖
Object control composite score		33.06 ± 2.67	31.96 ± 1.96‡	32.20 ± 2.09	37.73 ± 2.32§‖
Overall gross motor score		71.84 ± 3.33	71.82 ± 3.59	70.47 ± 3.09*	80.51 ± 3.35§‖

*Data are expressed as mean ± standard deviation. Before the intervention, control group vs. experimental group: * $P < 0.05$, † $P < 0.01$; within the control/experimental group, pre-intervention vs. post-intervention: ‡ $P < 0.05$, § $P < 0.01$; after the intervention, control group vs. experimental group: ¶ $P < 0.05$, ‖ $P < 0.01$.*

TABLE 5 | Results of physical fitness.

Test battery	Control group (*N* = 50)		Experimental group (*N* = 51)	
	Pre-intervention	**Post-intervention**	**Pre-intervention**	**Post-intervention**
Standing long jump test (cm)	100.84 ± 14.27	101.64 ± 11.30	99.78 ± 8.24	103.43 ± 12.01‡
Balance beam walking test (s)	9.61 ± 1.55	9.68 ± 1.10	10.00 ± 1.74	8.98 ± 0.87§‖
Tennis throwing test (m)	4.36 ± 1.56	4.76 ± 1.76	4.05 ± 1.24	4.85 ± 1.40§
Sit-and-reach test (cm)	3.36 ± 5.64	4.32 ± 6.29	4.84 ± 6.04	7.57 ± 5.49‡‖
10-m shuttle run test (s)	8.54 ± 1.10	7.91 ± 1.06§	8.63 ± 0.93	7.89 ± 0.68§
Double-leg timed hop test (s)	6.67 ± 1.65	6.12 ± 1.07	7.11 ± 1.40	5.80 ± 0.66§

Data are expressed as mean ± standard deviation. Within the control/experimental group, pre-intervention vs. post-intervention: ‡ $P < 0.05$, § $P < 0.01$; after the intervention, control group vs. experimental group: ‖ $P < 0.01$.

TABLE 6 | Results of sensory integration.

Domain	Control group (*N* = 50)		Experimental group (*N* = 51)	
	Pre-intervention	**Post-intervention**	**Pre-intervention**	**Post-intervention**
Vestibular function	57.26 ± 8.05	58.06 ± 7.19	59.00 ± 5.95	62.92 ± 3.37§‖
Tactile defensiveness	94.60 ± 9.44	94.76 ± 9.66	94.63 ± 10.03	99.40 ± 5.69§‖
Proprioception	55.10 ± 5.32	54.80 ± 5.19	56.20 ± 4.00	57.35 ± 3.46‖
Learning ability	36.52 ± 4.67	36.40 ± 4.31	34.80 ± 6.12	37.73 ± 2.61§

Data are expressed as mean ± standard deviation. Within the control/experimental group, pre-intervention vs. post-intervention: § $P < 0.01$; after the intervention, control group vs. experimental group: ‖ $P < 0.01$.

different components of fitness, including the standing long jump test, balance beam walking test, tennis throwing test, sit-and-reach test, 10-m shuttle run test, and double-leg timed hop test. A detailed measurement procedure can be found in an independent evaluation of the test (17).

Sensory integration was evaluated using the Child Sensory Integration Scale (18), which was established based on American psychiatrist Jean Ayres's classic sensory integration theory and has been validated in Chinese children aged 3 through 11 years (19). The sensory integration test requires parental cooperation, and due to the very subjective nature of parental self-assessment, the same rehabilitation therapist must help parents in completing an online questionnaire before and after the intervention to guarantee the scale is objectively consistent. The scale consists of the following five domains: vestibular function (14 items), which evaluates gross motor; tactile defensiveness (21 items), which evaluates emotional stability and a tendency to over-defend; proprioception (12 items), which evaluates body's proprioception and balance coordination; learning ability (8 items), which evaluates learning deficits due to poor sensory integration; and, issues particular to children beyond the age of 10 (8 items), which was not assessed in the present study population. Each of the 50 items was scored using a five-point Likert scale as follows: 5 = never (the child never responds in this manner when presented with the opportunity); 4 = seldom (the child responds occasionally in this manner); 3 = occasionally (the child responds sometimes); 2 = frequently; 1 = always (the child responds in the manner noted whenever presented with the opportunity). Total scores for each domain were theoretically between 8 and 105, with higher scores indicating better performance.

Statistics

The IBM SPSS Statistics 24.0 was used for the statistical analysis. A Shapiro-Wilk test was used to confirm data normality. First, a *t*-test was used to evaluate whether there were pre-intervention test differences between the groups. Second, a *t*-test was used to evaluate the training effect within the groups. Third, an analysis of covariance was used to evaluate the training effect between the groups, using the height (except for sensory integration), body weight (except for sensory integration), and corresponding pre-intervention test scores as continuous covariates. Results for the sit-and-reach test were compared using the paired Wilcoxon test within groups, and the Mann-Whitney *U* test between groups. $P < 0.05$ was considered statistically significant.

RESULTS

Table 4 summarizes the gross motor test results. Before the intervention, the control group scored considerably higher ($P < 0.01$) on the kick test than the experimental group. There were no significant differences ($P > 0.05$) in any of the other gross motor tests between the groups before the intervention.

Within the control group, the post-intervention locomotor composite score was higher ($P < 0.05$), with a higher ($P < 0.05$) gallop test score and no significant changes ($P > 0.05$) in the scores of the other five locomotor tests; the post-intervention object control composite score was lower ($P < 0.05$), with a lower ($P < 0.05$) striking a stationary ball test score, lower ($P < 0.05$) overhand throw test score, and considerably lower ($P < 0.01$) kick test score; and, there was no change ($P > 0.05$) in the overall gross motor score.

Within the experimental group, the post-intervention locomotor composite score, object control composite score, and overall gross motor score were all considerably higher ($P < 0.01$); and, all post-intervention locomotor and object control test scores were higher ($P < 0.05$).

After the intervention, the experimental group scored considerably higher ($P < 0.01$) on the locomotor composite score, object control composite score, and overall gross motor score than the control group; the experimental group scored higher ($P < 0.05$) on the run and stationary dribble tests than the control group; and, the experimental group scored considerably higher ($P < 0.01$) on the gallop, leap, kick, striking a stationary ball, overhand throw, and underhand roll tests than the control group.

Table 5 summarizes the physical fitness test results. Before the intervention, there were no significant differences ($P > 0.05$) in any of the physical fitness tests between the groups.

Within the control group, the post-intervention 10-m shuttle run test was considerably better ($P < 0.01$). Within the experimental group, the post-intervention standing long jump test and sit-and-reach test were better ($P < 0.05$), and the post-intervention balance beam walking test, tennis throwing test, 10-m shuttle run test, and double-leg timed hop test were considerably better ($P < 0.01$).

After the intervention, the experimental group performed considerably better ($P < 0.01$) on the balance beam walking test and sit-and-reach test than the control group.

Table 6 summarizes the sensory integration test results. Before the intervention, there were no significant differences ($P > 0.05$) in any of the sensory integration domains between the groups.

Within the control group, there was no change ($P > 0.05$) in the sensory integration. Within the experimental group, the post-intervention vestibular function, tactile defensiveness, and learning ability were considerably improved ($P < 0.01$).

After the intervention, the experimental group performed considerably better ($P < 0.01$) on the vestibular function, tactile defensiveness, and proprioception than the control group.

DISCUSSION

Motor development is the process through which individuals go from unstructured, untrained movements to regular, complicated, and deliberate movements (20). At the age of five, the fundamental motor skills gradually improve, and various motor skills gradually develop at the age of six (21). Given that gross motor activities are fundamental motor skills that are developed during the early stages of children's growth, the development of gross motor skills can be prioritized. In this study, kindergarten-based physical education curriculum can only improve certain crucial gross motor and physical fitness characteristics, while having minimal effect on sensory integration. Following a 12-week functional training program focused on motor development, healthy children aged 5 to 6 years performed better in terms of gross motor, physical fitness, and sensory integration. The implication is clear that kindergartens and communities should consider physical education programs with scientific rigor, such as this functional training program, in order for preschool children to develop important motor skills in a timely and sufficient manner, which could have significant effects on their physical and cognitive development.

The kindergarten-based physical education curriculum improved children's locomotor skills but not their object control skills, and the effect on children's gross motor development is not significant. The control group performed significantly better on the pre-intervention kick test than the experimental group. The reason for this could be that the kindergarten-based physical education curriculum had already begun teaching some children football classes. Consequently, some children in both the control and experimental groups were exposed to the kicking motion, resulting in disparities in their gross motor test scores before the intervention. In terms of the higher locomotor composite score, the regular parent-child sporting games held in the kindergarten establish a hurdle race, which is similar to the gallop test in the TGMD-2. As a result, the kindergarten-based physical education curriculum repeatedly consolidates the gallop movement skill while preparing for the sporting games and practicing hurdles, which has a beneficial effect on children's locomotor skills.

The functional training program integrates fundamental movement and balance skills and motor coordination activities for gross motor development. After the 12-week intervention, the locomotor composite score, object control composite score, and overall gross motor score were all higher in the experimental group, demonstrating that the functional training program focused on motor development can help preschool children's gross motor development. Meanwhile, the functional training program incorporates group-based ball games into the workout. Ball activities are very interactive and can not only pique young children's interest, but also improve their observation, judgment, and agility (22). Additionally, Wang et al. (14) has revealed that the rate at which children develop motor skills is related to the frequency with which they play with peers in Chinese preschool children aged 3 to 6 years. Epidemiological researches have generally found a suboptimal level of physical activity in Chinese preschool children aged 3 to 6 years (23, 24). Given the association between physical activity and motor skills, it is not unexpected that Chinese preschool children without adequate physical activity have suboptimal motor development. After adjusting for covariates, Rao et al. (25) discovered that the motor skill development scores of 4-year-old children were significantly lower in 2017 than in 2013. Our findings should be insightful for researchers and practitioners when designing motor development programs for preschool children in kindergartens or communities.

Early childhood is a vital period for physical fitness development. Adequate exercise can aid in the normal development of children's various organs, and physical fitness is a critical indicator of children's health (26). If young children lack physical activity and health-related fitness, they may be more susceptible to chronic diseases such as type 2 diabetes (27) and hypertension (28). Thus, regular physical activity is critical to developing motor skills in early childhood and promoting health throughout their life cycle (29). Meanwhile, motor skill development is a significant predictor of greater levels of health-related physical fitness and physical activity behaviors in preschool children, as well as improved health outcomes (30). It has been demonstrated that the development of 3–6-year-old children's motor skills is positively correlated with their physical health (31). Longitudinal studies also have demonstrated that children's ability to acquire motor skills continues to influence their development of physical fitness and health (32). This study provided evidence that the kindergarten-based physical education curriculum can only help children improve their speed quality, implying that the curriculum cannot address all facets of children's physical fitness. This paucity of high-quality physical activity in Chinese kindergartens is consistent with previous research. For example, Hu et al. (12) evaluated the quality of outdoor play in 91 Chinese kindergartens. They reported insufficient opportunities for outdoor play and a lack of physical activity among children aged 3 to 6 years. In comparison, the functional training program focused on motor development increased all physical characteristics of preschool children, with more noticeable outcomes in balance and flexibility. The functional training program is composed of supervised motor skill activities that can help children improve their sensitivity to external stimuli, develop new conditioned reflexes, and thus foster the development of their body's flexibility and coordination. Recent epidemiological studies on the incidence of developmental coordination disorder in Chinese children found that the overall incidence was 3.4%, and suspected cases were 5.4%, among 3–5-year-old children (33); and the overall incidence was 5.5%, and suspected cases were 10.4%, among 3–10-year-old children (34). This functional training program is particularly relevant to contemporary Chinese society for the healthy development of early childhood.

Sensory integration is critical for children's capacity to learn and social development across their lifespan (35). Children with sensory integration dysfunction are more vulnerable to external influences during movement, exhibiting intense mood swings, decreased self-control, a difficulty to maintain bodily balance, and, in severe cases, aggression. It is a significant public health problem worldwide, with a prevalence of sensory integration dysfunction ranging from 36.94% (36) to 55.8% (37) in Chinese preschool children aged 3 to 6 years. In this study, the functional training program focused on motor development was more effective at improving children's sensory integration than kindergarten-based physical education curriculum. This outcome is consistent with the literature. In Chinese children aged 3 to 6 years, it has been validated that TGMD-2 had a highly significant positive correlation with children's static balance, dynamic balance, and proprioception (38). On the one hand, the greater the risk of sensory integration dysfunction, the more difficult it is to acquire motor skills (39); on the other hand, the locomotor and object control of gross motor skills are correlated with vestibular function and proprioception in sensory integration (40). Functional training is structured around better neuromuscular responses, such as 2-foot hop, which aids children's spatial orientation, improve their balance, and stimulate their vestibular and proprioceptive senses. The present results suggest that a 12-week functional training can improve children's general sensory development, and that establishing a motor development-focused program could be a successful early life educational intervention strategy.

Notably, the functional training program enhanced the learning ability within the experimental group. Motor development is favorably associated with young children's learning ability. A regression analysis of 4–5-year-old children in the Northeast of England discovered that motor skill acquisition improved the number of children who are prepared to enter elementary school and that promoting gross and fine motor skills may increase the number of children who meet entry requirements and are more likely to achieve better educational outcomes (41). This observation was similarly validated among Chinese preschool children. Recently, Chou et al. (42) showed that 4–5-year-old children enrolling in kindergartens with better physical fitness programs had better executive function, which was associated with better academic skills. Furthermore, children with better motor skills had greater executive functions and obtained more academic skills in kindergartens (42). Thus, not only does the functional training program help preschool children's physical fitness, but it may also have a beneficial effect on their long-term learning ability.

This study has two limitations. First, there are six recommended self-reported levels of exercise intensity for Chinese preschool children aged 5 to 6 years, corresponding to an average heart rate of <120, 120, 120–140, 140, 140–160, and >160 beats·min^{-1} (43). Tan et al. (44) suggested that the target heart rate for physical activity in Chinese children aged 3 to 6 years should range between 126.3 and 165.8 beats·min^{-1}. As a result, this study designed the functional training program maintaining a target heart rate of 120–160 beats·min^{-1}. During the pilot test, both the kindergarten-based physical education curriculum and the functional training program fell within this target heart rate, and there were no statistically significant differences between the two exercise intensities. Due to the impossibility of concurrently recording all heart rate responses in the research context, we cannot rule out the possibility that the exercise intensity throughout the intervention period was different at certain periods. Second, this study examined the effect of a functional training program on 5–6-year-old healthy children, restricting the capacity to generalize these findings to other age groups or children with physical developmental disorders.

In conclusion, a 12-week functional training program focused on motor development improved gross motor, physical fitness, and sensory integrity in healthy Chinese preschool children. This study provided evidence that functional training can be used to accelerate motor development in this age group and has resulted in considerable advancements in a healthy Chinese population. Based on these findings, we recommend expanding this novel functional training program to kindergartens, schools, and communities in order to promote the healthy development of preschool children.

DATA AVAILABILITY STATEMENT

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

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Tianjin University of Sport. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

TF and DZ: conceptualization, methodology, and writing—original draft preparation. DZ, WW, HG, YL, and RS: data collection. TF, DZ, WW, HG, YL, RS, and TB: writing—review and editing. TF: project administration and funding acquisition. All authors have read and agreed to the published version of the manuscript.

FUNDING

This research was funded by the Humanities and Social Science Fund of the Ministry of Education of China an empirical study on the value, characteristics and curriculum system development of early childhood sports, grant number 20YJA890004.

REFERENCES

1. Goldfield GS, Harvey A, Grattan K, Adamo KB. Physical activity promotion in the preschool years: a critical period to intervene. *Int J Environ Res Public Health.* (2012) 9:1326–42. doi: 10.3390/ijerph9041326
2. McClelland MM, Cameron CE. Developing together: the role of executive function and motor skills in children's early academic lives. *Early Child Res Q.* (2019) 46:142–51. doi: 10.1016/j.ecresq.2018.03.014
3. Emck C, Bosscher R, Beek P, Doreleijers T. Gross motor performance and self-perceived motor competence in children with emotional, behavioural, and pervasive developmental disorders: a review. *Dev Med Child Neurol.* (2009) 51:501–17. doi: 10.1111/j.1469-8749.2009.03337.x
4. Gonzalez SL, Alvarez V, Nelson EL. Do gross and fine motor skills differentially contribute to language outcomes? a systematic review. *Front Psychol.* (2019) 10:2670. doi: 10.3389/fpsyg.2019.02670
5. Lei Y, Zhou L, Wang G. Research on the design of functional movement training program based on gross motor development for pre-school children. *J Chengdu Sport Univ.* (2018) 44:122–6. doi: 10.15942/j.jcsu.2018.01.020
6. Payne VG, Isaacs LD. *Human Motor Development: A Lifespan Approach*. New York, NY: Routledge. (2017). doi: 10.4324/9781315213040
7. Gupta S, Pande A. Moving skills—a contributing factor in developmental delay. *Soft Comput Theor Appl.* (2022) 1380:33—40. doi: 10.1007/978-981-16-1740-9_4
8. Tinderholt Myrhaug H, Østensjø S, Larun L, Odgaard-Jensen J, Jahnsen R. Intensive training of motor function and functional skills among young children with cerebral palsy: a systematic review and meta-analysis. *BMC Pediatr.* (2014) 14:1–19. doi: 10.1186/s12887-014-0292-5
9. Draper CE, Achmat M, Forbes J, Lambert EV. Impact of a community-based programme for motor development on gross motor skills and cognitive function in preschool children from disadvantaged settings. *Early Child Dev Care.* (2012) 182:137–52. doi: 10.1080/03004430.2010.547250
10. Goodway JD, Ozmun JC, Gallahue DL. *Understanding Motor Development: Infants, Children, Adolescents, Adults*. Burlington, MA: Jones & Bartlett Learning (2020).
11. Curriculum Framework Task Force. *Grade-Level Outcomes for K-12 Physical Education*. Reston, VA: SHAPE America (2013).

12. Hu BY Li K, De Marco A, Chen Y. Examining the quality of outdoor play in Chinese kindergartens. *Int J Early Child.* (2015) 47:53–77. doi: 10.1007/s13158-014-0114-9
13. Fang Y, Wang J, Zhang Y, Qin J. The relationship of motor coordination, visual perception, and executive function to the development of 4–6-year-old Chinese preschoolers' visual motor integration skills. *Biomed Res Int.* (2017) 2017:6264254. doi: 10.1155/2017/6264254
14. Wang H, Chen Y, Liu J, Sun H, Gao W. A follow-up study of motor skill development and its determinants in preschool children from middle-income family. *Biomed Res Int.* (2020) 2020:6639341. doi: 10.1155/2020/6639341
15. Li B, Diao Y, Li J, Hong J, Sun J, Liu Y. Analysis and Enlightenment of American Test of Gross Motor Development. *J Chengdu Sport Univ.* (2021) 47:58–64. doi: 10.15942/j.jcsu.2021.02.010
16. General Administration of Sport of China. *The National Physical Fitness Measurement Standards Manual (Preschool Children Version)*. Beijing: People's Sports Publishing House (2003).
17. Fang H, Ho IMK. Intraday reliability, sensitivity, and minimum detectable change of national physical fitness measurement for preschool children in China. *PLoS ONE.* (2020) 15:e0242369. doi: 10.1371/journal.pone.0242369
18. Ren G, Wang Y, Gu B, Shen Y. Abstracts of major original papers preliminary report on application of child sensory integration scale. *Chin Ment Health J.* (1994) 8:145–7.
19. Yang H, Wang H. Associations of developmental coordination disorders and sensory integration disorders with family environment for motor development. *Chin J Sch Health.* (2020) 1:86–9. doi: 10.16835/j.cnki.1000-9817.2020.01.023
20. Haywood KM, Getchell N. *Life Span Motor Development*. Champaign, IL: Human kinetics (2021).
21. Bolger LE, Bolger LA, O'Neill C, Coughlan E, O'Brien W, Lacey S, et al. Global levels of fundamental motor skills in children: a systematic review. *J Sports Sci.* (2021) 39:717–53. doi: 10.1080/02640414.2020.1841405
22. Gu Y, Chen Y, Ma J, Ren Z, Li H, Kim H. The influence of a table tennis physical activity program on the gross motor development of Chinese preschoolers of different sexes. *Int J Environ Res Public Health.* (2021) 18:2627. doi: 10.3390/ijerph18052627
23. Ji M, Tang A, Zhang Y, Zou J, Zhou G, Deng J, et al. The relationship between obesity, sleep and physical activity in Chinese preschool children. *Int J Environ Res Public Health.* (2018) 15:527. doi: 10.3390/ijerph15030527
24. Lu C, Wiersma R, Shen T, Huang G, Corpeleijn E. Physical activity patterns by objective measurements in preschoolers from China. *Child Adolesc Obes.* (2019) 2:1–17. doi: 10.1080/2574254X.2019.1585178
25. Rao N, Chan SWY, Su Y, Mirpuri S, Richards B, Sun J, et al. Early motor development in china: secular trends among 4-year-olds. *Early Child Dev Care.* (2022) 1—14. doi: 10.1080/03004430.2022.2064460
26. Carson V, Lee E-Y, Hewitt L, Jennings C, Hunter S, Kuzik N, et al. Systematic review of the relationships between physical activity and health indicators in the early years (0-4 years). *BMC Public Health.* (2017) 17:854. doi: 10.1186/s12889-017-4860-0
27. Zhang J, Wang H, Wang Z, Du W, Su C, Zhang J, et al. Prevalence and stabilizing trends in overweight and obesity among children and adolescents in China, 2011-2015. *BMC Public Health.* (2018) 18:571. doi: 10.1186/s12889-018-5483-9
28. Song C, Gong W, Ding C, Yuan F, Zhang Y, Feng G, et al. Physical activity and sedentary behavior among Chinese children aged 6–17 years: a cross-sectional analysis of 2010–2012 china national nutrition and health survey. *BMC Public Health.* (2019) 19:936. doi: 10.1186/s12889-019-7259-2
29. Barnett LM, Stodden D, Cohen KE, Smith JJ, Lubans DR, Lenoir M, et al. Fundamental movement skills: an important focus. *J Teach Phys Educ.* (2016) 35:219–25. doi: 10.1123/jtpe.2014-0209
30. Gao Z, Zeng N, Pope ZC, Wang R, Yu F. Effects of exergaming on motor skill competence, perceived competence, and physical activity in preschool children. *J Sport Health Sci.* (2019) 8:106–13. doi: 10.1016/j.jshs.2018.12.001
31. Jones D, Innerd A, Giles EL, Azevedo LB. Association between fundamental motor skills and physical activity in the early years: a systematic review and meta-analysis. *J Sport Health Sci.* (2020) 9:542–52. doi: 10.1016/j.jshs.2020.03.001
32. Utesch T, Bardid F, Büsch D, Strauss B. The relationship between motor competence and physical fitness from early childhood to early adulthood: a meta-analysis. *Sports Med.* (2019) 49:541–51. doi: 10.1007/s40279-019-01068-y
33. Zhu L, Du J, Zhang H, Wei X, Wang T, Dai X, et al. Developmental coordination disorder in preschool children in Taiyuan. *Chin J Prim Med Pharm.* (2022) 29:500–3. doi: 10.3760/cma.issn1008-6706.2022.04.005
34. Liu M, Hua J, Ke L, Duan W, Du W. Analysis of developmental coordination disorder in Chinese children. *Chin J Pediatr.* (2021) 59:928–34. doi: 10.3760/cma.j.cn112140-20210331-00277
35. Kilroy E, Aziz-Zadeh L, Cermak S. Ayres theories of autism and sensory integration revisited: what contemporary neuroscience has to say. *Brain Sci.* (2019) 9:68. doi: 10.3390/brainsci9030068
36. Jia X, Zhang Q, Sun Z, Wang D, Xie M, Wang B, et al. Factors associated with sensory processing dysfunction among preschool children in Qingdao. *Chin J Sch Health.* (2016) 37:691–4. doi: 10.16835/j.cnki.1000-9817.2016.05.016
37. Yu L, Li D, Li J, Ji H, Li X, Guo H, et al. Sensory integration disorder and its related factors among preschool children in amontanic county of Hubei Province. *Chin J Child Health Care.* (2020) 28:148–51. doi: 10.11852/zgetbjzz2019-0257
38. Jiang G-P, Jiao X-B, Wu S-K, Ji Z-Q, Liu W-T, Chen X, et al. Balance, proprioception, and gross motor development of Chinese children aged 3 to 6 years. *J Mot Behav.* (2018) 50:343–52. doi: 10.1080/00222895.2017.1363694
39. Jasmin E, Couture M, McKinley P, Reid G, Fombonne E, Gisel E. Sensori-motor and daily living skills of preschool children with autism spectrum disorders. *J Autism Dev Disord.* (2009) 39:231–41. doi: 10.1007/s10803-008-0617-z
40. Mache MA, Todd TA. Gross motor skills are related to postural stability and age in children with autism spectrum disorder. *Res Autism Spectr Disord.* (2016) 23:179–87. doi: 10.1016/j.rasd.2016.01.001
41. Jones D, Innerd A, Giles EL, Azevedo LB. The association between physical activity, motor skills and school readiness in 4–5-year-old children in the Northeast of England. *Int J Environ Res Public Health.* (2021) 18:11931. doi: 10.3390/ijerph182211931
42. Chou Y, Ying Hu B, Winsler A, Wu H, Greenburg J, Kong Z. Chinese preschool children's physical fitness, motor competence, executive functioning, and receptive language, math, and science performance in kindergarten. *Child Youth Serv Rev.* (2022) 136:106397. doi: 10.1016/j.childyouth.2022.106397
43. Li N, Kang Y, Luo D. Design of the self-report scale of intensity of preschool children's activity. *Sichuan Sports Sci.* (2016) 35:26–31. doi: 10.13932/j.cnki.sctykx.2016.01.07
44. Tan S, Yu X, Zhang Y, Wang P, Zhang W. Study on lactate threshold and related heart rate in children. *J Tianjin Inst Phys Educ.* (2001) 16:15–6. doi: 10.3969/j.issn.1005-0000.2001.03.003

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.

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 01 August 2022
DOI 10.3389/fpubh.2022.960870

Effect of mass sports activity on prosocial behavior: A sequential mediation model of flow trait and subjective wellbeing

Xiyan Duan[1†], Xiaohua Wang[2†], Xiaogang Li[3], Shichen Li[1*], Yiping Zhong[3*] and Te Bu[1]

[1]College of Physical Education, Hunan Normal University, Changsha, China, [2]School of Physical Education and Health, Wenzhou University, Wenzhou, China, [3]Cognition and Human Behavior Key Laboratory of Hunan Province, Department of Psychology, School of Education Science, Hunan Normal University, Changsha, China

Check for updates

OPEN ACCESS

EDITED BY
Dušan Stupar,
Sports Association Super Active, Serbia

REVIEWED BY
Nebojsa Maksimovic,
University of Novi Sad, Serbia
Yang Zhang,
Independent Researcher, Orlando, United States

*CORRESPONDENCE
Shichen Li
shichenli90@163.com
Yiping Zhong
ypzhong@163.com

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

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 03 June 2022
ACCEPTED 11 July 2022
PUBLISHED 01 August 2022

CITATION
Duan X, Wang X, Li X, Li S, Zhong Y and Bu T (2022) Effect of mass sports activity on prosocial behavior: A sequential mediation model of flow trait and subjective wellbeing. *Front. Public Health* 10:960870. doi: 10.3389/fpubh.2022.960870

Objectives: Participation in mass sports is one of the most efficient strategies for people to attain physical and mental health in China. Prosocial behavior has a positive effect on social development. This study developed a conceptual model with mass sports activity as the independent variable, prosocial behavior as the dependent variable, and flow trait and subjective wellbeing as the mediating variables.

Methods: Participants ($N = 351$) completed an online survey. Mass sports activity, flow trait, subjective wellbeing, and prosocial behavior were measured using the physical activity rank scale-3 (PARS-3), short dispositional flow scale (SDFS), index of wellbeing (IWB), and prosocial tendencies measure (PTM), respectively. Descriptive statistics compared differences between sports population (PARS-3, $\geq$ 36) and non-sports population (PARS-3, $<$ 36). Mediation effect was analyzed using the PROCESS (Template, Model 6).

Results: Sports population scored significantly higher (all $P \leq 0.05$) on SDFS, IWB, and PTM than non-sports population. Participation in mass sports stimulated flow trait and thus improved prosocial behavior, with a mediation effect value of 0.061 (95% *CI*, 0.028–0.104), which accounted for 30.18% of the total effect. Participation in mass sports enhanced subjective wellbeing and thus improved prosocial behavior, with a mediation effect value of 0.044 (95% *CI*, 0.007–0.090), which accounted for 21.96% of the total effect. Flow trait and subjective wellbeing mediated the relationship between mass sports activity and prosocial behavior in a sequential manner, with a mediation effect value of 0.059 (95% *CI*, 0.035–0.090), which accounted for 29.23% of the total effect.

Conclusion: The preliminary results of the mediation model validated the hypothesized sequential links between mass sports activity, flow trait, subjective wellbeing, and prosocial behavior. Greater participation in mass sports increases the likelihood of prosocial behavior.

KEYWORDS

health policy, mental health, physical activity, dispositional flow, empathy, leisure

Introduction

Prosocial behavior is a crucial aspect of an individual's socialization and refers to any behavior that matches social norms and is beneficial to individuals, groups, or society (1). Prosocial behavior typically demonstrates admirable attributes such as modesty, assisting, cooperation, and sharing in interpersonal interactions (2), which is a positive habit that society promotes for development. Social learning theory argues that individuals can develop prosocial behavior through witnessing the behaviors and outcomes of others during physical activity, learning, and reinforcing the behavioral outcomes (3). Individuals establish good interpersonal relationships with their peers through learning the rules of sports and imitating the role of sports (4). In physical activity, individuals also learn to deal with the relationship between competition and cooperation in a harmonious manner, and they acquire prosocial qualities such as humility, respect, solidarity, and helping others (5). Personal behavior, according to the theory of group dynamics, is the outcome of the interaction between the intrinsic demands of the individual and the external forces of the environment (6). On the basis of this notion, empirical studies have showed that physical activity facilitates the development of prosocial behavior in adolescents (7) and adults (8). For example, Moeijes and colleagues investigated longitudinal relationships between 10 and 12-year-olds' sports participation and prosocial behavior (9). Membership in a sports club and moderate or frequent sports participation were found to be longitudinally correlated with improved prosocial behavior. Although previous research have demonstrated the positive relationship between small group-based exercise, competitive sports, and prosocial behavior, the effect and its underlying mechanisms by which leisure physical activity influences prosocial behavior remain unexplained.

The concept of fitness for all has been integral to the development of the People's Republic of China since its inception. In 2016, the Central Committee of the Chinese Communist Party and the State Council issued the Outline of the "Healthy China 2030" Plan (10), which further encourages the Chinese public to participate actively in sports and scientific fitness. Mass sports activity is a type of popular sports activity (e.g., walking, Tai Chi, badminton, and marathon) that strives to increase physical fitness, health, leisure activities, and social feelings for all members of Chinese society (11). Zhu and Han researched the effects of different sports participation on prosocial behavior and showed that leisure sports participants scored higher than competitive sports participants on measures of prosocial behavior (12). Specifically, leadership, social facilitation, and group cohesion were found as three specific prosocial traits where leisure sports participants outperformed competitive sports participants. In light of this study, mass sports activity may not only be useful for promoting population physical health, but also for fostering social solidarity, which is absent from the current research context in China.

Flow theory is a field of research within positive psychology. Flow is the best condition of experience in which an individual is concentrating deeply on an activity, completely immersed, totally engaged, highly enjoyable, and experiencing favorable feelings during the action (13). State and trait of flow are distinct components of flow experience (14). Flow trait reflects the frequency with which individuals experience flow throughout an event, whereas flow state captures the sensation of flow during an event. Flow in sports and its applications to prosocial behavior are a relatively young area of research. A few studies on elite athletes suggest that physical activity may positively influence the flow experience (15, 16). Li and Zhang (17) found that easy-to-learn tennis instruction can motivate novices to learn and increase the likelihood of students experiencing the state of flow. Therefore, simple and popular mass sports activity may be beneficial at attracting the interest of individuals and stimulating their flow experience. Meanwhile, flow experience has been recommended to be more conducive to promoting prosocial behavior (18). Traditionally, research on flow in the context of sports has focused on its effects on the performance outcomes of elite athletes, whereas its social psychological benefits associated with leisure physical activity have received less attention. There is a need for rigorous study to determine whether the flow experience induced by mass sports activity could be a precursor to prosocial behavior.

Subjective wellbeing is a holistic evaluation of an individual's quality of life and is a comprehensive psychological indicator of personal and social quality (19). In healthy persons, there is a beneficial correlation between physical activity and subjective wellbeing (20). Chatzisarantis and Hagger found that leisure sports participants experienced greater psychological wellbeing than competitive sports participants (21). In recent years, the central and municipal governments of China have increased expenditure on sports infrastructure in an effort to foster mass sports activity (22). As a result, the nationwide urban fitness trails has expanded from 823,500 in 2019 (23) to 929,300 in 2021 (24). The provision of urban sports facilities at the grassroots level could promote not only leisure sports activity and physical health (25), but also social engagement (26). A case study conducted in Zhuhai City, China showed that community sports parks have a positive influence on the subjective wellbeing of community members (27). Participation in mass sports could therefore improve mental health in contemporary Chinese society. Meanwhile, subjective wellbeing reinforces prosocial behavior (28). The relationship between subjective wellbeing and prosocial behavior among Chinese population has been proven to be both positive and bidirectional (29, 30). Despite this, the influence of leisure physical activity on positive psychology is an understudied topic. Particularly in light of the growing acknowledgment of antisocial behavior as a serious public health concern, positive psychology-based research on mass sports activity is warranted.

Therefore, this study analyzed the mechanism underlying the influence of mass sports activity on prosocial behavior and developed a theoretical foundation for increasing mental health through physical health. It was hypothesized that mass sports activity has a positive direct relationship with prosocial behavior, and that flow trait and subjective wellbeing mediate the relationship between mass sports activity and prosocial behavior. The multiple mediator model covers parallel mediator model and serial mediator model. In a parallel mediation model, the mediating variables have no effect on one another. The serial mediation model indicates that the mediating variables exert mutually influential effects. Wu et al. (31) suggested that the greater the degree of flow experience, the greater the likelihood that it can induce subjective wellbeing, and that the two are linked. Further, it was theorized that the flow experience induced by mass sports activity could enhance the subjective wellbeing of individuals, hence sequentially mediating and encouraging prosocial behavior.

Methods

Participants

The research was approved by the Ethics Committee of Hunan Normal University. All study participants or their legal guardians, if they were younger than 18 years old, provided informed consent (signed online during the survey). Using G*Power (version 3.1), the multiple linear regression R^2 one-sample procedure was chosen to predict the sample size with significance level of 0.05 and a statistical test power of 0.95. The *priori* analysis estimated a sample size of at least 107 to detect a predictive effect of mass sports activity and prosocial behavior ($f^2 = 0.15$). Data were collected using an online survey platform (Credamo, China) between March and May 2021. Credamo delivered surveys at random to personnel in all regions of China, and 367 surveys were collected in total. Excluding 16 surveys whose testing questions were unsatisfactory or too brief, a total of 351 valid surveys were retrieved, yielding an effective response rate of 95.64%. A total of 172 males and 179 females participated in this survey. There were 20 participants under the age of 18, 231 participants between the ages of 19 and 30, 95 participants between the ages of 31 and 45, three participants between the ages of 46 and 59, and two participants over the age of 60. This sample includes 102 students, 244 full-time workers, and five individuals who were unemployed or retired.

Instruments

Respondents' participation in mass sports over the last month was measured using the physical activity rank scale-3 (PARS-3) (32). PARS-3 ranked the intensity of physical activity ("What level of physical exertion do you engage in?" score range: 1–5 points), duration of physical activity ("How many minutes at a time do you engage in the physical activity described above?" score range: 1–5 points), and frequency of physical activity ("How frequently do you participate in the aforementioned physical activities?" score range: 0–4 points). The total score (PARS-3 = intensity × time × frequency) ranges from 0 to 100. China's National Fitness Program (33) defines the sports population as individuals who exercise moderately at least three times per week for at least 30 min per session. In this study, individuals with scores of 36 or more were considered part of the sports population, while those with scores of <36 were considered part of the non-sports population. The questionnaire has proven good test-retest reliability ($r = 0.82$) (32) and has been widely utilized in China to assess physical activity.

Flow trait was measured using the short dispositional flow scale (SDFS; 5-point Likert scale: 1, never experienced a flow; 5, always experienced a flow) (34). SDFS measured nine dimensions of flow: challenge—skill balance, merging of action and awareness, clear goals, unambiguous feedback, concentration on the task at hand, sense of control, loss of self-consciousness, transformation of time, and autotelic experience. All dimensions were added together to determine the total score. Higher scores indicate an individual's perception of flow trait in physical activity. Cronbach alpha of this study population was 0.76.

Subjective wellbeing was measured using the index of wellbeing (IWB; 7-point Likert scale: 1, strongly unsatisfied; 7, strongly satisfied) (35). IWB is comprised of index of general affect (containing of eight items with a score weight of 1) and index of life satisfaction (containing of one item with a score weight of 1.1). The total score (IWB = mean of eight items in the index of general affect × 1 + one item in the index of life satisfaction × 1.1) ranges from 2.1 to 14.7. The higher the score, the happier the respondent. Cronbach alpha of this study population was 0.92.

Prosocial behavior was measured using the prosocial tendencies measure (PTM; 5-point Likert scale: 1, does not describe me at all; 5, describes me greatly) (36). PTM consists of a total of 23 items, which are categorized into six dimensions: altruism, dire, compliant, emotional, public, and anonymous. All dimensions were added together to determine the total score. Higher scores imply that the respondent's prosocial tendencies are more evident. Cronbach alpha of this study population was 0.86.

Statistics

Data were analyzed using the IBM SPSS Statistics (version 25.0) and Hayes' PROCESS (version 4.1). Statistical significant level was set at $P < 0.05$. First, a two-tailed Welch's t-test was conducted to determine if the sports and non-sports populations differed significantly in the PARS-3, SDFS, IWB, and PTM. Then, the correlations between mass sports activity, flow trait,

TABLE 1 Means ± standard deviations of variables.

	Sports population			Sex		
	No ($n = 287$)	Yes ($n = 64$)	P	Female ($n = 179$)	Male ($n = 172$)	P
Physical activity rank scale-3	15.72 ± 8.45	41.61 ± 9.38	<0.001	18.66 ± 12.47	22.30 ± 13.72	0.01
Short dispositional flow scale	3.88 ± 0.48	4.09 ± 0.45	0.001	3.83 ± 0.51	4.01 ± 0.44	0.001
Index of wellbeing	11.69 ± 2.00	12.13 ± 1.54	0.05	11.40 ± 2.12	12.15 ± 1.62	<0.001
Prosocial tendencies measure	83.63 ± 10.84	87.94 ± 10.50	0.004	83.08± 10.65	85.81 ± 11.00	0.019

subjective wellbeing, and prosocial behavior were computed, and a linear regression was used to determine if mass sports activity had a significant influence on prosocial behavior. Finally, the PROCESS (Template, Model 6) was utilized to examine whether trait flow and subjective wellbeing served as sequential mediators between mass sports activity and prosocial behavior. The study utilized a bias-corrected non-parametric percentile bootstrap method appropriate for testing the significance level of the mediation effect, with 5,000 random resampling from the total sample size ($N = 351$), and the mediation effect was significant if the 95% confidence interval did not cross zero (37).

Results

Common method bias

Survey research often introduces data bias due to the characteristics of the survey items or the consistency of the data sources. In order to increase the truthfulness of the survey, it was constructed with lie detector and individuals were instructed to complete it anonymously. The Credamo was used to collect surveys nationwide in order to avoid consistency in questionnaire origin. Harman's single-factor test was employed to confirm the common method bias. The unrotated factor analysis examined a total of 10 common factors with eigenvalues were >1, the first of which explained 24.81% of the variance, which is below the critical threshold of 40%. This suggests that the common method bias did not cause significant issue in this study.

Descriptive statistics

Table 1 shows the descriptive statistics of variables. The SDFS, IWB, and PTM scores of sports population were significantly higher than those of non-sports population. On the PARS-3, male scored significantly higher than female. Likewise, male's SDFS, IWB, and PTM scores were significantly higher than female's. These findings indicate that participation in mass sports could effectively influence the extent to which trait flow, subjective wellbeing, and prosocial behavior tendencies are experienced.

TABLE 2 Matrix of Pearson correlation coefficient for variables.

	1	2	3	4
Mass sports activity	1			
Flow trait	0.339***	1		
Subjective wellbeing	0.307***	0.560***	1	
Prosocial behavior	0.243***	0.460***	0.542***	1

***Denotes P < 0.001.

Correlation analysis

Table 2 summarizes correlations among factors. The correlation analysis between the variables revealed significant positive relationships between mass sports activity, trait flow, subjective wellbeing, and prosocial behavior (all $P < 0.001$). The regression coefficients between the variables were determined using a linear regression model, and the results are presented in Table 3. The variance inflation factor values of all predictor variables in this study are below five, hence there is no multicollinearity issue (38). The result of simple linear regression supports hypothesis one, demonstrating that mass sport activity significantly predicted prosocial behavior, $\beta = 0.243$, $t_{(349)} = 4.687$, $P < 0.001$.

Two-mediator sequential model

Table 4 presents the mediation effects based on the bootstrap method. The 95% confidence intervals of all three indirect paths do not contain zero, indicating that all three paths have significant mediation effects. Furthermore, the significance of mass sports activity on prosocial behavior disappeared ($c' = 0.037$, $P = 0.338$) after the inclusion of two mediators, indicating that flow trait and subjective wellbeing had a fully mediation effect in this study. Therefore, the validity of hypotheses two,

TABLE 3 Results of regression analysis.

Outcome variable	Independent variables	*R*	R^2	*F*	*β*	*t*	*P*	*df*	VIF
Prosocial behavior	Mass sports activity	0.243	0.059	21.971	0.243	4.69	<0.001	349	1.00
Flow trait	Mass sports activity	0.339	0.115	45.441	0.339	6.74	<0.001	349	1.00
Subjective wellbeing	Mass sports activity	0.574	0.329	85.414	0.131	2.82	0.005	348	1.13
	Flow trait	-	-	-	0.516	11.05	<0.001	348	1.13
Prosocial behavior	Mass sports activity	0.575	0.331	57.176	0.045	0.96	0.338	347	1.16
	Flow trait	-	-	-	0.216	3.99	<0.001	347	1.53
	Subjective wellbeing	-	-	-	0.407	7.58	<0.001	347	1.49

VIF, variance inflation factor.

TABLE 4 Results of sequential mediation analysis.

Indirect effect path	Effect	Boot *SE*	Boot 95% *CI*	Ratio of indirect to total effect of *X* on *Y*
Ind1: $X \rightarrow M_1 \rightarrow Y$	0.061	0.019	[0.028, 0.101]	30.18%
Ind2: $X \rightarrow M_2 \rightarrow Y$	0.044	0.021	[0.007, 0.089]	21.96%
Ind3: $X \rightarrow M_1 \rightarrow M_2 \rightarrow Y$	0.059	0.014	[0.035, 0.089]	29.23%
Indirect effects of *X* on *Y*	0.163	0.031	[0.108, 0.230]	81.37%
Total effect of *X* on *Y*	0.201	0.043	[0.117, 0.285]	-

X, mass sports activity; M_1, flow trait; M_2, subjective well-being; Y, prosocial behavior.

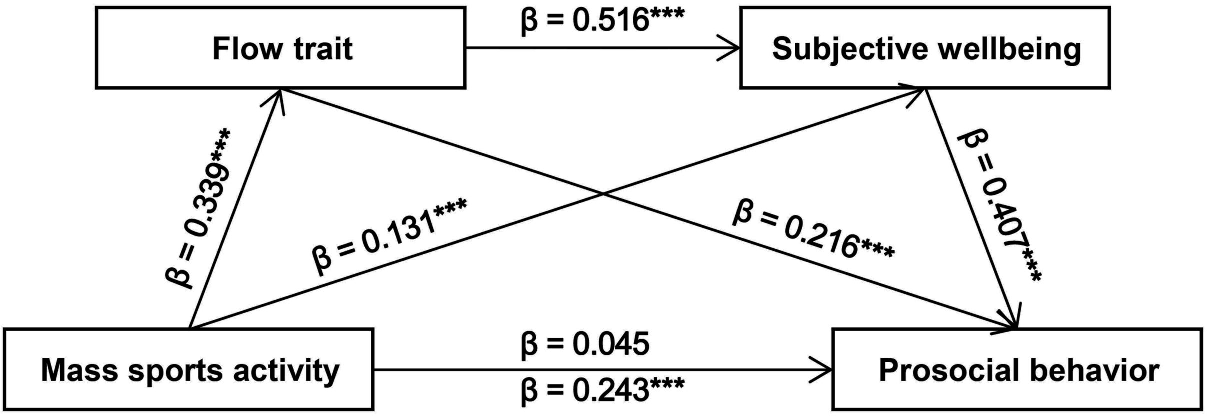

FIGURE 1
Conceptual diagram of double mediation using the PROCESS (Template, Model 6). Beta values above the solid line represent indirect effects, while the beta value below the solid line represent the total effect. ***Denotes $P < 0.001$.

three, and four is supported by these findings. Figure 1 depicts the two-mediator sequential model.

Discussion

In this study, we showed that participation in mass sports can promote prosocial behavior. Based on the subgroup analysis, it was also identified that the sports population scored significantly higher on flow trait, subjective wellbeing, and prosocial behavior, highlighting the value of leisure physical activity. The current study is the first to demonstrate positive psychological outcomes in addition to physical health benefits associated with mass sports activity, so providing the theoretical underpinning to support the fitness for all policy of the Chinese government.

Sports participation throughout the lifespan is regarded to enhance moral character and the capacity to work collaboratively toward a common objective (39–41). Individual sports participation is governed by the sport's laws and ethics, which are gradually reinforced as the number of sports activity increases (42). This is congruent with the social norms theory (43), which argues that norms can be internalized into an individual's consciousness (44) and can be adhered to even in the absence of external rewards (45). Thus, individuals with active inclusion in mass sports exhibit more pronounced prosocial behavior. Furthermore, mass sports are sports activities conducted in public, and people can be influenced by the watching eyes effect (46) when participating in sports, thereby creating an implicit social pressure to be supervised, and are more likely to develop prosocial behavior as a result of this supervision mechanism (47).

In the present study, flow trait and subjective wellbeing independently mediated the relationship between mass sports activity and prosocial behavior, respectively. According to the flow theory, this is mostly due to the fact that when people engage in easy-to-learn mass sports activity, they concentrate on the task at hand while experiencing a sense of joy and fulfillment (48). During the flow process, the individual's sense of control rises (49), and he or she is also more inclined to exhibit prosocial behaviors such as helping, cooperation, and humility (50). Furthermore, numerous research has demonstrated that regular physical activity, such as walking (51), could bring about array of benefits on an individual's physical and mental health, resulting in a relaxed and content state of mind and body. Meta-analysis of leisure sports participation and subjective wellbeing suggested that the leisure domain is an essential target for boosting subjective wellbeing (52), which has been demonstrated in the Chinese (53) and European (54) population. Mass sports activity is a form of leisure physical activity in which individuals of all ages can participate at any time. Physical activity improves individuals' subjective wellbeing, and in turn, when people are in a state of happiness, they are more inclined to engage in prosocial behavior (55).

Through the sequential mediation effect of flow trait and subjective wellbeing, the present study shows that mass sports activity can predict prosocial behavior. Our conclusion is consistent with the literature that flow is a strong predictor of subjective wellbeing (31). The sense of flow that people develop while exercise results in a heightened sense of wellbeing, which encourages prosocial behavior. This effect can also be explained by the theory of empathy training (56). Empathy is the capacity of the observer to feel and comprehend the feelings of the observed, as well as the mental process by which humans recognize and experience the emotions and feelings of others. Sport education (57) and regular participation in organized physical activity (58) can enhance an individual's personal and social responsibility, and a higher level of physical activity correlates with a greater capacity for empathy (59). Given the relationship between heightened flow experience and empathy (60), as well as the link between positive empathy, subjective wellbeing, and prosocial behavior (61), mass sports activity contributes to more prosocial behavior.

This study's findings have significant practical implications. First, our data revealed a significant gender difference in physical activity, which resulted in a significant decrease in females' flow trait, subjective wellbeing, and prosocial behavior. Insufficient physical activity among females is prevalent not only in China, but worldwide (62). In response to this global trend, governments should implement more effective health campaigns to encourage female physical activity. Not only could active sports participation improve physical health, but it could also have a positive influence on mental health, as demonstrated in the present study. This recommendation also applies to disadvantaged populations, such as those with physical disabilities or who live in economically underdeveloped areas with fewer public fitness facilities. Second, the sequential mediation effect of flow trait and subjective wellbeing suggests that individuals may choose appropriate exercise form (e.g., pacing sports) (16), extend the exercise duration, and increase the exercise intensity (63) when performing mass sports activity in order to achieve a deep state of flow in sports, which can increase the level of subjective wellbeing after exercise and improve the prosocial behavior of individuals. Third, these findings have implications for physical education classes in schools and team-building training in businesses. By organizing extracurricular and leisure physical activity, schools and businesses can increase the level of prosocial behavior among students and employees, hence enhancing the efficacy of the class and business (64).

The Chinese government has promoted the construction of "Healthy China" and developed an innovative public health model with Chinese characteristics to intervene in life and guide social behavior through sports, which not only has a positive impact on China's social progress and development, but also serves as an excellent example for the international community. On the basis of the Chinese experience, the promotion of an active lifestyle and social cohesion can be more effectively done through a series of societal and institutional policies that remove contextual barriers to produce habitual engagement in leisure physical activity. Fitness for all can lead to a nation that is more vibrant and inclusive. The economic, cultural, and social life of other nations can be enhanced immeasurably by the formation of a national fitness campaign that is tailored to national needs.

It should be acknowledged that, the study employed conventional questionnaire-based assessments, which may differ from the actual situation. Longitudinal experimental research on the effect of leisure physical activity on prosocial and antisocial behaviors is warranted to confirm our findings.

In conclusion, individuals who regularly participate in mass sports enjoy greater flow, which improves their subjective wellbeing and increases their prosocial behavior. Since the implementation of the National Fitness Program, China's public fitness system has been increasingly refined, and the number of individuals who regularly engage in mass sports activity has risen. The larger significance of this study provides empirical data to support the National Fitness Program's policy priority of increasing sports population in order to improve physical health and social cohesion. Moving forward, China's fitness for all that promotes a healthy society ought to be a global goal.

Data availability statement

The data that support the findings of this study are openly available in figshare at doi: 10.6084/m9.figshare.20218715.v1.

Ethics statement

The studies involving human participants were reviewed and approved by Hunan Normal University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

XD, XW, XL, SL, and YZ: conceptualization. XD and YZ: methodology. XD and SL: investigation. XD, XW, and SL: formal analysis. XD: writing—original draft preparation. XW, XL, SL, YZ, and TB: writing—review and editing. YZ: project administration. XW: funding acquisition. All authors have read and agreed to the published version of the manuscript.

Funding

This research was funded by the Department of Education of Zhejiang Province: Research on the construction of the carrier for the co-education of civic and political science from the Sanquan Education perspective, Grant Number Y202147685.

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.

References

1. Wispe LG. Positive forms of social behavior: an overview. *J Soc Issues.* (1972) 28:1–19. doi: 10.1111/j.1540-4560.1972.tb00029.x

2. Penner LA, Dovidio JF, Piliavin JA, Schroeder DA. Prosocial behavior: multilevel perspectives. *Annu Rev Psychol.* (2005) 56:365–92. doi: 10.1146/annurev.psych.56.091103.070141

3. Majed E, Ruiz Y, Amireault S, Reed JB, Snyder FJ, McDonough MH, et al. Examining positive youth development interventions with a physical activity component to address bullying among pre-and early adolescents: a critical review of the literature. *J Early Adolesc.* (2022) 42:389–413. doi: 10.1177/02724316211036748

4. Spitzer US, Hollmann W. Experimental observations of the effects of physical exercise on attention, academic and prosocial performance in school settings. *Trends Neurosci Educ.* (2013) 2:1–6. doi: 10.1016/j.tine.2013.03.002

5. Goldstein JD, Iso-Ahola SE. Promoting sportsmanship in youth sports: perspectives from sport psychology. *J Phys Educ Recreat Dance.* (2006) 77:18–24. doi: 10.1080/07303084.2006.10597902

6. Eys M, Bruner MW, Martin LJ. The dynamic group environment in sport and exercise. *Psychol Sport Exerc.* (2019) 42:40–7. doi: 10.1016/j.psychsport.2018.11.001

7. Sukys S, Majauskiene D, Dumciene A. The effects of a three-year integrated olympic education programme on adolescents' prosocial behaviours. *Eur J Sport Sci.* (2017) 17:335–42. doi: 10.1080/17461391.2016.1254280

8. Di Bartolomeo G, Papa S. The effects of physical activity on social interactions: the case of trust and trustworthiness. *J Sports Econ.* (2019) 20:50–71. doi: 10.1177/1527002517717299

9. Moeijes J, van Busschbach JT, Bosscher RJ, Twisk JWR. Sports participation and psychosocial health: a longitudinal observational study in children. *BMC Public Health.* (2018) 18:702. doi: 10.1186/s12889-018-5624-1

10. The State Council of the People's Republic of China. *The Central Committee of the Cpc and the State Council Print and Issue the Outline of the "Healthy China 2030" Plan: The State Council of the People's Republic of China*. (2016). Available online at: http://www.gov.cn/zhengce/2016-10/25/content_5124174.htm (accessed October 25, 2016).

11. General Administration of Sport of China. Study on development of mass sports in China. *Sports Cult Guide.* (2019) 11:1–10. doi: 10.3969/j.issn.1671-1572.2019.11.002

12. Zhu Q, Han J. Effects of different sport participations on prosocial and antisocial behaviors. *Int J Appl Sports Sci.* (2019) 31:1–12. doi: 10.24985/ijass.2019.31.1.1

13. Nakamura J, Csikszentmihalyi M. *The Concept of Flow. Flow and the Foundations of Positive Psychology*. Berlin: Springer (2014). p. 239–63. doi: 10.1007/978-94-017-9088-8_16

14. Jackson SA, Ford SK, Kimiecik JC, Marsh HW. Psychological correlates of flow in sport. *J Sport Exerc Psychol.* (1998) 20:358–78. doi: 10.1123/jsep.20.4.358

15. Jackson SA. Factors influencing the occurrence of flow state in elite athletes. *J Appl Sport Psychol.* (1995) 7:138–66. doi: 10.1080/10413209508406962

16. Cathcart S, McGregor M, Groundwater E. Mindfulness and flow in elite athletes. *J Clin Sport Psychol.* (2014) 8:119–41. doi: 10.1123/jcsp.2014-0018

17. Li W, Zhang M. Research on the influence and mechanism of "Tennis Xpress" on physical fitness, technical skills and flow experience of non-sports college students. *Zhejiang Sport Sci.* (2021) 43:101–7. doi: 10.3969/j.issn.1004-3624.2021.01.019

18. Mesurado B, Richaud MC. The relationship between parental variables, empathy and prosocial-flow with prosocial behavior toward strangers, friends, and family. *J Happiness Stud.* (2017) 18:843–60. doi: 10.1007/s10902-016-9748-7

19. Diener E, Oishi S, Tay L. Advances in subjective well-being research. *Nat Hum Behav.* (2018) 2:253–60. doi: 10.1038/s41562-018-0307-6

20. Buecker S, Simacek T, Ingwersen B, Terwiel S, Simonsmeier BA. Physical activity and subjective well-being in healthy individuals: a meta-analytic review. *Health Psychol Rev.* (2021) 15:574–92. doi: 10.1080/17437199.2020.1760728

21. Chatzisarantis NLD, Hagger MS. The moral worth of sport reconsidered: contributions of recreational sport and competitive sport to life aspirations and psychological well-being. *J Sports Sci.* (2007) 25:1047–56. doi: 10.1080/02640410600959954

22. Cao R. Application and development of Ppp mode in sports industry. In: Wang T, Han Z, Yang Y, Wang S, Li K, editors, *Annual Report on the Development of Ppp in China*. Singapore: Springer Singapore (2020). p. 125–44. doi: 10.1007/978-981-15-5724-8_7

23. General Administration of Sport of China. *2019 National Sports Venue Statistics Survey Data: General Administration of Sport of China*. (2020). Available online at: https://www.sport.gov.cn/n315/n329/c968164/content.html (accessed November 2, 2020).

24. General Administration of Sport of China. *2021 National Sports Venue Statistics Survey Data: General Administration of Sport of China (2022)*. Available online at: https://www.sport.gov.cn/jjs/n5043/c24251191/part/24251201.pdf (accessed April 29, 2022).

25. Wang K, Wang X. Providing sports venues on mainland china: implications for promoting leisure-time physical activity and national fitness policies. *Int J Environ Res Public Health.* (2020) 17:5136. doi: 10.3390/ijerph17145136

26. Sun Y, Tan S, He Q, Shen J. Influence mechanisms of community sports parks to enhance social interaction: a bayesian belief network analysis. *Int J Environ Res Public Health.* (2022) 19:1466. doi: 10.3390/ijerph19031466

27. Zhang Z, Wang M, Xu Z, Ye Y, Chen S, Pan Y, et al. The influence of community sports parks on residents' subjective well-being: a case study of Zhuhai City, China. *Habitat Int.* (2021) 117:102439. doi: 10.1016/j.habitatint.2021.102439

28. Aknin LB, Van de Vondervoort JW, Hamlin JK. Positive feelings reward and promote prosocial behavior. *Curr Opin Psychol.* (2018) 20:55–9. doi: 10.1016/j.copsyc.2017.08.017

29. Su T, Tian L, Huebner ES. The reciprocal relations among prosocial behavior, satisfaction of relatedness needs at school, and subjective well-being in school: a three-wave cross-lagged study among chinese elementary school students. *Curr Psychol.* (2021) 40:3734–46. doi: 10.1007/s12144-019-00323-9

30. Feng L, Zhang L. Prosocial tendencies and subjective well-being: the mediating role of basic psychological needs satisfaction. *Soc Behav Pers.* (2021) 49:1–10. doi: 10.2224/sbp.9986

31. Wu J, Xie M, Lai Y, Mao Y, Harmat L. Flow as a key predictor of subjective well-being among chinese University students: a chain mediating model. *Front Psychol.* (2021) 12:743906. doi: 10.3389/fpsyg.2021.743906

32. Liang D. Stress level of college students and their relationship with physical exercise. *Chin Ment Health J.* (1994) 8:5–6.

33. The State Council of the People's Republic of China. *Circular of the State Council on Printing and Issuing the National Fitness Program (2021-2025): The State Council of the People's Republic of China*. (2021). Available online at: http://www.gov.cn/zhengce/content/2021-08/03/content_5629218.htm (accessed August 3, 2021).

34. Liu W. Revision on Chinese edition of the short flow state scale and the short dispositional flow scale. *Chin Sports Sci.* (2010) 30:64–70. doi: 10.3969/j.issn.1000-677X.2010.12.009

35. Campbell A, Converse PE, Rodgers WL. *The Quality of American Life: Perceptions, Evaluations, and Satisfactions*. New York, NY: Russell Sage Foundation (1976).

36. Carlo G, Randall BA. The development of a measure of prosocial behaviors for late adolescents. *J Youth Adolesc.* (2002) 31:31–44. doi: 10.1023/A:1014033032440

37. Preacher KJ, Rucker DD, Hayes AF. Addressing moderated mediation hypotheses: theory, methods, and prescriptions. *Multivar Behav Res.* (2007) 42:185–227. doi: 10.1080/00273170701341316

38. Shrestha N. Detecting multicollinearity in regression analysis. *Am J Appl Math Stat.* (2020) 8:39–42. doi: 10.12691/ajams-8-2-1

39. Panza MJ, Graupensperger S, Agans JP, Doré I, Vella SA, Evans MB. Adolescent sport participation and symptoms of anxiety and depression: a systematic review and meta-analysis. *J Sport Exerc Psychol.* (2020) 42:201–18. doi: 10.1123/jsep.2019-0235

40. Zarrett N, Liu Y, Vandell DL, Simpkins SD. The role of organized activities in supporting youth moral and civic character development: a review of the literature. *Adolesc Res Rev.* (2021) 6:199–227. doi: 10.1007/s40894-020-00142-1

41. Kim ACH, Park SH, Kim S, Fontes-Comber A. Psychological and social outcomes of sport participation for older adults: a systematic review. *Ageing Soc.* (2020) 40:1529–49. doi: 10.1017/S0144686X19000175

42. Spruit A, Kavussanu M, Smit T, Ijntema M. The relationship between moral climate of sports and the moral behavior of young athletes: a multilevel meta-analysis. *J Youth Adolesc.* (2019) 48:228–42. doi: 10.1007/s10964-018-0968-5

43. Blay AD, Gooden ES, Mellon MJ, Stevens DE. The usefulness of social norm theory in empirical business ethics research: a review and suggestions for future research. *J Bus Ethics.* (2018) 152:191–206. doi: 10.1007/s10551-016-3286-4

44. McDonald RI, Crandall CS. Social norms and social influence. *Curr Opin Behav Sci.* (2015) 3:147–51. doi: 10.1016/j.cobeha.2015.04.006

45. Touré-Tillery M, Fishbach A. Three sources of motivation. *Consum Psychol Rev.* (2018) 1:123–34. doi: 10.1002/arcp.1007

46. Conty L, George N, Hietanen JK. Watching eyes effects: when others meet the self. *Conscious Cogn.* (2016) 45:184–97. doi: 10.1016/j.concog.2016.08.016

47. Zhang X, Liu C. The watching eyes effect on prosociality. *Adv Psychol Sci.* (2017) 25:475–85. doi: 10.3724/SP.J.1042.2017.00475

48. Engeser S, Schiepe-Tiska A, Peifer C. Historical lines and an overview of current research on flow. In: Peifer C, Engeser S, editors, *Advances in Flow Research*. Cham: Springer International Publishing (2021). p. 1. doi: 10.1007/978-3-030-53468-4_1

49. Swann C, Keegan RJ, Piggott D, Crust L. A systematic review of the experience, occurrence, and controllability of flow states in elite sport. *Psychol Sport Exerc.* (2012) 13:807–19. doi: 10.1016/j.psychsport.2012.05.006

50. Heywood L. Affective infrastructures: toward a cultural neuropsychology of sport. *Front Evol Neurosci.* (2011) 3:4. doi: 10.3389/fnevo.2011.00004

51. Kelly P, Williamson C, Niven AG, Hunter R, Mutrie N, Richards J. Walking on sunshine: scoping review of the evidence for walking and mental health. *Br J Sports Med.* (2018) 52:800–6. doi: 10.1136/bjsports-2017-098827

52. Wiese CW, Kuykendall L, Tay L. Get active? a meta-analysis of leisure-time physical activity and subjective well-being. *J Posit Psychol.* (2018) 13:57–66. doi: 10.1080/17439760.2017.1374436

53. Wang P, Wei X, Yingwei X, Xiaodan C. The impact of residents' leisure time allocation mode on individual subjective well-being: the case of China. *Appl Res Qual Life.* (2022) 17:1831–66. doi: 10.1007/s11482-021-10003-1

54. Ruseski JE, Humphreys BR, Hallman K, Wicker P, Breuer C. Sport participation and subjective well-being: instrumental variable results from german survey data. *J Phys Act Health.* (2014) 11:396–403. doi: 10.1123/jpah.2012-0001

55. Zhou X, Hu S, Liang L, Yuan K, Bian Y. Prosocial behaviors and subjective well-being in junior high school students: a cross-lagged analysis during three years. *Chin J Clin Psychol.* (2020) 28:561–5. doi: 10.16128/j.cnki.1005-3611.2020.03.026

56. Sevdalis V, Raab M. Empathy in sports, exercise, and the performing arts. *Psychol Sport Exerc.* (2014) 15:173–9. doi: 10.1016/j.psychsport.2013.10.013

57. García-López LM, Gutiérrez D. The effects of a sport education season on empathy and assertiveness. *Phys Educ Sport Pedagogy.* (2015) 20:1–16. doi: 10.1080/17408989.2013.780592

58. Amado-Alonso D, León-del-Barco B, Mendo-Lázaro S, Sánchez-Miguel PA, and Iglesias Gallego D. Emotional intelligence and the practice of organized physical-sport activity in children. *Sustainability.* (2019) 11:1615. doi: 10.3390/su11061615

59. Shima T, Nakao H, Tai K, Shimofure T, Jesmin S, Arai Y, et al. The influences of changes in physical activity levels with easing restriction of access to the University campus on empathy and social supports in college students during the covid-19 pandemic. *Asia Pac J Public Health.* (2022) 34:406–10. doi: 10.1177/10105395221083381

60. Wang X-M, Hu Q-N, Hwang G-J, Yu X-H. Learning with digital technology-facilitated empathy: an augmented reality approach to enhancing students' flow experience, motivation, and achievement in a biology program. *Interact Learn Environ.* (2022) 2022:1–17. doi: 10.1080/10494820.2022.2057549

61. Morelli SA, Lieberman MD, Zaki J. The emerging study of positive empathy. *Soc Personal Psychol Compass.* (2015) 9:57–68. doi: 10.1111/spc3.12157

62. Guthold R, Stevens GA, Riley LM, Bull FC. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1·9 million participants. *Lancet Glob Health.* (2018) 6:e1077–e86. doi: 10.1016/S2214-109X(18)30357-7

63. Stamatelopoulou F, Pezirkianidis C, Karakasidou E, Lakioti A, Stalikas A. "Being in the Zone": a systematic review on the relationship of psychological correlates and the occurrence of flow experiences in sports' performance. *Psychology.* (2018) 9:2011–30. doi: 10.4236/psych.2018.98115

64. Yaakobi E, Weisberg J. Organizational citizenship behavior predicts quality, creativity, and efficiency performance: the roles of occupational and collective efficacies. *Front Psychol.* (2020) 11:758. doi: 10.3389/fpsyg.2020.00758

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 30 August 2022
DOI 10.3389/fpubh.2022.949130

Effect of physical activity combined with extra ciliary-muscle training on visual acuity of children aged 10–11

Rongbin Yin†, Jianrong Xu†, Hongyun Wang, Sheng Zhou, Meng Zhang and Geng Cai*

School of Physical Education, Soochow University, Suzhou, China

This study is intended for exploring the effects of the physical activity combined with extra ciliary-muscle training with different frequencies on children's kinetic visual acuity and uncorrected distance visual acuity, and eventually figuring out the optimal frequency of ciliary-muscle training for each physical education class. To do the present research, A total of 160 students aged 10–11 from a school in Suzhou (a major city located in southeastern Jiangsu Province, East China) were randomly selected and divided into control group ($n = 33$), 15-frequency group ($n = 44$), 30-frequency group ($n = 40$) and 60-frequency group ($n = 43$), and the latter three experimental groups participated in a specially designed physical activity plan based on the training principles of ciliary muscle, while the control group participated in normal physical activity as usual. The experimental intervention period was 16 weeks, and all students' kinetic visual acuity and uncorrected distance visual acuity were measured before and after the experiment. The result showed that the kinetic visual acuity of the students in the 30 and 60-frequency groups got improved significantly after the experiment ($p < 0.05$), with the highest improvement occurring in the 30-frequency group, while there was no significant change in the 15-frequency group and the control group; The uncorrected distance visual acuity of the students in the 30 and 60-frequency groups was significantly improved after the experiment ($p < 0.05$), and the improvement range in these two groups was similar. In contrast, there was no significant change in the 15-frequency group, while the control group showed a significant decrease ($p < 0.05$). Physical activity combined with extra ciliary-muscle training has a positive effect on improving children's vision; at the same time, ciliary-muscle training with different frequencies bring out different outcomes on children's vision improvement, among which ciliary-muscle training with frequency of 30 in each physical education class is the best choice to enhance children's kinetic visual acuity and uncorrected distance visual acuity.

KEYWORDS

children, physical activity, ciliary-muscle training, kinetic visual acuity, uncorrected distance visual acuity

OPEN ACCESS

EDITED BY
Dušan Stupar,
Sports Association Super Active, Serbia

REVIEWED BY
Wei Wang,
Xuzhou Medical University, China
Jovan Gardasevic,
University of Montenegro, Montenegro

*CORRESPONDENCE
Geng Cai
caigeng@suda.edu.cn

†These authors have contributed equally to this work

SPECIALTY SECTION
This article was submitted to Children and Health, a section of the journal Frontiers in Public Health

RECEIVED 20 May 2022
ACCEPTED 15 August 2022
PUBLISHED 30 August 2022

CITATION
Yin R, Xu J, Wang H, Zhou S, Zhang M and Cai G (2022) Effect of physical activity combined with extra ciliary-muscle training on visual acuity of children aged 10–11. *Front. Public Health* 10:949130. doi: 10.3389/fpubh.2022.949130

Introduction

Eye health is an essential part of citizens' overall wellbeing, which has a far-reaching and extensive impact on individuals' life, health and society's sustainable development (1). In recent years, myopia has become a major public health issue worldwide. It is estimated that by 2050, the global myopia will increase significantly to 4.758 billion, accounting for 49.8% of the world's total population (2). Based on the investigations on current situation of myopia in the world, myopia presents clear regional characteristics, that is, the detection rate of myopia in Asia is much higher than that of Africa, Europe and America (3). For instance, in China, there are about 500 million patients suffer from refractive errors, of which 90% are myopic (4). Even worse, the morbidity of myopia is increasing, and persons with eye problems tend to be younger. The myopia rate of Chinese children and adolescents ranks first in the world (5). The large-scale prevalence of myopia has become a key factor triggering the downturn of eye health among children and adolescents.

With a progressive feature, the degree of myopia gradually rises with the increase of age, changing into moderate and high myopia, even into pathological myopia. The earlier children devolop myopia, the higher the risk of high myopia, pathological myopia and even blindness (6). Visual problems generate adverse effects on individual's health, wellbeing and economic development, including reduced educational and employment opportunities, social isolation and lower life expectancy, which will cause their quality of life to go down, and place a large barrier to the advancement of individuals, families and societies (7). In this situation, it is urgent to prevent the occurrence of children's myopia, slow down its progressive process and control the growth rate of myopia.

The vast majority of children's myopia is due to the long-term contraction of ciliary muscle under the condition of close visual activities without relaxing, which weakens the stretching ability of ciliary mustle and results in its loss of relaxation ability (8). In this case, improving the ciliary-muscle adjusting function is the key to prevent and slow down the formation of myopia (9). Kinetic visual acuity (KVA) and uncorrected distance visual acuity (UDVA), as the main indicators of visual acuity, are closely related to the adjusting function of ciliary muscle (10). Kinetic visual acuity is the ability to perceive the details of moving objects, which mainly depends on the regulating function of ciliary muscle (11), while the uncorrected distance visual acuity is the ability to perceive the details of static objects, which requires the ciliary-muscle adjustment to ensure a clear vision at both far and near visual distances. Kinetic visual acuity can help to predict uncorrected distance visual acuity to some extent (12). Existing studies have shown that the visual environment created in the process of physical activities is quite consistent with the principle of ciliary-muscle regulation, so specialized physical activities can improve people's kinetic visual acuity (13, 14), and also improve uncorrected distance visual acuity, as well as create a series of changes in eye parameters (15–19). Therefore, special physical activities designed under the guidance of ciliary-muscle regulation principle, can improve children's uncorrected distance visual acuity by promoting their kinetic visual acuity, which is an effective measure to ameliorate children's vision. Compared with ciliary-muscle training relying on apparatus (20, 21), physical exercise is more interesting, much safer, simpler and more acceptable to children, which can better benefit children and promote their visual health.

At present, the research on the prevention and control of children's myopia with physical activities mostly focused on impacts of different sports on children's visual acuity (22), but there are few quantitative studies on the intervention programs of physical activities. Obviously, to prevent and control children's myopia through physical activities, it is critical to define a reasonable range of intervention intensity, so as to make the myopia prevention and control program more practical and scientific. This study recorded and analyzed the effects of 15-frequency ciliary-muscle training, 30-frequency and 60-frequency ciliary-muscle training on children's kinetic visual acuity and uncorrected distance visual acuity in school physical education classes, and figured out the optimal threshold of training frequency of ciliary muscle in physical education classes, expecting to provide practical experience for the formulation of physical activities concerning the prevention and control of children's myopia.

Materials and methods

Participants

A total of 160 children aged 10–11 years old from four classes of Grade 5 at Experimental Primary School of Suzhou Science and Technology Town were randomly recruited as experimental subjects. Taking the class as a unit, they were randomly divided into three experimental groups and one control group (n = 33). The experimental included the 15-frequency group (low frequency, $n = 44$), the 30-frequency group (medium frequency, $n = 40$) and the 60-frequency group (high frequency, $n = 43$). Homogeneity tests were performed using one-way ANOVA. There was no significant ($p>0.05$)difference in the uncorrected distance visual acuity and kinetic visual acuity among the groups, which ensured that subsequent experiments could be carried out smoothly. Subjects' details are shown in Table 1.

Inclusion criteria of eligible subjects in this study: (1) no astigmatism, amblyopia, hyperopia and other eye pathological symptoms; (2) no wearing orthokeratology lenses; (3) no cognitive and motor dysfunction, and being able to successfully complete the experimental tasks. This study protocol was in accordance with the *Declaration of Helsinki* and approved by the Ethics Committee of Soochow University (No.SU-DA20201010H01).

TABLE 1 Participants demographic characteristics ($N = 160$, M ± SD).

Variables	15-frequency group	30-frequency group	60-frequency group	Control group	Value of *P*
Total	44	40	43	33	
Boys	24	24	24	22	
Girls	20	16	19	11	
KVA	0.289 ± 0.246	0.268 ± 0.214	0.333 ± 0.304	0.274 ± 0.276	0.359
UDVA	4.875 ± 0.334	4.775 ± 0.306	4.807 ± 0.335	4.794 ± 0.302	0.766

KVA, kinetic visual acuity; UDVA, uncorrected distance visual acuity.

Ciliary-muscle training method

Physical activity combined with ciliary-muscle training is designed in the present study, as studies have found that both closed-skill sports and open-skill sports can effectively improve students' kinetic visual acuity and uncorrected distance visual acuity after adding visual tasks (6). Generally, closed-skill sports include running, jumping and throwing. In detail, specific exercise tasks involve fast running, endurance running, obstacle running, standing long jump, single jump and double fall, rapid long jump, throwing sandbags or softball on the upper step, etc. On the strength of these regular physical activities, some visual targets were designed as digital cards, and some were printed action names, and solid balls, sandbags and other sports facilities were attached with visual targets signs as well. For example, in the obstacle running exercise, when students clearly saw the numbers and action names presented on the visual target in the process of running forward, which were set at each obstacle point in advance, and they should complete the described actions for the corresponding number of times. And the same to the jumping exercise and throwing exercise, students observed the number and content of the visual targets while jumping forward to complete the prescribed actions; during the throwing process, students were asked to track the movement of medicine balls, sandbags or softballs with eyes, carefully read the content of visual targets and did the written task on it.

Open-skill sports include football, basketball, volleyball and table tennis, the specific exercises of which are kicking the ball with the inside foot, catching the ball, dribbling the ball in front of the instep, dribbling the ball in basketball, shooting *in situ*, passing and catching the ball, self-cushion and two-person cushion in volleyball, throwing and catching ball and two-person play in table tennis. In these activities, the visual target was a card with numbers or a ball affixed with a visual-target design. Engaging in the exercise, students followed the movement of the ball with both eyes, or observed the hand-held visual target, and read the content of the visual target clearly (Table 2).

The principles of the visual-task design and implementation consisted of four categories: (1) to ensure the completion of the exercise task and individual's safety; (2) regarding kinetic visual acuity, the change of depth or distance in the exercise was the main concern; (3) the emphasis of training placed on the changing process from "visible" to "see details of the visual target clearly"; (4) the times of each exercise was determined by the frequency of each group. Taking throwing and catching the ball as an example, the key of intervention is to guide the participant to track the movement and landing point of the ball with eyes when throwing and catching the ball. The ball from near to far or from far to near was recognized as one time of visual intervention.

Study design

The determination of training frequency of ciliary muscle was in light of the practical experience of previous related studies, which indicated that the training frequency of ciliary muscle was generally 15–40 times in each physical education class according to different sports items and teaching contents (23, 24). Taking the limited time of physical education class and the requirements of teaching tasks into further consideration, this study would set the frequency of 30 as the benchmark threshold, and the upper and lower amplitudes were adjusted twice, so the experimental groups were assigned as the 15-frequency group (low frequency), the 30-frequency group (medium frequency) and the 60-frequency group (high frequency), respectively. In this situation, the effects of low, medium and high frequency of ciliary-muscle training on participants' kinetic visual acuity and uncorrected distance visual acuity were observed. The three experimental groups took part in additional ciliary-muscle training activities with the frequency of 15 (low frequency), the frequency of 30 (medium frequency) and the frequency of 60 (high frequency) designed based on the principle of ciliary-muscle training, while the control group carried out routine physical education activities.

For this study, the selected physical activities was from the regular school physical education for children aged 10–11, which consisted of open-skill sports like basketball, football, volleyball, table tennis and other ball games, and closed-skill sports, such as running, jumping, throwing in athletics. The intervention period of the experiment is 16 weeks, and the experimental group and the control group were arranged to conduct physical

TABLE 2 Experiment content.

Classification	Projects	Exercise content	Exercise time	Movement frequency	Duration of ciliary muscle intervention
Open motor skills	Basketball	Passing, dribbling, shooting, etc.	Total 4 weeks; 40 min each time	Three times a week	Control group without ciliary muscle intervention and normal participation in physical education classes. The hourly value of ciliary muscle intervention in the experimental group was 3 s/time; since the ciliary muscle intervention was carried out as a motor exercise, the exact time could not be accurately estimated and depended on the content of the exercise. For example, the 60-frequency group performed volleyball reversal exercises with 40 people divided into four groups of 10 people at a time for 5 min each, for a total of 20 min.
	Soccer	Shooting, passing, dribbling, etc.	Total 4 weeks; 40 min each time	Three times a week	
	Volleyball	Matting, serving, passing, etc.	Total 4 weeks; 40 min each time	Three times a week	
	Table tennis	Throwing and catching balls, pairs, games, etc.	Total 4 weeks; 40 min each time	Three times a week	
Closed motor skills	Run	Obstacle run, speed run, relay run etc.	Total 4 weeks; 40 min each time	Three times a week	
	Jump	Height adjustment, long jump, etc.	Total 4 weeks; 40 min each time	Three times a week	
	Cast	Sandbag, softball, solid ball	Total 4 weeks; 40 min each time	Three times a week	
	Sports games	Emphasis on the far-sighted–near-sighted game	Total 4 weeks; 40 min each time	Three times a week	

education class three times a week, with each class lasting 40 min. The intervention of the experimental group was carried out in physical education class. According to the research purpose, on the premise of not affecting the teaching content of normal physical education courses, combined with the characteristics of various sports movements and skills learning requirements, ciliary muscle training tasks were reasonably added to the experimental group in practice, and appropriate visual aids were added. Physical education class's exercises of the control group did not include ciliary muscle training tasks. For example, when the experimental group and the control group were practicing football passing at the same time, the football in the experimental group should be pasted with numbers or letters, and students were required to catch the moving track of the ball during the football rolling process. They need to see clearly the content of the visual mark on the football and experience the change of farsightedness and nearsightedness. However, there was no visual mark on the football in the control group, because the students in the control group did not need to complete the ciliary muscle training task. The exercise load, exercise duration, exercise frequency and items of the experimental group and the control group should be consistent to ensure the accuracy of the experimental results. At the same time, we keep tracking of students' physical activity during out-of-school hours, such as after school and weekends, through regular communication with parents and students to prevent experimental errors caused by sudden changes in subjects' physical activity (e.g., participation in or withdrawal from sports clubs, etc.).

Measure method

This study measured the participants' uncorrected distance visual acuity and kinetic visual acuity from four groups before the experimental intervention (before the first week) and after the experimental intervention (after the 16th week). In order to minimize the error of experimental data, the detection methods and process were strictly carried out in accordance with the standards, and the same person conducted all the measurement and recording of various data before and after the experiment.

Measurement of uncorrected distance visual acuity

Participants' uncorrected distance visual acuity test was completed by the full-time school doctor, using the light box of current "Standard Logarithmic Visual Acuity Chart" for testing, and the whole operation process followed the ophthalmic examination standards. The measurement result of the right eye was taken as the final value of the subjects' uncorrected distance visual acuity.

Measurement of kinetic visual acuity

Kinetic visual acuity was tested with XP.14-TD-J905, the kinetic visual acuity detector produced by Shanghai Hump Automation Technology Co., Ltd. The range of kinetic visual acuity was between 0.1 and 1.6, and the higher the value, the better the kinetic visual acuity. Before the eyesight test, the tester explained the operation method. The student sat in front of the detector and look through the measuring window. After the test began, students would see a Landolt ring in a bright yellow circular shape. The Landolt ring approached the subject from the front, moving from a 50 meters distance at a velocity of 30 km/h. The students were instructed to rapidly press the joystick when they identified the orientation of the Landolt ring (four directions: up, down, left, right). Only the correct measurement values were recorded. Then, each student was tested three times in a row, and the average value was taken as the final value of the student's kinetic visual acuity.

Statistical analysis

Excel spreadsheet was used for data entry and collation, and SPSS25.0, statistical software, was used for data analysis. All data were expressed as mean ± standard deviation (M ± SD). Before the experiment, the data were tested for homogeneity, and the data obeyed normal distribution and had the same homogeneity of variance. Repeated-measures analysis of variance (ANOVA) and paired sample t-test were used to analyze the test results of participants' kinetic visual acuity and uncorrected distance visual acuity before and after the experiment. The significance size of main effects and interactions was evaluated using ηp2 to evaluate the significance size of main effects and interactions, in which $\eta p2 \leq 0.06$ was a small effect, $0.06 < \eta p2 \leq 0.14$ was a medium effect, and $\eta p2 > 0.14$ was a large effect. The significance level is $\alpha = 0.05$.

TABLE 3 Results of repeated-measures ANOVA on participants' kinetic visual acuity.

Elements	Value of F	Value of *P*	η_p^2
Time	16.210*	0.000	0.094
Group	1.727	0.164	0.032
Time×Group	3.405*	0.019	0.061

*indicates significant difference ($p < 0.05$).

Results

Intervention effect analysis of ciliary-muscle training with different frequencies on kinetic visual acuity

Table 3 presents the results of the repeated-measures ANOVA on participants' kinetic visual acuity. As seen in Table 3, the main effect of time was significant ($F = 16.210$, $p < 0.05$), which indicated that participants' kinetic visual acuity changed significantly with the passage of time. The interaction of time and group (shown as time × group) was significant ($F = 3.405$, $p < 0.05$), which indicated that under the interaction of time and group, different frequency of ciliary-muscle training in physical education had different effects on students' kinetic visual acuity.

Further simple effect analysis (Table 4) found that at the level of baseline test, there was no statistically significant difference in kinetic visual acuity among the groups ($F = 0.520$, $p > 0.05$); At the post-test level, there was a significant difference in the kinetic visual acuity among the groups ($F = 3.701$, $p < 0.05$). Multiple comparison shows there was a remarkable difference in the kinetic visual acuity between the control group and the 30-frequency group ($p < 0.05$). The paired sample T test of kinetic visual acuity before and after the experiment showed that the kinetic visual acuity of the students in both the 30 and the 60-frequency groups was significantly improved ($p < 0.05$), while that of the students in the 15-frequency group and the control group had no significant change ($p>0.05$) (Figure 1).

TABLE 4 Simple effect analysis and paired-sample *t*-test on subjects' kinetic acuity.

Measure time	Groups	M ± SD	Value of F	Value of *P*	η_p^2
Pre-experiment	15-frequency group	0.289 ± 0.246	0.520	0.669	0.010
	30-frequency group	0.268 ± 0.214			
	60-frequency group	0.333 ± 0.304			
	Control group	0.274 ± 0.276			
Post-experiment	15-frequency group	0.361 ± 0.248	3.701	0.013	0.066
	30-frequency group	0.486 ± 0.327[ab]			
	60-frequency group	0.424 ± 0.324[a]			
	Control group	0.275 ± 0.200			

[a]means that compared with pre-experiment, $p < 0.05$. [b]means significant difference in comparison with the control group after the experiment ($p < 0.05$).

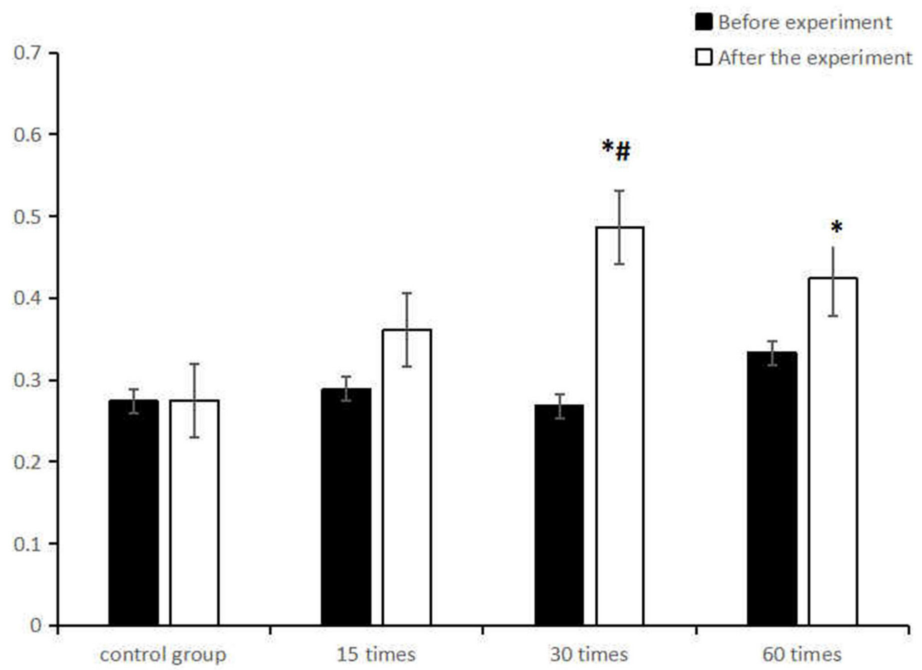

FIGURE 1
Comparison of the mean (M ± SD)kinetic visual acuity between the control group and the ciliary muscle training group with different frequencies before and after the experiment. *represents significant difference in intra-group comparison ($p < 0.05$), #represents significant difference in comparison with the control group after the experiment ($p < 0.05$).

TABLE 5 Repeated measures analysis of variance on participants' uncorrected distance visual acuity.

Elements	Value of F	Value of *P*	η_p^2
Time	14.076*	0.000	0.083
Group	2.334	0.076	0.043
Time×Group	12.219*	0.000	0.190

*indicates significant difference ($p < 0.05$).

Intervention effect analysis of ciliary-muscle training with different frequencies on uncorrected distance visual acuity

Participants' uncorrected distance visual acuity in each group was analyzed by repeated measurement analysis of variance before and after the experiment, which reflected that the main effect of time was significant (F=14.076, $p < 0.05$), in other words, participants' uncorrected distance visual acuity changed significantly with the passage of time. Moreover, the interaction of time and group (shown as time × group) was significant (F=12.219, $p < 0.05$), which demonstrated that under the interaction of time and group, different frequencies of ciliary-muscle training in physical education had different effects on students' uncorrected distance visual acuity (Table 5).

Further simple effect analysis (Table 6) showed that at the level of baseline test, there was no statistically significant difference in uncorrected distance visual acuity among the groups (F = 0.776, $p > 0.05$); At the post-test level, a significant difference appeared in subjects' uncorrected distance visual acuity among the groups (F = 7. 095, $p < 0.05$), and there was a remarkable difference in the uncorrected distance visual acuity between the control group and the three experimental groups ($p < 0.05$). The paired sample *t* test of uncorrected distance visual acuity before and after the experiment found that students' uncorrected distance visual acuity in both the 30 and the 60-frequency groups was significantly improved ($p < 0.05$), while that of the students in the 15-frequency group had no significant change (p>0.05), but the control group displayed a significant decrease ($p > 0.05$) (Figure 2).

Discussion

Development of 10–11-year-old children's visual health

More attention should be paid to the relationship between visual acuity and age in terms of prevention and cure for

TABLE 6 Simple effect analysis and paired-sample *t*-test on subjects' uncorrected distance visual acuity.

Measure time	Groups	M ± SD	Value of F	Value of *P*	$\eta_p{}^2$
Pre-experiment	15-frequency group	4.875 ± 0.334	0.776	0.509	0.015
	30-frequency group	4.775 ± 0.306			
	60-frequency group	4.807 ± 0.335			
	Control group	4.794 ± 0.302			
Post-experiment	15-frequency group	4.927 ± 0.311	7.095	0.000	0.120
	30-frequency group	4.937 ± 0.269[ab]			
	60-frequency group	4.958 ± 0.280[ab]			
	Control group	4.685 ± 0.277[ab]			

[a]means that compared with pre-experiment, $p < 0.05$. [b]means significant difference in comparison with the control group after the experiment ($p < 0.05$).

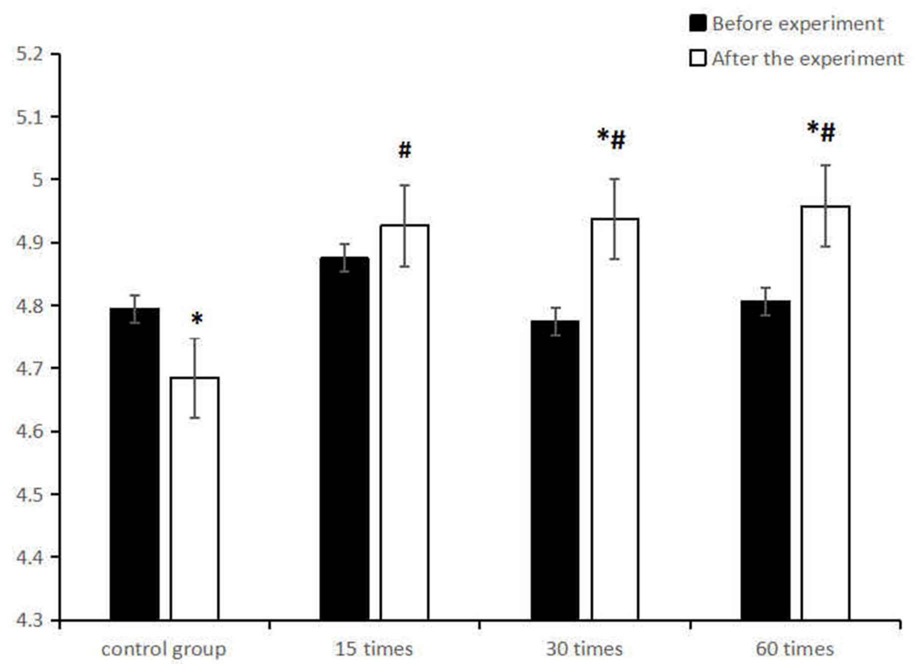

FIGURE 2
Comparison of the mean (M ± SD) uncorrected distance visual acuity between the control group and the ciliary muscle training group with different frequencies before and after the experiment. *represents significant difference in intra-group comparison ($p < 0.05$), #represents significant difference in comparison with the control group after the experiment ($p < 0.05$).

children's myopia, as the development of vision shows different characteristics in different age groups. Before the age of 6, it is the key development period of children's uncorrected distance visual acuity (25). Later, at the age of 10–14, their uncorrected distance visual acuity decreases significantly with age (26). It should be noted that myopia develops rapidly among children aged 7–12 years (27). A scholar investigated the current status of children's poor vision in a Chinese city and found that the rate of poor vision among children aged 9–12 was as high as 51.28% (28). This study showed that participants' overall visual health in the control group without any intervention displayed a downward trend, which may be related to the stage characteristics of visual development and the abnormal adjusting function of eyes. According to Kepler's near-work hypothesis (29), myopia was based on the continuous contraction of ciliary muscle, which created higher intraocular pressure during overloaded near work. Children's myopia took shape around school-age was mostly caused by ciliary-muscle dysfunction, coincidentally the peak period of myopic morbidity coincided with the peak period of individual's physical growth and development and also the individual's high-intensity academic learning (30, 31). In addition, external environmental factors such as near work, education intensity, long screen time, lack of physical activity and outdoor exercise were all recognized as risk factors for children's myopia. Particularly, children aged 10–11 are just in the period of rapid physical growth and development, and at the same time they step into the stage of increasing academic pressure, with more time for close work and less time for outdoor physical activities. In this situation, their ciliary muscle cannot be fully relaxed due to continuous contraction, consequently the range, flexibility and accuracy of ciliary-muscle regulation are reduced or its regulation ability will lose, and that's why children's visual acuity is prone to fluctuation. It is no doubt that at this stage, if we can provide helpful treatment strategies, the prevention and control of children's myopia can achieve better benefits.

Effect of physical activity combined with ciliary-muscle training on children's visual health

The present study found that ciliary-muscle training in physical education class had a positive effect on improving children's visual health. As is known, the root of myopia is ciliary muscle spasm. Fortunately, special ciliary-muscle training can relieve this problem. In the past, some previous researchers were misled to believe that ciliary muscle cannot be changed by exercise, since structurally ciliary muscle belongs to smooth muscle (32). However, in recent years, it has been found that the muscle cells of ciliary muscle are different from the smooth muscle of other parts such as blood vessels, which are regularly arranged dense bands and dense bodies, similar to the Z band in striated muscle; moreover, in the ultrastructure, the number of mitochondria and endoplasmic reticulum in ciliary muscle cells is more abundant than that in ordinary smooth muscle (33). Due to the fact that ciliary muscle not only has the smooth muscle characteristics controlled by parasympathetic nerve, but also has many physiological structure, histochemistry and efferent nerve characteristics of striated muscle, increasing scholars convince that it can be regulated by special training.

Physical activity is the best medium for ciliary-muscle training in childhood. Studies have found that both open-skill sports and closed-skill sports can effectively improve students' kinetic visual acuity and uncorrected distance visual acuity after adding visual tasks (24). Besides, ball games with the nature of open-skill sports are accompanied by the alternation of close and distant vision in the process of practice, in which the ciliary muscle needs to be constantly adjusted to make the vision clear, which is conducive to the recovery of regulatory function (34). Admittedly, compared with open movement, closed movement requires less vision adjustment in the process of practice, but embedding the task of alternating near-far vision in closed movement, and increasing the frequency of eye use in closed movement can also improve the vision of myopic students (23).

According to the findings of previous studies (24), it is not difficult to see that different types of sports can show different effects on improving children's visual acuity, and this kind of differentiation is likely to be related with the frequency of ciliary-muscle training during exercise. In addition, some scholars (35) believed that in the process of physical activities, the adaptation of human eyes to changes in the external environment increased the frequency of ciliary muscle regulation, coupled with the strengthening of nerve regulation and the relaxation of psychological state, which may improve the spasm of ciliary muscle to a certain extent, thus having a positive impact on the level of visual health.

Effects of ciliary-muscle training with different frequencies on children's kinetic visual acuity and uncorrected distance visual acuity

The results of this study showed that different frequencies of ciliary-muscle training had different effects on students' visual acuity. That was partly because of different amount of ciliary-muscle regulation triggered by different training intensity. In fact, the process of visual training is essentially the process of sports training, and the only main difference is that the training part concentrated on eyes. Although the eye muscle group belongs to the small muscle group, it can still support a suitable amount of exercise, so different amount of exercise done by the ciliary-muscle will create diverse stimulation, which is why in a certain period of intervention, different training frequencies have different effects on vision.

Another finding of this study was that 30 times of ciliary-muscle training in each physical education class had the best effect on improving students' kinetic visual acuity, and 30 times and 60 times of ciliary-muscle training had similar effects on improving students' the uncorrected distance visual acuity. In general, ciliary-muscle training with 30-frequency had better effects on the two kinds of vision than that of the 15 and the 60-frequency groups, which can be well explained. From a physiological point of view, eye muscles belong to small muscle groups, with poor tolerance, fatigue and other characteristics, frequency of 30 may be the appropriate intensity for ciliary-muscle training with physical activities as the carrier, which is more likely to produce the ideal effect on improving the adjustment ability of ciliary muscle.

Also, from the experimental point of view, ciliary-muscle training with frequency of 30 can be widely accepted in the experiment, and children had a high degree of execution and can complete the experimental task with high quality. Through the intervention, the ciliary muscle was not only fully relaxed, but also the sensitivity and accuracy of eye adjustment can be enhanced. In comparison, the 60-frequency training group was affected by the longer experimental time, resulting in a lower degree of participants' execution, in which children were unable to fully adjust and relax their eyes, and the quality of task completion was worse than that of the 30-frequency group. As for the 15-frequency group, 15 times of ciliary-muscle training can only make the strained and spasmodic ciliary muscle experience a simple warm-up effect. After 15 times of training, intervention on the ciliary muscle immediately stopped, but the muscle just reached the state of preparation, so the relaxation of ciliary muscles failed to continue, resulting in insufficient stimulation intensity. Therefore, 15-frequency training failed to reach the threshold of cillary muscle training. Based on the explanation above, it is a more reasonable and scientific choice to take 30 times in each physical class as the benchmark threshold for ciliary-muscle training combined with physical activities. The reason for the visual acuity loss in the control group may be that Chinese students have fewer opportunities to participate in extracurricular physical activities, and the ciliary muscle conditioning in daily school physical activities cannot counteract the negative effects of students due to close eye use and excessive time spent on visual screens.

At present, the traditional teaching mode of physical education at school has limited effect on improving children's visual acuity. Being aware of this undesirable situation, this study asserts that it is necessary to combine ciliary-muscle training with regular physical activities to form a new physical education teaching mode that not only enables children to master sports skills, but also works in children's myopia prevention and control. By this way, it will motivate children's active participation in the new mode, and help them cultivate a good habit of self-regulation to improve myopia.

Although great effort was made, the present study was far from satisfactory. Only 10–11-year-old children were selected for the experiment, but no comparative study of multi-population, larger sample and different methods was carried out. Due to these limitations, in terms of research content, it is recommended that future studies further explore the effects of different intervention frequencies on the visual acuity levels of children at various ages, even refining to different genders and visual acuity levels, and also expanding to the relationship between different intervention hourly values and intensities and the visual acuity levels of children and adolescents at various school levels. All of the aspects are worth exploring experimentally. In terms of related index measurements, future studies can perform ciliary muscle paralysis on the measurement subjects to obtain more accurate data.

Conclusions

On the basis of the experiment data analysis, this study revealed that physical activity combined with extra ciliary-muscle training has a positive effect on improving children's visual health. At the same time, different frequencies of ciliary-muscle training produces different effects on children's visual acuity. In particular, the 30-frequency ciliary-muscle training is the optimal choice to improve children's kinetic visual acuity and uncorrected distance visual acuity in each physical education class.

Data availability statement

The data that support the findings of this study are available on request from the first author. The data are not publicly available because they contain information that could compromise the privacy of research participants. Requests to access the datasets should be directed to RY, yrb@suda.edu.cn.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of Soochow University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

Conceptualization and validation: RY and JX. Methodology and writing—original draft preparation: RY. Formal analysis and data curation: SZ and MZ. Investigation and visualization: HW. Resources: GC. Writing—review and editing: JX. Supervision: RY and JX. Project administration and funding acquisition: GC. All authors have read and agreed to the published version of the manuscript.

Funding

This research was supported by the National Social Science Fund of China (No. 19BTY078).

Acknowledgments

We would like to express our gratitude to Experimental Primary School of Suzhou Science and Technology Town for their assistance with this study.

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. Burton MJ, Ramke J, Marques AP, Bourne RRA, Congdon N, Jones I, et al. The Lancet Global Health Commission on global eye health: vision beyond 2020. *Lancet Glob Heal.* (2021) 9:e489–551. doi: 10.1016/S2214-109X(20)30488-5

2. Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology.* (2016) 123:1036–42. doi: 10.1016/j.ophtha.2016.01.006

3. Ding BY, Shih YF, Lin LLK, Hsiao CK, Wang IJ. Myopia among schoolchildren in East Asia and Singapore. *Surv Ophthalmol.* (2017) 62:677–97. doi: 10.1016/j.survophthal.2017.03.006

4. Li L. *National Vision Health Report*. Beijing: Peking University Press. (2016).

5. Pan CW, Wu RK, Liu H, Li J, Zhong H. Types of lamp for homework and myopia among Chinese school-aged children. *Ophthalmic Epidemiol.* (2018) 25:250–6. doi: 10.1080/09286586.2017.1420204

6. Zhang M, Fu Q, Zhou S, Tan Q, Cai G. Meta-analysis of sports activities for the prevention and control of myopia in children and adolescents. *Sport Res.* (2022) 43:55–64.

7. Chua SYL, Sabanayagam C, Cheung YB, Chia A, Valenzuela RK, Tan D, et al. Age of onset of myopia predicts risk of high myopia in later childhood in myopic Singapore children. *Ophthalmic Physiol Opt.* (2016) 36:388–94. doi: 10.1111/opo.12305

8. González-Méijome JM. New research routes to fight myopia. *EBioMedicine.* (2017) 16:24–5. doi: 10.1016/j.ebiom.2017.01.022

9. Yin R. Bin, Sun L, Wang GX, Cai G, Huang K, Yang T, et al. Effect of physical activities on myopia in children: based on ICF theory. *Chinese Rehabil Theory Pract.* (2018) 24:1223–7. doi: 10.3969/j.issn.1006-9771.2018.10.018

10. Sun L, Cai G, Yin R. Bin, Pan JL, Wang GX, Chen G, et al. Correlation between static visual acuity and dynamic visual acuity in children and its implications for physical activity. *Chinese Rehabil Theory Pract.* (2018) 24:1485–8. doi: 10.3969/j.issn.1006-9771.2018.12.025

11. Cutler GH, Ley AH. Kinetic visual acuity. *Br J Physiol Opt.* (1963) 20:119–27.

12. Palidis DJ, Wyder-Hodge PA, Fooken J, Spering M. Distinct eye movement patterns enhance dynamic visual acuity. *PLoS ONE.* (2017) 12:e0172061. doi: 10.1371/journal.pone.0172061

13. Freeman EE, Muñoz B, Turano KA, West SK. Dynamic measures of visual function and their relationship to self-report of visual functioning. *Investig Ophthalmol Vis Sci.* (2006) 47:4762–6. doi: 10.1167/iovs.06-0436

14. Quevedo-Junyent L, Aznar-Casanova JA, Merindano-Encina D, Cardona G, Solé-Fortó J. Comparison of dynamic visual acuity between water polo players and sedentary students. *Res Q Exerc Sport.* (2011) 82:644–51. doi: 10.1080/02701367.2011.10599801

15. Chuang AYC. How to effectively manage myopia. *Taiwan J Ophthalmol.* (2017) 7:44–7. doi: 10.4103/tjo.tjo_24_17

16. Yurova O V, Andjelova D V, Chayka AA. The influence of physical loads on the functional parameters of the eyes in the children and adolescents regularly engaged in sports activities. *Vopr Kurortol Fizioter Lech Fiz Kult.* (2017) 94:44–8. doi: 10.17116/kurort201794344-48

17. Hsu CC, Huang N, Lin PY, Tsai DC, Tsai CY, Woung LC, et al. Prevalence and risk factors for myopia in second-grade primary school children in Taipei: a population-based study. *J Chinese Med Assoc.* (2016) 79:625–32. doi: 10.1016/j.jcma.2016.02.011

18. Cheng HC, Chang K, Shen E, Luo KS, Ying YH. Risk factors and behaviours of schoolchildren with myopia in Taiwan. *Int J Environ Res Public Health.* (2020) 17:1967. doi: 10.3390/ijerph17061967

19. Read SA, Collins MJ. The short-term influence of exercise on axial length and intraocular pressure. *Eye.* (2011) 25:767–74. doi: 10.1038/eye.2011.54

20. Lin SY, Su HR, Lo CC, Yeh SM, Lee CH, Wu R, et al. Effects of extended viewing distance on accommodative response and pupil size of myopic adults by using a double-mirror system. *Int J Environ Res Public Health.* (2022) 19:2942. doi: 10.3390/ijerph19052942

21. Yeh SM, Lo CC, Lee CH, Chen YJ, Lin FC, Huang SY. Reduction in accommodative response of schoolchildren by a double-mirror system. *Int J Environ Res Public Health.* (2021) 18:9951. doi: 10.3390/ijerph18199951

22. Wang BN, Wang LJ, Chen RZ, Zhou YL. The relationship between physical activity and myopia in children and adolescents: a systematic review and meta-analysis. *China Sport Technol.* (2022) 58:62–72. doi: 10.16470/j.csst.2019160

23. Zhou S, Zhou C, Tan Q, Qiu FB, Cai G. The effect of closed skill physical activity combined with dynamic visual task on visual function of fourth grade myopic children. *Chinese Rehabil Theory Pract.* (2020) 26:1283–9.

24. Jin G, Pan JL, Cai G. Practical significance and empirical research of physical exercise on pupils'visual health. *J Cap Inst Phys Educ.* (2021) 33:40–8.

25. Wang J, Li Y, Musch DC, Wei N, Qi X, Ding G, et al. Progression of myopia in school-aged children after COVID-19 home confinement. *JAMA Ophthalmol.* (2021) 139:293–300. doi: 10.1001/jamaophthalmol.2020.6239

26. Zhou S, Chen J, Zhang J, Tan Q, Chen G, Pan JL, et al. Age and gender differences in visual function of school-age children participating in physical activities. *Chinese Rehabil Theory Pract.* (2019) 25:1255–9.

27. Tricard D, Marillet S, Ingrand P, Bullimore MA, Bourne RRA, Leveziel N. Progression of myopia in children and teenagers: a nationwide longitudinal study. *Br J Ophthalmol.* (2021) 318256. doi: 10.1136/bjophthalmol-2020-318256

28. Zhu JN. Status and influencing factors of poor vision among primary and secondary school students in Nanning in 2019. *J Prev Med Inf.* (2021) 37:1668–73.

29. Mark HH. Johannes kepler on the eye and vision. *Am J Ophthalmol.* (1971) 72:869–78. doi: 10.1016/0002-9394(71)91682-5

30. Jan C, Li SM, Kang MT, Liu L, Li H, Jin L, et al. Association of visual acuity with educational outcomes: a prospective cohort study. *Br J Ophthalmol.* (2019) 103:1666–71. doi: 10.1136/bjophthalmol-2018-313294

31. Lin LL, Shih YF, Hsiao CK, Chen CJ, Lee LA, Hung PT. Epidemiologic study of the prevalence and severity of myopia among schoolchildren in Taiwan in 2000. *J Formos Med Assoc.* (2001) 100:684–91.

32. Albrecht May C. Morphologic characteristics of the human ciliary muscle. *New Front Ophthalmol.* (2017) 3:1–6. doi: 10.15761/NFO.1000168

33. Flügel-Koch CM, Croft MA, Kaufman PL, Lütjen-Drecoll E. Anteriorly located zonular fibres as a tool for fine regulation in accommodation. *Ophthalmic Physiol Opt.* (2016) 36:13–20. doi: 10.1111/opo.12257

34. Pan JL, Cai G, Yin R. Bin, Sun L, Wang GX. Research on the relationship between physical exercise and children's dynamic vision under the background of vision rehabilitation and enlightenment. *Sport Sci Res.* (2019) 40:90–5.

35. Khalid K, Padda J, Pokhriyal S, Hitawala G, Khan MS, Upadhyay P, et al. Pseudomyopia and its association with anxiety. *Cureus.* (2021) 13:17411. doi: 10.7759/cureus.17411

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 15 September 2022
DOI 10.3389/fpubh.2022.1010236

Check for updates

OPEN ACCESS

EDITED BY
Stevo Popovic,
University of Montenegro, Montenegro

REVIEWED BY
Cristian Petri,
Universidad Pablo de Olavide, Spain
Mario Mauro,
University of Bologna, Italy

*CORRESPONDENCE
Flavia Figlioli
flavia.figlioli@unipa.it

SPECIALTY SECTION
This article was submitted to Children and Health, a section of the journal Frontiers in Public Health

RECEIVED 02 August 2022
ACCEPTED 29 August 2022
PUBLISHED 15 September 2022

CITATION
Patti A, Giustino V, Figlioli F, Miceli M, Barca M, Drid P, Palma A and Bianco A (2022) The role of school physical education on adolescents' fitness levels during the pandemic period from COVID-19: An observational study of the Italian scientific high school—section sport and physical activity.
Front. Public Health 10:1010236.
doi: 10.3389/fpubh.2022.1010236

The role of school physical education on adolescents' fitness levels during the pandemic period from COVID-19: An observational study of the Italian scientific high school—section sport and physical activity

Antonino Patti[1], Valerio Giustino[1], Flavia Figlioli[1]*, Matteo Miceli[1], Martina Barca[1], Patrik Drid[2], Antonio Palma[1] and Antonino Bianco[1]

[1]Sport and Exercise Sciences Research Unit, Department of Psychology, Educational Science and Human Movement, University of Palermo, Palermo, Italy, [2]Faculty of Sport and Physical Education, University of Novi Sad, Novi Sad, Serbia

Objectives: In Italy, in 2013, a new school curriculum with a sport character was established in high schools, called Sports High School (SHS). The aims of this study were: (1) to assess the fitness levels of SHS students who, respecting all the safety rules to limit the spread of COVID-19, practiced physical education (PE) at school with continuity for almost all of 2021, and to compare them with Traditional High School (THS) students; (2) to evaluate as the SHS may have influenced the fitness levels in adolescents.

Methods: This is a case-control study in which thirty participants were enrolled (SHS: $n = 15$; THS: $n = 15$). To assess the fitness levels, the following tests were administered: the Static Baropodometric and Stabilometric Analyses, the Counter Movement Jump (CMJ), and the Handgrip test. All these tests were administered when the non-pharmaceutical interventions (NPIs) for COVID-19 allowed the resumption of PE lessons (T0) and 2 months after their resumption (T1).

Results: Unpaired *t*-test between SHS (T0) vs. THS (T0) showed significant differences between: Handgrip test Dx and Handgrip test Sx (both $p < 0.001$), Surface Sx foot and Surface Dx foot (both $p < 0.05$), and CMJ ($p < 0.001$). These results were also confirmed in T1. The performance analysis between T0 and T1 of both SHS and THS showed improvements in SHS: Handgrip test Dx ($p < 0.05$; $d = 0.57$), Handgrip test Sx ($p < 0.01$; $d = 0.87$), and CMJ ($p < 0.05$; $d = 0.59$). Pearson's analysis of the results of the tests showed significant strong correlations between: Handgrip test Dx and Handgrip test Sx ($R = 0.959$; $p < 0.001$), Handgrip test Dx and CMJ ($R = 0.881$; $p < 0.001$), Handgrip test Sx and CMJ ($R = 0.893$; $p < 0.001$). The same analysis showed significant but moderate correlations between: Surface foot Sx and CMJ ($R = 0.489$; $p < 0.01$), Surface foot Sx and y-mean ($R = 0.485$; $p < 0.01$), Surface foot Dx and CMJ ($R = 0.444$; $p < 0.05$).

Conclusions: This study is in agreement with the literature showing that the quarantine period and the NPIs for COVID-19 caused a decrease in fitness levels in adolescents. Our results showed that students of SHS recorded higher strength performance both in the Handgrip test and in the CMJ.

KEYWORDS

school, physical education, physical activity, Handgrip strength, vertical jump height, vertical jump performance, jumping performance, body posture

Introduction

In Italy, the objectives of school education are defined by the National Guidelines. Physical activity (PA) is related with several health benefits and is widely recognized as an essential determinant of adolescents physical and psychosocial health and wellbeing (1, 2). According to these National Guidelines, the general aim of the school is the harmonious and comprehensive development of the individual (3). In Italy, in 2013, a new school curriculum with a sport character was established in high schools, called Sports High School (SHS) (4). This curriculum is aimed at the study of sports sciences and PA. In addition, unlike the traditional curriculum, that is Traditional High School (THS), it provides for the practice of sport and PA and from 2 to 6 h weekly in the first 2 years, and 5 h in the last 3 years, significantly increasing the annual hours that students dedicate to physical education (PE) at school.

In 2019, to counteract the coronavirus disease-2019 (COVID-19), the Italian government adopted containment measures to control the virus' spread known as non-pharmaceutical interventions (NPIs). Among the NPIs, schools and SHS have been closed and PE have been suspended (5). Even when school activity returned to normal, PE continued to have severe limitations throughout 2021. However, in the same year, the Italian Ministry of Public Education issued a clarification regarding the specific skills that can only be achieved through regular and constant practice (6). In particular, at the end of the 5-year period, students in SHS must acquire the specific knowledge and skills of the various individual and team sports envisaged by their characterizing school curriculum. To this end, these students have had priority in accessing school sports facilities while respecting social distancing and contingency of sports spaces (7).

The literature suggests that schools play an essential role in combating physical inactivity and in ensuring good health (1). In 2016, the World Health Organization (WHO) identified schools as the optimal context to implement and guarantee adequate levels of PA (8). Adequate levels of PA are considered to be at least 60 min per day, most of this PA should be aerobic (9).

These unique circumstances have allowed us to study some aspects of the influence of the PE programs of the Italian school. The purpose of this study was double: (1) the first aim was to assess the fitness levels of SHS students who, respecting all the safety rules to limit the spread of COVID-19, practiced PE at school with continuity for almost all of 2021, and to compare them with THS students who have experienced greater limitations in practicing PE as a result of the restrictions; (2) analyzing a 2-month of follow-up, the second aim was to evaluate as a specific school curriculum aimed at the study of sports sciences and PA, that increases the annual hours that students dedicate to PE at high school, may have influenced the fitness levels in young adolescents compared to students of traditional school curriculum. To the best of our knowledge, this is the first study that evaluated the effects of this specific school curriculum, established in Italy in 2013 with the name of "Scientific high school—section sport and physical activity" (4).

Materials and methods

Study design and procedure

This is a case-control study in which participants were students of the same high school located in Sicily Region (Italy). Participants of the SHS group were part of a high school class with a sport curriculum, while the THS group was composed of students attending classes with a traditional PE curriculum. Written informed consent was obtained before participating in the study from parents' participants. The STROBE guidelines were used to ensure a high-quality presentation of the conducted observational study (10). The study was carried out in compliance with the principles of the Declaration of Helsinki and approved by the Bioethics Committee of the University of Palermo (Num. 77/2022 - Prot. 35307).

10.3389/fpubh.2022.1010236

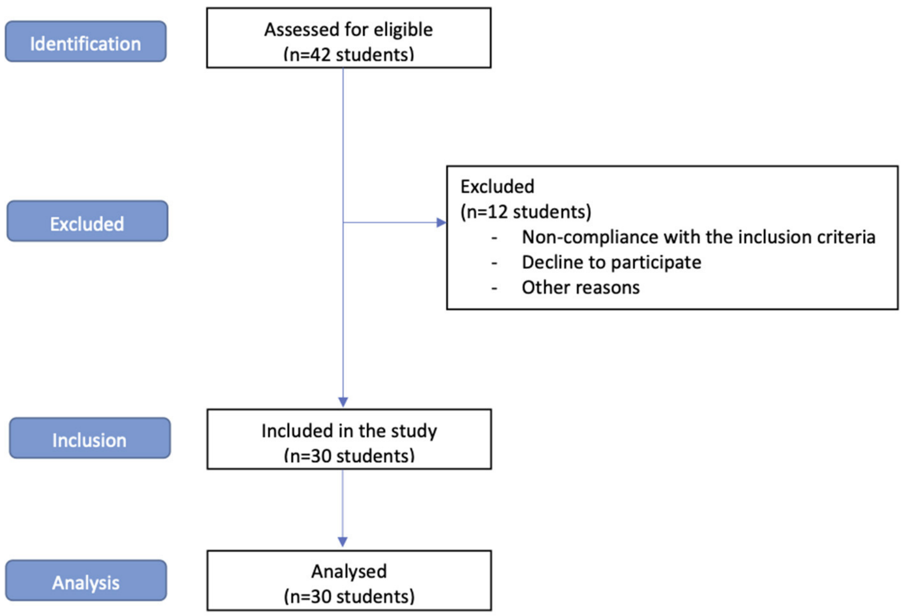

FIGURE 1
STROBE flow chart.

Participants

Forty-two subjects were considered for the study but twelve of them did not meet the inclusion criteria or declined their participation. Hence, thirty subjects were enrolled in this study (Figure 1). Fifteen attended classes with a sport curriculum and fifteen attended classes with a traditional PE curriculum. To be eligible for the study, students met the following inclusion criteria: (a) they did not have to play professional sports or structured PA in sports clubs during after-school hours; (b) they were not have any deficits or illnesses affecting sports and fitness performance; (c) during the pandemic period they had not carried out any PA with sports professionals other than those activities authorized by the school.

Sports high school vs. traditional high school

The SHS was established in Italy in 2013 with the name of "Scientific high school—section sport and physical activity" (4). The SHS is a 5-year upper secondary school that combines the theme of the traditional Italian scientific high school with a substantial increase in the hours of lessons dedicated to PE and the study of sport and PA in general. This topic is also dealt in other disciplines, such as Sports Law and Economics. The SHS aims to combine an in-depth and harmonious culture, both in the humanistic and scientific fields, through the promotion of the educational value of sport. This specific high school is characterized by the strengthening of physical and sports sciences. In particular, at the end of the course, students who attend a scientific high school with a sport curriculum must: (a) know how to apply the methods of sport practice in various fields, (b) know how to elaborate the critical analysis of sport, the methodological on sport and the experimental procedures on it, (c) know how to search for strategies aimed at promoting the discovery of the multidisciplinary and social role of sport, (d) knowing how to deepen the knowledge and practice of the various sports (4). In detail, in the first 2 years, the students of this curriculum dedicate 3 h per week to PE and further 3 h dedicated to specific sports activities. In the following 3 years, the hours dedicated to PE became two per week while those dedicated to specific sports activities remained three. On the other hand, the traditional curriculum of Italian high schools provides only 2 h per week of PE.

Measurements

To assess the fitness levels, the following tests were administered: the Static Baropodometric and Stabilometric Analyses, the Counter Movement Jump (CMJ), and the Handgrip test. All these tests were administered when the non-pharmaceutical interventions (NPIs) for COVID-19 allowed the resumption of PE lessons for all students enrolled in the study

10.3389/fpubh.2022.1010236

(T0) and 2 months after the resumption of PE lessons in which they restarted normally and continuously for both groups (T1).

Static Baropodometric and Stabilometric Analyses were carried out using the FreeMed system (FreeStep v.1.0.3 software, Sensor Medica, Guidonia Montecelio, Roma, Italy). The platform's sensors are 24 K gold and this allows a high reliability. Using the Romberg test position, all participants were administered a baropodometric and a stabilometric analysis (11). The parameters considered were: Surface Sx foot (left), Surface Dx foot (right) for the baropodometric analysis, and Sway Path Length (mm), Ellipse Surface Area (mm^2), x-mean (mm), y-mean (mm), and Average Speed of Movement (mm/s) for the stabilometric analysis (12).

Counter Movement Jump (CMJ) test was administered with the Microgate system. It is an optical detection system composed of a transmitting and a receiving bar. The system allows the measurement of flight and contact times during the execution of a series of jumps, with a precision of 1/1,000 of a second. Starting from these fundamental basic data, the dedicated software allows to obtain a series of parameters related to performance with maximum precision and in real-time (13).

TABLE 1 Unpaired *t*-test analysis of the anthropometric measures between SHS (T0) and THS (T0).

	SHS (T0) (*n* = 15)	THS (T0) (*n* = 15)	*p*
Age, y	17 ± 1.25	16.2 ± 1.42	0.14
Height, cm	167.93 ± 8.40	167.86 ± 10.41	0.98
Weight, kg	61.80 ± 9.15	61.20 ± 12.29	0.87
Shoe number	40.86 ± 2.99	40.60 ± 3.64	0.83
BMI	21.83 ± 2.07	21.59 ± 2.91	0.80
BMI Z-Score	0.11 ± 0.81	0.09 ± 1.03	0.95

SHS, Sports High School; THS, Traditional High School.

TABLE 2 Unpaired t-test analysis between SHS (T0) vs. THS (T0).

	SHS (T0) (*n* = 15)	THS (T0) (*n* = 15)	*p*	Effect size *Cohen's d*
Handgrip Dx (kg)	38.72 ± 7.74	21.26 ± 6.83	0.001	2.75
Handgrip Sx (kg)	35.44 ± 6.52	19.24 ± 6.62	0.001	2.32
Surface left (Sx, cm^2)	84.33 ± 21.40	64.67 ± 12.93	0.05	0.75
Surface right (Dx, cm^2)	82.13 ± 20.95	64.86 ± 9.76	0.05	0.76
CMJ (cm)	37.6 ± 8.70	19.66 ± 4	0.001	3.55
Sway path length (mm)$^{\Phi}$	402.53 ± 118.5	385.1 ± 98.85	0.6	0.12
Ellipse surface area (mm^2)$^{\Phi}$	245.33 ± 191.89	273.94 ± 261.12	0.9	0.08
x-mean (mm)	−1 ± 13.75	−1.08 ± 12.76	0.98	0.003
y-mean (mm)	−26.95 ± 25.36	−24.51 ± 14.40	0.73	0.08
Average speed of movement (mm/s)$^{\Phi}$	8.03 ± 2.32	7.73 ± 1.99	0.86	0.11

SHS, Sports High School; THS, Traditional High School; CMJ, Counter Movement Jump; Dx, right; Sx, left; Φ, non-parametric analysis.

TABLE 3 Unpaired t-test analysis between SHS (T1) vs. THS (T1).

	SHS (T1) (*n* = 15)	THS (T1) (*n* = 15)	*p*	Effect size *Cohen's d*
Handgrip Dx (kg)	41.08 ± 8.29	20.58 ± 6.15	0.001	2.98
Handgrip Sx (kg)	38 ± 6.56	20.21 ± 6.47	0.001	2.22
Surface left (Sx, cm^2)	89 ± 24.17	61.46 ± 9.15	0.01	0.91
Surface right (Dx, cm^2)	83.86 ± 24.68	65.13 ± 8.99	0.05	0.67
CMJ (cm)	44 ± 9.04	21.17 ± 5.71	0.001	1.88
Sway path length (mm)$^{\Phi}$	375.60 ± 118.5	401.2 ± 103.27	0.33	0.16
Ellipse surface area (mm^2)$^{\Phi}$	218.55 ± 186.27	231.31 ± 165.31	0.6	0.04
x-mean (mm)	−1.41 ± 12.31	0.61 ± 10.93	0.69	0.10
y-mean (mm)	−24.81 ± 21.54	−24.51 ± 14.40	0.99	0.003
Average speed of movement (mm/s)$^{\Phi}$	8.5 ± 2.84	8.49 ± 1.65	0.40	0.004

SHS, Sports High School; THS, Traditional High School; CMJ, Counter Movement Jump; Dx, right; Sx, left.
Φ, non-parametric analysis.

Handgrip test aims to measure the maximum isometric strength exerted by the upper limb muscles. The literature suggests that the Handgrip test has a predictive value and correlation with the fitness levels (14–17).

Statistical analysis

All numerical data were entered into an Excel sheet before being analyzed. Descriptive statistics were reported as mean ± standard deviation. Shapiro–Wilk's normality test was used to analyze data distribution. *Post hoc* sample size power analysis was computed to estimate the level of power achieved for the sample size using G*Power software 3.1.9.2 (Heinrich Heine University, Düsseldorf, Germany). The comparison of the two groups at T0 and at T1 was performed with unpaired Student's *t*-test, and Mann-Whitney test has been used when appropriate. The comparison of the same group over time (T0 to T1) was performed with paired Student's *t*-test, and Wilcoxon matched-pairs test has been used when appropriate. For each outcome, Cohen's *d* was calculated. Pearson's correlation coefficient was used to analyze any correlations between the variables of the tests. A *p*-value lower than 0.05 (95% confidence) was considered useful. Statistical analyses were conducted using Jamovi software (version 2.3.0.0) and GraphPad Prism 8.0.

Results

Post-hoc sample size power analysis ($f = 0.25$, $\alpha = 0.05$) showed that, with a total sample size of 30 participants (SHS: $n = 15$; THS: $n = 15$), we achieved a power of 75%. Table 1 shows anthropometric characteristics of the participants. No significant differences on anthropometric characteristics between groups were found. Table 2 and Figure 2 show unpaired *t*-test analysis between SHS (T0) vs. THS (T0). Table 3 shows the analysis between SHS (T1) vs. THS (T1). Table 4 and Figure 3 show the performance analysis between T0 and T1 of both the SHS and the THS. Pearson's analysis of the results of the tests showed significant strong correlations between: Handgrip test Dx and Handgrip test Sx ($R = 0.959$; $p < 0.001$), Handgrip test Dx and CMJ ($R = 0.881$; $p < 0.001$), Handgrip test Sx and CMJ ($R = 0.893$; $p < 0.001$). The same analysis showed significant but moderate correlations between: Surface foot Sx and CMJ ($R = 0.489$; $p < 0.01$), Surface foot Sx and y-mean ($R = 0.485$; $p < 0.01$), Surface foot Dx and CMJ ($R = 0.444$; $p < 0.05$).

Discussion

The literature suggests that physical fitness is a significant health marker already in adolescents (18).

To the best of our knowledge, there are no studies in the literature that analyzed the effects of specific school curriculum

TABLE 4 Paired Student's *t*-test analysis between SHS (T0) vs. SHS (T1) and THS (T0) vs. THS (T1).

	SHS (T0) ($n = 15$)	SHS (T1) ($n = 15$)	$p <$	Effect size Cohen's *d*	THS (T0) ($n = 15$)	THS (T1) ($n = 15$)	p	Effect size Cohen's *d*
Handgrip Dx (kg)	38.72 ± 7.74	41.08 ± 8.29	0.05	0.57	21.26 ± 6.83	20.58 ± 6.15	0.48	0.18
Handgrip Sx (kg)	35.44 ± 6.52	38 ± 6.56	0.01	0.87	19.24 ± 6.62	20.21 ± 6.47	0.23	0.32
Surface left (Sx, cm^2)	84.33 ± 21.40	89 ± 24.17	0.60	0.13	64.67 ± 12.93	61.46 ± 9.15	0.51	0.17
Surface right (Dx, cm^2)	82.13 ± 20.95	83.86 ± 24.68	0.85	0.04	64.86 ± 9.76	65.13 ± 8.99	0.94	0.01
CMJ (cm)	37.6 ± 8.70	44 ± 9.04	0.05	0.59	19.66 ± 4	21.17 ± 5.71	0.39	0.25
Sway path length (mm) $^{\Phi}$	402.53 ± 118.5	375.60 ± 118.5	0.48	0.16	385.1 ± 98.85	401.2 ± 103.27	0.93	0.13
Ellipse surface area (mm^2) $^{\Phi}$	245.33 ± 191.89	218.55 ± 186.27	0.84	0.09	273.94 ± 261.12	231.31 ± 165.31	0.56	0.16
x-mean (mm)	−1 ± 13.75	−1.41 ± 12.31	0.92	0.02	−1.08 ± 12.76	0.61 ± 10.93	0.70	0.10
y-mean (mm)	−26.95 ± 25.36	−24.81 ± 21.54	0.81	0.06	−24.51 ± 14.40	−24.51 ± 14.40	0.96	0.01
Average speed of movement (mm/s) $^{\Phi}$	8.03 ± 2.32	8.5 ± 2.84	0.76	0.12	7.73 ± 1.99	8.49 ± 1.65	0.28	0.36

SHS, Sports High School; THS, Traditional High School; CMJ, Counter Movement Jump; Dx, right; Sx, left.
Φ, non-parametric analysis.

aimed at the study of sports sciences and PA on the fitness levels in adolescents. Moreover, the period in which the study was conducted allowed us to estimate the possible contribution of both this sport curriculum and the traditional PE of Italian high schools in adolescents.

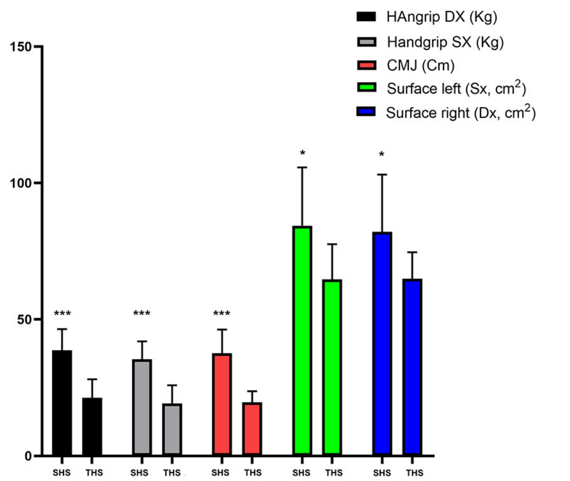

FIGURE 2
Analysis between SHS (T0) vs. THS (T0). * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

In our opinion, the results of this study are particularly interesting. In fact, the main results of this study are related to the performance of SHS and THS students. Our results showed that students of SHS recorded higher strength performance both in the CMJ test and in the Handgrip test. In detail, as for the CMJ test, the THS showed significant lower values than the SHS. This result is critical for the health of adolescents. As a matter of fact, some studies described how lower limb performance is an important health marker (18–21). Indeed, it is widely known that muscle strength and cardiorespiratory endurance are considered key indicators of human health (22). In the same way, the handgrip test is used as a marker of fitness level or predictor of future health conditions. Many research groups have emphasized the work of assessing the health status of adolescents and children (11, 23). These authors developed some fitness battery tests applicable in children and adolescents as the ALPHA fitness test battery, the ASSO project, and the PREFIT (11, 14, 23, 24).

As concern the PA levels during COVID-19, of particular interest for the Italian population is the study by Giustino et al. in which authors showed significantly lower levels of PA among the physically active Sicilian population during the quarantine compared to before the quarantine at all ages

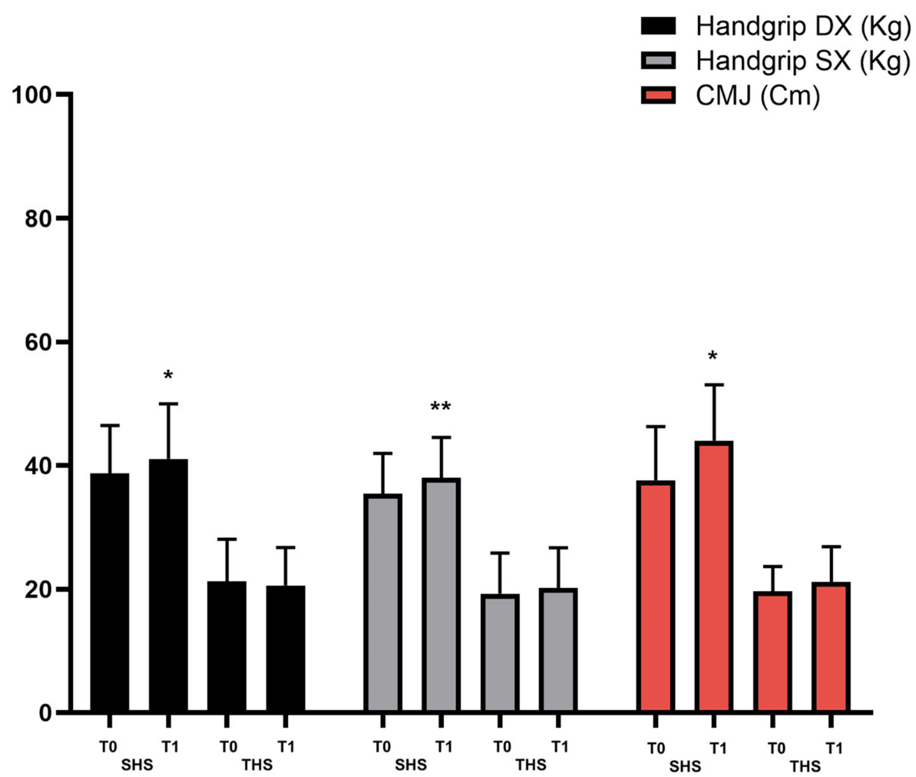

FIGURE 3
Analysis between SHS (T0) vs. SHS (T1) and THS (T0) vs. THS (T1). * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

(25). This trend also occurs in other countries. In fact, other research groups around the world have found a decrease in the practice of physical activity as a consequence of COVID-19 (26). Our results are in line with these studies, in fact, the students who practiced PE (SHS) have minimized the deficits in their fitness levels compared to peers who did not practice PE (THS) during the pandemic period. In fact, as abovementioned, this study allowed us to estimate the effects of school PE both in SHS and THS. In Table 4, the results showed that 2 months of traditional school PE did not improve fitness levels in adolescents. On the other hand, in the same period considered, the students who attended the SHS classes showed improved performance in handgrip test Dx, handgrip test Sx, and CMJ. Cohen's *d* analysis showed a medium/large effect size in these measures.

The limitation of this study is that we only evaluated strength and balance performance and we did not considered the assessment of cardiorespiratory performance. Further studies also with a larger sample are needed to confirm our findings.

Conclusion

This study confirmed previous research present in the literature in which is reported that the quarantine period and the NPIs for COVID-19 caused a decrease in fitness levels in adolescents. However, this new school curriculum with a sport character established in Italy in high schools and called Sports High School (SHS) has shown not only to have positive effects in preserving the fitness levels of adolescents during the pandemic period, but also after 2-month of follow-up the students of SHS showed significant improvements in both lower and upper limb strength. This trend was not present in the THS group. School PE plays an important role in improving fitness levels in children and adolescents. However, our results suggest the need to increase hours per week of school PE as a strategy for improving fitness levels in adolescents.

Data availability statement

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

Ethics statement

The studies involving human participants were reviewed and approved by Independent Ethics Committee the University of Palermo (No. 77/2022 -Prot. 35307). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

AB and APat: conceptualization. VG, FF, and MM: data collection. APat: data analysis. APat, VG, and MB: methodology. AB: supervision. PD and APal: visualization. APat: writing—original draft. VG and APal: writing—review and editing. All authors contributed to the article and approved the submitted version.

Funding

The publication was made with the co-financing of the European Union - FESR or FSE, PON Research and Innovation 2014-2020 - DM 1062/2021.

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. Schmidt SK, Bratland-Sanda S, Bongaardt R. Young adolescents' lived experience with teacher-led classroom-based physical activity: a phenomenological study. *Teach Teach Educ.* (2022) 116:103777. doi: 10.1016/j.tate.2022.103777

2. Biddle SJ, Asare M. Physical activity and mental health in children and adolescents: a review of reviews. *Br J Sports Med.* (2011) 45:886–95. doi: 10.1136/bjsports-2011-090185

3. D'Elia F. Teachers' perspectives about contents and learning aim of physical education in Italian primary school. *J Hum Sport Exerc.* (2020) 15:S279–88. doi: 10.14198/jhse.2020.15.Proc2.19

4. D.P.R. Regolamento di organizzazione dei percorsi della sezione ad indirizzo sportivo del sistema dei licei. Gazzetta Ufficiale (2013). 3, comma 2, del decreto del Presidente della Repubblica 15 marzo (2010). n. 89.

5. Ordinanza 20 Marzo (2020). Gazzetta Ufficiale Della Repubblica Italiana, Serie Generale - n. 73 del 20 Marzo (2020). Available online at: https://www.gazzettaufficiale.it/eli/gu/2020/03/20/73/sg/pdf (2020).

6. Decreto del Presidente del Consiglio dei Ministri del 03/12/2020 - Presidenza Consiglio dei Ministri. Available online at: https://def.finanze.it/DocTribFrontend/getAttoNormativoDetail.do?ACTION=getSommario&id=3DFAFC03-AD15-429A-815B-AB9489AB0B50 (2020).

7. Nota Miur 1779 del 27-01-2021 Available online at: http://www.istruzionepiemonte.it/wp-content/uploads/2021/02/m_pi.AOODGOSV.REGISTRO-UFFICIALEU.0001779.27-01-2021-1.pdf. (2021).

8. Organization WH. Physical activity strategy for the WHO European Region 2016-2025. (2016).

9. Tremblay MS, Carson V, Chaput JP, Connor Gorber S, Dinh T, Duggan M, et al. Canadian 24-hour movement guidelines for children and youth: an integration of physical activity, sedentary behaviour, and sleep. *Appl Physiol Nutr Metab.* (2016) 41:S311–27. doi: 10.1139/apnm-2016-0151

10. Cuschieri S. The STROBE guidelines. *Saudi J Anaesth.* (2019) 13:S31–4. doi: 10.4103/sja.SJA_543_18

11. Patti A, Maggio MC, Corsello G, Messina G, Iovane A, Palma A. Evaluation of fitness and the balance levels of children with a diagnosis of juvenile idiopathic arthritis: a pilot study. *Int J Environ Res Public Health.* (2017) 14:806. doi: 10.3390/ijerph14070806

12. Patti A, Bianco A, Messina G, Iovane A, Alesi M, Pepi A, et al. Evaluation of podalic support and monitoring balance control in children with and without dyslexia: a pilot study. *Sustainability.* (2020) 12:1191. doi: 10.3390/su12031191

13. Montalvo S, Gonzalez MP, Dietze-Hermosa MS, Eggleston JD, Dorgo S. Common vertical jump and reactive strength index measuring devices: a validity and reliability analysis. *J Strength Cond Res.* (2021) 35:1234–43. doi: 10.1519/JSC.0000000000003988

14. Bianco A, Mammina C, Jemni M, Filippi AR, Patti A, Thomas E, et al. A fitness index model for Italian adolescents living in Southern Italy: the ASSO project. *J Sports Med Phys Fitness.* (2016) 56:1279–88.

15. Garcia-Pinillos F, Delgado-Floody P, Martinez-Salazar C, Latorre-Roman PA. Responsiveness of the countermovement jump and handgrip strength to an incremental running test in endurance athletes: influence of sex. *J Hum Kinet.* (2018) 61:199–208. doi: 10.1515/hukin-2017-0121

16. Zhou M, Zha F, Chen Y, Liu F, Zhou J, Long J, et al. Handgrip strength-related factors affecting health outcomes in young adults: association with cardiorespiratory fitness. *Biomed Res Int.* (2021) 2021:6645252. doi: 10.1155/2021/6645252

17. Katsimpris A, Jurgens C, Ludtke L, Martin B, Ittermann T, Glaser S, et al. Association between cardiorespiratory fitness and handgrip strength with age-related macular degeneration: a population-based study. *Br J Ophthalmol.* (2021) 105:1127–32. doi: 10.1136/bjophthalmol-2020-316255

18. Ortega FB, Ruiz JR, Castillo MJ, Sjostrom M. Physical fitness in childhood and adolescence: a powerful marker of health. *Int J Obes.* (2008) 32:1–11. doi: 10.1038/sj.ijo.0803774

19. Petrigna L, Karsten B, Marcolin G, Paoli A, D'Antona G, Palma A, et al. A review of countermovement and squat jump testing methods in the context of public health examination in adolescence: reliability and feasibility of current testing procedures. *Front Physiol.* (2019) 10:1384. doi: 10.3389/fphys.2019.01384

20. King MM, Levy SM, Carr LJ, Janz KF, Barr-Anderson D. Vertical jump test as a health-promotion screening tool for predicting bone strength in young adults. *Med Sci Sports Exerc.* (2017) 49:400. doi: 10.1249/01.mss.0000517975.40993.e8

21. Giustino V, Messina G, Patti A, Padua E, Zangla D, Drid P, et al. Effects of a postural exercise program on vertical jump height in young female volleyball players with knee valgus. *Int J Environ Res Public Health.* (2022) 19:3953. doi: 10.3390/ijerph19073953

22. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.* (1985) 100:126–31.

23. Ruiz JR, Espana Romero V, Castro Pinero J, Artero EG, Ortega FB, Cuenca Garcia M, et al. [ALPHA-fitness test battery: health-related field-based fitness tests assessment in children and adolescents]. *Nutr Hosp.* (2011) 26:1210–4. doi: 10.1590/S0212-16112011000600003

24. Ortega FB, Artero EG, Ruiz JR, Espana-Romero V, Jimenez-Pavon D, Vicente-Rodriguez G, et al. Physical fitness levels among European adolescents: the HELENA study. *Br J Sports Med.* (2011) 45:20–9. doi: 10.1136/bjsm.2009.062679

25. Giustino V, Parroco AM, Gennaro A, Musumeci G, Palma A, Battaglia G. Physical activity levels and related energy expenditure during COVID-19 quarantine among the Sicilian active population: a cross-sectional online survey study. *Sustainability.* (2020) 12:4356. doi: 10.3390/su12114356

26. Gjaka M, Feka K, Bianco A, Tishukaj F, Giustino V, Parroco AM, et al. The effect of COVID-19 lockdown measures on physical activity levels and sedentary behaviour in a relatively young population living in Kosovo. *J Clin Med.* (2021) 10:763. doi: 10.3390/jcm10040763

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 24 September 2022
DOI 10.3389/fpubh.2022.995755

OPEN ACCESS

EDITED BY
Bojan Masanovic,
University of Montenegro, Montenegro

REVIEWED BY
Narlon C. Boa Sorte Silva,
University of British Columbia, Canada
Célia Kingsbury,
Université de Montréal, Canada
Kam Pui Eric Lee,
The Chinese University of Hong Kong, China

*CORRESPONDENCE
Xingqi Wang
6020160037@jsnu.edu.cn
Yujia Liu
liuyujia89@jsnu.edu.cn

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

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 16 July 2022
ACCEPTED 09 September 2022
PUBLISHED 24 September 2022

CITATION
Zhou L, Feng W, Xiang N, Cheng Y, Ya X, Wang M, Wang X and Liu Y (2022) Association between physical activity dimensions and the risk of hypertension among middle and older adults: A cross-sectional study in China. *Front. Public Health* 10:995755. doi: 10.3389/fpubh.2022.995755

Association between physical activity dimensions and the risk of hypertension among middle and older adults: A cross-sectional study in China

Linlin Zhou[1†], Wei Feng[2†], Na Xiang[3], Yue Cheng[1], Xudong Ya[1], Mingxia Wang[1], Xingqi Wang[4]* and Yujia Liu[1]*

[1]Institute of Physical Education, Jiangsu Normal University, Xuzhou, China, [2]Department of Physical Education, Suzhou University, Suzhou, China, [3]Caoxian People's Hospital, Heze, China, [4]School of Life Science, Biomedical R&D Center, Jiangsu Normal University, Xuzhou, China

Background: It is known that insufficient physical activity is associated with the risk of hypertension, but the relationship to different physical activity dimensions within hypertension risk remains to be elucidated.

Objective: The objective of this study is to identify the association between physical activity intensity, frequency, duration, and volume with hypertension risk. Meanwhile, a dose-response experiment is conducted to determine the relationship between physical activity level and hypertension risk.

Methods: Data came from the 2018 China Health and Retirement Longitudinal Study (CHARLS, 2018), which included 14266 participants over the age of 45. Binary logistic regression models were established to assess the associations between different dimensions of physical activity and the risk of hypertension. Restricted cubic spline analysis was used to examine possible non-linear associations between physical activity volume and hypertension risk.

Results: For frequency, lower hypertension risk was associated with performing vigorous physical activity 6–7d/w (OR 0.82, 95%CI 0.73–0.93) and moderate physical activity 6–7d/w (OR 0.89, 95%CI 0.80–0.99). No significant association between any light physical activity frequency and hypertension was observed before and after being adjusted. For the duration, lower hypertension risk was observed in performing vigorous physical activity ≥240 min/d (OR 0.85, 95%CI 0.75–0.97) and moderate physical activity ≥240 min/d (OR 0.83, 95%CI 0.71–0.97). For volume, the risks of hypertension in the participants who reported TPA in the 3th and 4th of quantiles were reduced by 18% (OR 0.82, 95%CI 0.72–0.95) and 22% (OR 0.78, 95%CI 0.68–0.91). A non-linear dose-response association between total physical activity and the risk of hypertension was shown among all of the participants (P non-linearity < 0.05).

Conclusion: Higher frequency and longer duration of vigorous physical activity or moderate physical activity were significantly associated with a lower risk of hypertension. Higher physical activity levels were associated with a lower risk of hypertension and there was an inverse non-linear dose-response relationship between weekly total physical activity and the risk of hypertension.

These findings provide further proof that hypertension could be prevented through increased physical activity.

KEYWORDS

hypertension risk, middle and older adults, restricted cubic spline, dose-response relationship, physical activity

Introduction

Hypertension is one of the most common chronic diseases worldwide (1), and it is the leading risk factor for cardiovascular disease (2). Hypertension can lead to serious health problems such as heart disease, stroke, as well as possible death if left uncontrolled (3). About 1 billion people are living with hypertension worldwide (4), and more than 1.56 billion people will have elevated hypertension in 2025 (1, 5). Likewise, hypertension is common in China. A large-scale epidemiological survey in 2013 showed that the prevalence of hypertension among Chinese adults was as high as 27.8% (6). Studies have shown that many factors are related to the risk of hypertension such as obesity, alcohol consumption, sodium intake, and physical inactivity (7–10). However, previous data showed that more than 40% of the elderly in China are still physically inactive (11). In addition, the prevalence of hypertension increases with age (12). Promoting adequate physical activity in middle-aged and older adults to prevent hypertension is a key issue.

Increased physical activity (PA) was effective in the treatment and prevention of hypertension, this viewpoint has been confirmed by many studies (13–15). An inverse dose-response association between levels of PA and hypertension was demonstrated in a meta-analysis (16). But this association may vary according to sex and age. An early study suggested that increased total amount of energy expenditure during PA was statistically associated with reduced risk of hypertension among men but not among women (17). Additionally, Cohen et al. (18) found age differences in the association between PA and hypertension, the association between high levels of PA and the prevention of hypertension was weaker among older women when compared to younger women. What's more, there were also inconsistent results regarding the association between the intensity of PA and the risk of hypertension. It was reported that vigorous physical activity (VPA) is associated with a reduced risk of hypertension, and VPA was far more effective than moderate physical activity (MPA) or light physical activity (LPA) in the prevention of hypertension (19). An earlier study, however, found that the addition of VPA cannot offer additional benefits in the prevention of hypertension (20). The optimal prescription (intensity, duration, frequency and volume) for the prevention and treatment of hypertension remains elusive.

Further investigation of the association between physical activity to hypertension is still required. We hypothesized that higher intensity, frequency, duration and volume of physical activity would each be associated with reduced hypertension risk. Therefore, this study aimed to assess the association of hypertension with various dimensions of PA and to assess whether there were gender and age differences in the dose-response relationship between PA and the risk of developing hypertension.

Abbreviations: PA, physical activity; CHARLS, China Health and Retirement Longitudinal Study; RCS, restricted cubic spline; VPA, vigorous physical activity; MPA, moderate physical activity; LPA, light physical activity; TPA, total physical activity; MET, Metabolic equivalent of task; OR, Odds ratio; Cis, confidence intervals.

Materials and methods

Participants

This cross-sectional study was done based on the China Health and Retirement Longitudinal Study (CHARLS) survey in 2018. CHARLS is a nationally representative survey of Chinese middle-aged and elderly people conducted by the National School for Development (China Center for Economic Research) in collaboration with Peking University's Institute for Social Science Survey. The survey covers 450 urban communities and rural areas in 28 provinces, municipalities, and autonomous regions in China. It was approved by the Biomedical Ethics Review Committee of Peking University (approval number: IRB00001052-11015), and informed consent was required of all participants.

To be included in this study, participants (age $\geq$ 45 years) should have complete data on physical activity record, gender, place of residence, marital status, educational level, sleep status, smoking status, drinking status, annual income, hypertension record. Participants younger than 45 years or with missing data for any of the above will be excluded.

Among 19,752 participants in 2018, we excluded 226 participants aged $<$ 45 years, 5,243 participants with missing hypertension diagnoses data, 12 participants with missing sleep data, and 5 participants with missing smoking data. Finally, 14,266 participants were included in this cross-sectional study. Based on the *post hoc* analysis of sample power using G Power 3.1, the present study population provided a statistical power of 0.99.

Physical activity

A modified version of the validated International Physical Activity Questionnaire Short Form (IPAQ-SF) (21) was used to measure participants' physical activity (see Supplementary material). Each participant was asked, "Do you usually take this type of activity for at least 10 min every week?" Specific types of physical activity include (1) VPA: activities that cause shortness of breath and may include carrying heavy stuff, digging, hoeing, aerobic workout, bicycling at a fast speed, and riding a cargo bike or motorcycle. (2) MPA: activities that make you breathe faster than usual and may include carrying light stuff, bicycling at a normal speed, mopping, Tai-Chi, and speed walking. (3) LPA: such as walking from one place to another place at a workplace or home, and taking a walk for leisure, sports, exercise, or entertainment. If participants answered "no", they would be considered as not engaged in this type of PA during the week. If participants answered "yes", they were further asked about the frequency and duration of each PA intensity. The frequency of PA ranged from 0–7 d/w and was divided into 4 levels: no activity (0 d/w); 1–2 d/w; 3–5 d/w; and 6–7 d/w. The duration of PA was categorized into 5 levels by CHARLS: no activity; 10–29 min/d; 30–119 min/d; 120–239 min/d; and ≥240 min/d. Metabolic equivalent of task (MET) was cited to calculate the volume of physical activity with considerations of intensity. Resting energy expenditure during quiet sitting was defined as one MET. According to the Physical Activity Guidelines Advisory Committee Scientific Report of 2018 (22), we assigned 6.0 METs, 3.1 METs, and 1.6 METs for 1 min of VPA, MPA, and LPA, respectively. The weekly PA volume for each intensity category equals the product of PA frequency, the daily duration of PA, and the value assigned for each category. The total volume of PA (TPA) equals the sum of VPA, MPA, and LPA. Finally, the TPA was classified by quartiles.

Hypertension

Hypertension was defined based on self-reported medical history and measurement of blood pressure (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg). Participants were asked the question "Have you been diagnosed with hypertension by a doctor?" We considered that the individual had hypertension when the response was "yes".

Covariates

Covariates in the present study were age, sex (male, female), marital status (married, separated/divorced/widowed, never married), education (junior high school or less, senior high school and vocational school, college or higher), residency (urban, rural), smoking status (current smoker, quit smoking, never smoked), drinking frequency (≤1/month,>1/month, never) and sleep duration (<7 h,7–8 h, ≥8 h), annual income (<5000 yuan, 5000–10000 yuan, 10000–30000 yuan, 30000–50000 yuan, ≥50000 yuan).

Statistical analysis

The software STATA16.0 was used for data processing and analysis. Categorical variables were expressed as counts and percentages and were compared using the Pearson's chi-squared test. Continuous data are expressed as mean ± SD and analyzed with Student's *t*-test. Binary logistic regression analysis was used to explore the associations between various dimensions of PA and the risk of hypertension, while adjusting for potential confounders. Model 1 was adjusted for demographic characteristics (including age, sex, marital status, education, residency); Model 2 was further adjusted for health-related behaviors (smoking status, drinking frequency, sleep duration). A restricted cubic spline (RCS) was used to assess the dose-response relationship between the risk of hypertension and PA, using the 25th, 50th, and 75th percentiles of the TPA as fixed knots. The RCS models were adjusted for age, sex, marital status, education, residency, smoking status, drinking frequency and sleep duration. Analyses stratified by sex and age were conducted. Missing data were imputed using multiple imputation by chained equations. To test the robustness of the results, we performed a sensitivity analysis with imputed data. All tests were two-tailed, and a probability value of $p < 0.05$ was considered statistically significant. Graph Pad prism 8 was used to draw cubic splines.

Results

Baseline characteristics

Table 1 showed the demographic data of participants. Among 14 266 participants in this study, 2,175 (15.25%) reported having hypertension. The risk of hypertension was significantly correlated with age ($P < 0.001$), sex ($P = 0.006$), marital status ($P < 0.001$), smoking status ($P < 0.001$) and annual income ($P = 0.019$). However, there was no significant difference in drinking frequency, residency, education, and sleep duration between participants with and without hypertension (all $P > 0.05$). Compared with non-hypertensive participants, hypertensive patients had lower weekly TPA. Women and older adults had lower weekly TPA (Supplementary Table S1).

TABLE 1 Baseline characteristics of participants.

Characteristic	Total (N = 14,266)	Hypertension (N = 2,175)	Non-hypertension (N = 12,091)	P-value
Age, years, n (%)				<0.001
<65	9,483	1,224 (56.28)	8,259 (68.31)	
≥65	4,783	951 (43.72)	3,832 (31.69)	
Sex, n (%)				0.006
Male	6,903	1,111 (51.08)	5,792 (47.90)	
Female	7,363	1,064 (48.92)	6,299 (52.10)	
Marital status, n (%)				<0.001
Married or cohabiting	12,371	1,801 (82.80)	10,570 (87.42)	
Separated, divorced or widowed	1,808	364 (16.74)	1,444 (11.94)	
Never married	87	10 (0.46)	77 (0.64)	
Drinking frequency, n (%)				0.192
≤1/month	3,905	575 (26.44)	3,330 (27.54)	
>1/month	1,132	158 (7.26)	974 (8.06)	
Never	9,229	1,442 (66.30)	7,787 (64.40)	
Smoking status, n (%)				<0.001
Current smoker	4,076	585 (26.90)	3,491 (28.87)	
Quit	1,891	385 (17.70)	1,506 (12.46)	
Never	8,299	1,205 (55.40)	7,094 (58.67)	
Residency, n (%)				0.667
Urban	4,003	602 (27.68)	3,401 (28.13)	
Rural	10,263	1,573 (72.32)	8,690 (71.87)	
Education, n (%)				0.566
Junior high school or less	12,421	1,909 (87.77)	10,512 (86.94)	
Senior high school or vocational school	1,723	248 (11.40)	1,475 (12.20)	
College or higher	122	18 (0.83)	104 (0.86)	
Sleep duration, hours, n (%)				0.339
< 7	7,921	1,239 (56.97)	6,682 (55.26)	
7-8	2,507	370 (17.01)	2,137 (17.67)	
≥ 8	3,838	566 (26.02)	3,272 (27.06)	
Annual income, yuan, n (%)				
< 5000	8,972	1,430 (65.75)	7,542 (62.38)	0.019
5000–30000	2,973	430 (19.77)	2,543 (21.03)	
30000–50000	1,444	199 (9.15)	1,245 (10.30)	
≥ 50000	877	116 (5.33)	761 (6.29)	
TPA, MET-mins/week, mean (SD)	5,122 (5629)	4,520 (5365)	5,230 (5669)	<0.001

Logistic regression analysis of physical activity and hypertension

Total physical activity and the risk of hypertension

Table 2 shows the results of logistic regression analysis between TPA and the risk of hypertension. Participants who reported TPA in the 3th and 4th of quartiles had a 25% (OR 0.75, 95%CI 0.65–0.86) and 31% (OR 0.69, 95%CI 0.60–0.79) lower risk of hypertension compared to the first quartile of TPA. After adjusting for confounding factors including age, sex, marital status, education, residency, smoking status, drinking frequency, sleep duration and annual income, the risks of hypertension in the participants who reported TPA in the 3th and 4th of quantiles were reduced by 18% (OR 0.82, 95%CI 0.72–0.95) and 22% (OR 0.78, 95%CI 0.68–0.91), respectively (all $P < 0.01$). The reduction in the risk of hypertension in participants with TPA in second quantile was not statistically significant before and after adjustment ($P > 0.05$). In addition, an inverse association between the TPA level and the risk

TABLE 2 Logistic regression analysis for the associations between TPA and the risk of hypertension.

TPA	*N*	Univariate		Model 1		Model 2	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Q1	2,591	1		1		1	
Q2	4,542	0.91 (0.79, 1.03)	0.136	0.95 (0.83, 1.08)	0.421	0.96 (0.84, 1.09)	0.526
Q3	3,564	0.75 (0.65, 0.86)	<0.001	0.82 (0.71, 0.94)	0.004	0.82 (0.72, 0.95)	0.007
Q4	3,569	0.69 (0.60, 0.79)	<0.001	0.77 (0.67, 0.89)	<0.001	0.78 (0.68, 0.91)	0.001
P for trend		<0.001		<0.001		0.001	

OR, odds ratio; CI, confidence interval; Model 1 was adjusted for age, sex, education, marital status, and residency; Model 2 was further adjusted for smoking status, drinking frequency, sleep duration and annual income.

of hypertension was observed in all three models (P for trend < 0.001).

Frequency of PA and the risk of hypertension

Table 3 indicates the binary logistic regression results for the associations between PA frequency and the risk of hypertension. Compared with inactivity, there was an association between taking part in VPA 1–2 d/w (OR 0.80, 95%CI 0.65–0.99) and the risk of hypertension, but the association became insignificant after adjustment for confounders (Model 1: OR 0.85, 95%CI 0.69 to 1.06; Model 2: OR 0.86, 95%CI 0.69 to 1.07). Taking part in VPA 6–7 d/w (OR 0.77, 95%CI 0.68–0.87) was associated with a lower risk of hypertension, and the association remained statistically significant after adjusting for confounders (Model 1: OR 0.81, 95%CI 0.72–0.92; Model 2: OR 0.82, 95%CI 0.73–0.93). Taking part in MPA 6–7 d/w (OR 0.81, 95%CI 0.73–0.89) was associated with a lower risk of hypertension. After adjustment for confounders, the association attenuated slightly but remained significant (Model 1: OR 0.89, 95%CI 0.80–0.99; Model 2: OR 0.89, 95%CI 0.80–0.99). No association between any LPA frequency and hypertension was observed before and after adjusting.

Duration of PA and the risk of hypertension

Lower risk of hypertension was observed in participants spending 30–119 min (OR 0.82, 95%CI 0.67–0.99) or over 240 min per day (OR 0.79, 95%CI 0.69–0.89) for VPA. Spending 120–239 min (OR 0.84, 95%CI 0.73–0.98) or over 240 min (OR 0.74, 95%CI 0.63–0.86) on MPA each time was correlated with smaller odds of hypertension. Participants performing over 240 min LPA each time had a lower risk of hypertension (OR 0.83, 95%CI 0.70–0.97). After adjusting for age, sex, marital status, education, residency, smoking status, drinking frequency and sleep duration, spending over 240 min on VPA each time and over 240 min on MPA each time was correlated with smaller odds of hypertension (Table 3).

Dose-response relationship between TPA and hypertension

Figure 1 displays the RCS regression analysis result. We observed a non-linear dose-response association between TPA and the risk of hypertension among all of the participants (P non-linearity < 0.05). As the increase of TPA per week, the OR of hypertension markedly decreased. The point estimate of the risk ratio reached 0.85 (95% CI = 0.75–0.95) for activity at 3000 MET-minutes per week, indicating that the probability of having hypertension was 15% lower at that level of physical activity. When TPA reached 4500 MET-minutes per week, the risk of hypertension decreased by 19% (OR 0.81, 95%CI 0.70–0.93). The risk of hypertension no longer decreased significantly when the TPA was increased further.

Subgroup and sensitivity analysis

As shown in Supplementary Figure S1, after sex stratification, there was a linear dose-response association between TPA and the risk of hypertension in male participants (P non-linearity > 0.05). The OR of hypertension decreased sharply as the TPA per week increased. However, no significant relationship was found in female participants. In the age-stratified analyses (Supplementary Figure S2), a nonlinear dose-response relationship was observed in those aged 45–64 (P non-linearity < 0.05). A linear dose-response relationship was observed in those aged ≥ 65 (P non-linearity > 0.05). All of the dose-response relationships revealed an inverse relationship between TPA and the risk of hypertension.

Missing values were imputed by multiple imputation, 19,466 participants were included in the sensitivity analysis. A non-linear dose-response relationship between TPA and the risk of hypertension was similar to the main analysis (Supplementary Figure S3).

TABLE 3 Logistic regression analysis for the associations between PA and the risk of hypertension.

Variables	*N*	Univariate		Model 1		Model 2	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Frequency							
VPA							
No activity	9,374	1		1		1	
1–2 d/w	778	0.80 (0.65, 0.99)	0.043	0.85 (0.69, 1.06)	0.153	0.86 (0.69, 1.07)	0.178
3–5 d/w	1,144	0.95 (0.79, 1.12)	0.517	1.01 (0.85, 1.20)	0.902	1.02 (0.86, 1.21)	0.819
6–7 d/w	2,970	0.77 (0.68, 0.87)	<0.001	0.81 (0.72, 0.92)	0.001	0.82 (0.73, 0.93)	0.003
MPA							
No activity	7,081	1		1		1	
1–2 d/w	945	0.93 (0.77, 1.12)	0.417	0.99 (0.82, 1.19)	0.902	0.99 (0.82, 1.19)	0.885
3–5 d/w	1,460	0.88 (0.75, 1.03)	0.117	0.96 (0.82, 1.12)	0.609	0.96 (0.82, 1.13)	0.619
6–7 d/w	4,780	0.81 (0.73, 0.89)	<0.001	0.89 (0.80, 0.99)	0.034	0.89 (0.80, 0.99)	0.038
LPA							
No activity	2,380	1		1		1	
1–2 d/w	483	0.79 (0.59, 1.06)	0.117	0.83 (0.63, 1.11)	0.214	0.85 (0.64, 1.13)	0.257
3–5 d/w	1,141	1.06 (0.87, 1.28)	0.581	1.15 (0.95, 1.39)	0.162	1.17 (0.96, 1.41)	0.117
6–7 d/w	10,262	0.92 (0.81, 1.04)	0.168	0.96 (0.85, 1.09)	0.560	0.98 (0.87, 1.11)	0.744
Duration							
VPA							
No activity	9,347	1		1		1	
10–29 min/d	139	0.77 (0.47, 1.27)	0.132	0.83 (0.50, 1.37)	0.462	0.84 (0.51, 1.39)	0.509
30–119 min/d	905	0.82 (0.67, 0.99)	0.046	0.87 (0.71, 1.06)	0.176	0.88 (0.72, 1.07)	0.209
120–239 min/d	1,074	0.89 (0.75, 1.07)	0.230	0.93 (0.77, 1.11)	0.400	0.93 (0.77, 1.11)	0.419
≥240 min/d	2,774	0.79 (0.69, 0.89)	<0.001	0.84 (0.74, 0.96)	0.009	0.85 (0.75, 0.97)	0.016
MPA							
No activity	7,081	1		1		1	
10–29 min/d	824	0.84 (0.69, 1.04)	0.107	0.90 (0.73, 1.11)	0.328	0.91 (0.77, 1.12)	0.385
30–119 min/d	2,910	0.90 (0.79, 1.01)	0.083	0.99 (0.87, 1.11)	0.822	0.98 (0.87, 1.11)	0.803
120–239 min/d	1,655	0.84 (0.73, 0.98)	0.029	0.92 (0.79, 1.07)	0.257	0.91 (0.78, 1.06)	0.238
≥240 min/d	1,796	0.74 (0.63, 0.86)	<0.001	0.82 (0.71, 0.96)	0.014	0.83 (0.71, 0.97)	0.017
LPA							
No activity	2,380	1		1		1	
10–29 min/d	1,353	1.09 (0.92, 1.31)	0.313	1.13 (0.95, 1.36)	0.168	1.15 (0.96, 1.37)	0.138
30–119 min/d	5,768	0.95 (0.83, 1.08)	0.442	0.99 (0.87, 1.14)	0.951	1.01 (0.89, 1.16)	0.849
120–239 min/d	2,658	0.87 (0.75, 1.01)	0.076	0.90 (0.77, 1.06)	0.201	0.92 (0.78, 1.07)	0.274
≥240 min/d	2,107	0.83 (0.70, 0.97)	0.023	0.91 (0.77, 1.07)	0.258	0.92 (0.78, 1.09)	0.363

OR, odds ratio; CI, confidence interval; Model 1 was adjusted for age, sex, education, marital status, and residency; Model 2 was further adjusted for smoking status, drinking frequency, sleep duration, annual income.

Discussion

This cross-sectional study evaluated the association between the risk of hypertension with various dimensions of PA in middle and older-aged Chinese people. Several important findings of the current study include: (1) Higher frequency and longer duration of VPA or MPA were significantly associated with a lower risk of hypertension. (2) There was an inverse association between TPA and risk for hypertension. (3) A non-linear dose-response relationship between TPA and the risk of hypertension was observed in all participants, the downward hypertension risk flattened when TPA was approximately 4500 MET-minutes/week. (4) There were sex and age differences in the dose-response relationship between physical activity and hypertension risk.

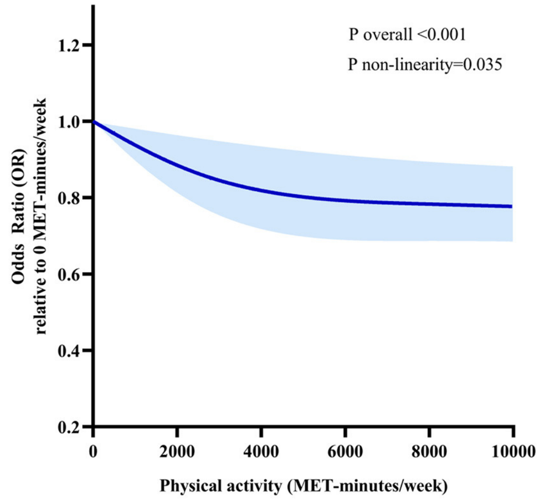

FIGURE 1
Dose-response relationships between TPA and the risk of hypertension. Models are adjusted for age, sex, marital status, education, residency, smoking status, drinking frequency, sleep duration and annual income. The solid line and long dash line represent the estimated odds ratio and its 95% confidence interval. Knots are at the 25th, 50th and 75th percentiles for TPA.

Intensity, frequency, and duration of PA are important factors affecting the benefits of PA. We found that VPA and MPA were associated with a lower risk of hypertension after adjustment for covariates. The result is consistent with those of previous studies, moderate-to-vigorous PA is beneficially associated with many health statuses (23). However, the association between moderate-to-vigorous PA with hypertension risk was only observed at 6–7days per week and duration ≥240 min. A single session of exercise can cause a sustained drop in blood pressure, a phenomenon known as post-exercise hypotension (24). Repeated induction of post-exercise hypotension at a higher frequency may be best in hypertensive patients. Sharman et al. (25) support the idea that hypertensive patients should be physically active most days of the week for optimal health benefits. The guideline (26) also encourage adults with high blood pressure to do moderate-to-vigorous aerobic exercise most days of the week, and preferably all days.

In terms of duration, the physical activity guidelines recommend that adults should do at least 150–300 min MPA per week, or 75–150 min. VPA per week for substantial health benefits (27). Taylor-Tolbert et al. (28) found that just 45 min of acute exercise immediately reduced blood pressure load in elderly male hypertensive patients. Our findings differ significantly from the previous reports. Smith et al. (29) compared self-reported and objectively measured physical activity trajectories in prostate cancer survivors, and they found that self-reported measures greatly overestimated moderate to vigorous physical activity. However, a systematic review noted that self-reported measures of physical activity were higher or lower than directly measured physical activity levels, depending on the measure of physical activity employed, the level of physical activity measured, and the gender of participants (30). The physical activity indicators associated with lowering hypertension in our results still need to be further validated with objective monitoring data. No significant association was observed in any frequency and duration of LPA after adjustment for confounders. Despite the evidence that even LPA is associated with numerous positive health outcomes (31), it remains unclear whether LPA can have a beneficial effect on hypertension.

Our result shows an inverse association between TPA level and the risk of hypertension, which is consistent with previous research (32, 33). Importantly, the effect of PA on hypertension is dose-dependent (16). We used RCS to explore this relationship and found the relationship to be non-linear, which decreases initially and then stabilizes. When TPA reached 3000 MET-minutes per week, the risk of hypertension decreased by 15%. The energy expenditure far exceeds the recommendations of current physical activity guidelines, suggestive that exceeding current guidelines in terms of energy expenditure incurs greater contribution. But the curve reached a plateau when TPA per week was approximately 4500 MET-mins. This is probably a volume for optimal health benefits, equivalent to 2.5 h a day of moderate-intensity, or 1.3 h a day of vigorous-intensity physical activity. A beneficial effect of physical exercise on hypertension appears in the regulation of endothelial function (34). Physical exercise augments blood flow and laminar shear stress, and it can also elicit systemic molecular pathways connected with angiogenesis and chronic anti-inflammatory action (35).

It is worth noting that sex and age differences were found in the dose-response relationship between physical activity and hypertension risk. A linear dose-response relationship between PA and hypertension was observed in the male population. No significant dose-response relationship was found in female participants, which was consistent with the findings of Haapanen et al. (17). Physical activity may differ between men and women. A previous report on the physical activity of middle and older Chinese indicated that men were more active in VPA and women were more active in MPA (36). In addition, the dose-response relationship between physical activity and the risk of hypertension in aged 45–64 participants is linear, but it was non-linear in those aged ≥65 participants. The age difference in the relation between PA and hypertensive risk may result from an age-related increase in arterial stiffness (18). Casey et al. (37) found that the vasodilator responses were slower in older adults at all exercise intensities compared with younger adults. The decreasing physical function makes it difficult for older adults to engage in moderate-to-vigorous PA (38), which also limits the higher benefits they can get from PA.

This study has the strength of including a representative sample of middle-aged and older adults in the Chinese population, which increased the statistical power. We conducted subgroup analyses based on age and sex to explore whether a difference in association could be observed in subgroups with a different age or sex. Furthermore, the sensitivity analyses have confirmed the robustness of this study's findings. This study has some limitations. First, because of the cross-sectional design, the cause-effect relationships between PA and the risk of hypertension not be determined. Further longitudinal studies are needed to determine the direction of causality for these associations. Second, questionnaire-based assessments of physical activity may be subject to recall and social desirability bias. Although the IPAQ is widely used, validation studies have shown poor agreement with objective measures (39). Third, these data do not allow us to distinguish the source of physical activity, it's hard to determine if the observed effects are independent of the type of occupation. Moreover, we were unable to include some important covariates, such as BMI, history of metabolic conditions, salt intake, medication use, and other potential confounders that may interfere with the effect of physical activity on hypertension risk. Our results cannot be excluded from being influenced by unknown or unmeasured confounders, despite the multivariable adjustments we made. Finally, results are limited to Chinese middle-aged and elderly groups, and may not generalize to other countries or populations.

Implications

It is expected that the prevalence of hypertension will continually increase in the future as the Chinese population ages rapidly. Our findings reinforce a growing body of independent evidence that supports the effectiveness of moderate-to-vigorous-intensity physical activity in preventing and managing the risk of hypertension. This study also has significant practical implications. We analyzed the associations between multiple dimensions of physical activity and the risk of hypertension, and found gender and age differences in the dose-response relationship between accumulated physical activity over the week and the risk of hypertension. This may provide more detailed guidance for the prevention and control of hypertension in different populations. Physical activity as a non-pharmacological intervention has been shown to be effective in reducing the risk of hypertension. Objective measurement of physical activity should be considered and incorporated into the management of hypertensive patients.

Conclusion

The results of this study assessed associations between different dimensions of PA and the risk of hypertension. After adjustment for potential confounders, higher frequency and longer duration of VPA or MPA were significantly associated with a lower risk of hypertension. Higher PA levels were associated with a lower risk of hypertension and there was an inverse dose-response relationship between weekly TPA and the risk of hypertension. When TPA reached approximately 4500 MET-minutes per week, the risk of hypertension in the overall population decreased by 19%, while continued increases in PA did not appear to produce any further marked reduction in the risk. These findings provide further proof that hypertension could be prevented through increased PA.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found at: https://g2aging.org.

Ethics statement

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

Author contributions

LZ, YL, and WF designed the research. LZ, WF, NX, XY, and MW performed all the statistical analysis. LZ, WF, YL, and XW interpreted the data analysis. LZ, WF, YC, YL, and XW wrote the manuscript with critical input from YL. All authors read and approved the final manuscript.

Funding

This work was supported by the Jiangsu Provincial Natural Science Foundation of China (grant number, BK20190999), the Xuzhou Natural Science Foundation (grant number, KC21029), and the Natural Science Foundation of the Jiangsu Education Institutions of China (grant number, 22KJB180017).

Acknowledgments

We would like to acknowledge the China Health and Retirement Longitudinal Study (CHARLS) team for providing high-quality, nationally representative data.

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.2022.995755/full#supplementary-material

SUPPLEMENTARY FIGURE S1
Dose-response relationships between TPA and the risk of hypertension for different sex groups **(A)** Males. **(B)** Females. Models were adjusted for age, marital status, education, residency, smoking status, drinking frequency, sleep duration and annual income. The solid line and long dash line represent the estimated odds ratio and its 95% confidence interval. Knots are at the 25th, 50th, and 75th percentiles for TPA.

SUPPLEMENTARY FIGURE S2
Dose-response relationships between TPA and the risk of hypertension for different age groups **(A)** Participants aged < 65 years. **(B)** Participants aged 65 years and older. Models were adjusted for sex, age, marital status, education, residency, smoking status, drinking frequency, sleep duration and annual income. The solid line and long dash line represent the estimated odds ratio and its 95% confidence interval. Knots are at the 25th, 50th and 75th percentiles for TPA.

SUPPLEMENTARY FIGURE S3
Sensitivity analyses of dose-response relationships between TPA and the risk of hypertension. Models are adjusted for age, sex, marital status, education, residency, smoking status, drinking frequency, sleep duration and annual income. The solid line and long dash line represent the estimated odds ratio and its 95% confidence interval. Knots are at the 25th, 50th and 75th percentiles for TPA.

SUPPLEMENTARY TABLE S1
Physical activity level of participants.

References

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J, et al. Global burden of hypertension: analysis of worldwide data. *Lancet.* (2005) 365:217–23. doi: 10.1016/S0140-6736(05)17741-1

2. Staessen JA, Wang J, Bianchi G, Birkenhäger WH. Essential hypertension. *Lancet.* (2003) 361:1629–41. doi: 10.1016/S0140-6736(03)13302-8

3. Williams B, Mancia G, Spiering W, Agabiti RE, Azizi M, Burnier M, et al. 2018 esc/esh guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the european society of cardiology and the european society of hypertension: the task force for the management of arterial hypertension of the european society of cardiology and the european society of hypertension. *J Hypertens.* (2018) 36:1953–2041. doi: 10.1097/HJH.0000000000001940

4. Whelton PK, Carey RM, Aronow WS, Casey DJ, Collins KJ, Dennison HC, et al. 2017 acc/aha/aapa/abc/acpm/ags/apha/ash/aspc/nma/pcna guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the american college of cardiology/american heart association task force on clinical practice guidelines. *Hypertension.* (2018) 71:e13–115. doi: 10.1161/HYP.0000000000000076

5. Kuo PL, Pu C. The contribution of depression to mortality among elderly with self-reported hypertension: analysis using a national representative longitudinal survey. *J Hypertens.* (2011) 29:2084–90. doi: 10.1097/HJH.0b013e32834b59ad

6. Li Y, Yang L, Wang L, Zhang M, Huang Z, Deng Q, et al. Burden of hypertension in china: a nationally representative survey of 174,621 adults. *Int J Cardiol.* (2017) 227:516–23. doi: 10.1016/j.ijcard.2016.10.110

7. Hall ME, Do CJ Da SA, Juncos LA, Wang Z, Hall JE, et al. Obesity, hypertension, and chronic kidney disease. *Int J Nephrol Renovasc Dis.* (2014) 7:75–88. doi: 10.2147/IJNRD.S39739

8. Shimbo D, Levitan EB, Booth JR, Calhoun DA, Judd SE, Lackland DT, et al. The contributions of unhealthy lifestyle factors to apparent resistant hypertension: findings from the reasons for geographic and racial differences in stroke (regards) study. *J Hypertens.* (2013) 31:370–6. doi: 10.1097/HJH.0b013e32835b6be7

9. Batis C, Gordon-Larsen P, Cole SR, Du S, Zhang B, Popkin B, et al. Sodium intake from various time frames and incident hypertension among Chinese adults. *Epidemiology.* (2013) 24:410–8. doi: 10.1097/EDE.0b013e318289e047

10. O'Donovan C, Lithander FE, Raftery T, Gormley J, Mahmud A, Hussey J, et al. Inverse relationship between physical activity and arterial stiffness in adults with hypertension. *J Phys Act Health.* (2014) 11:272–7. doi: 10.1123/jpah.2012-0075

11. Li X, Liu Q, Wang K, Li R, Hou Y, Li Z, et al. Prevalence and correlates of physical inactivity among elderly Chinese. *Osteoarthr Cartilage.* (2017) 25:S203. doi: 10.1016/j.joca.2017.02.349

12. Cheng YL, Leung CB, Kwan TH, Chau KF, Tong KL Li CS, et al. Screening for high blood pressure (bp): the Hong Kong experience. *Int J Cardiol.* (2009) 137:S126. doi: 10.1016/j.ijcard.2009.09.429

13. Treff C, Benseñor IM, Lotufo PA. Leisure-time and commuting physical activity and high blood pressure: the Brazilian longitudinal study of adult health (elsa-brasil). *J Hum Hypertens.* (2017) 31:278–83. doi: 10.1038/jhh.2016.75

14. Chase NL, Sui X, Lee DC, Blair SN. The association of cardiorespiratory fitness and physical activity with incidence of hypertension in men. *Am J Hypertens.* (2009) 22:417–24. doi: 10.1038/ajh.2009.6

15. Williams PT, A. cohort study of incident hypertension in relation to changes in vigorous physical activity in men and women. *J Hypertens.* (2008) 26:1085–93. doi: 10.1097/HJH.0b013e3282fb81dc

16. Pescatello LS, Buchner DM, Jakicic JM, Powell KE, Kraus WE, Bloodgood B, et al. Physical activity to prevent and treat hypertension: a systematic review. *Med Sci Sports Exerc.* (2019) 51:1314–23. doi: 10.1249/MSS.0000000000001943

17. Haapanen N, Miilunpalo S, Vuori I, Oja P, Pasanen M. Association of leisure time physical activity with the risk of coronary heart disease, hypertension and diabetes in middle-aged men and women. *Int J Epidemiol.* (1997) 26:739–47. doi: 10.1093/ije/26.4.739

18. Cohen L, Curhan GC, Forman JP. Influence of age on the association between lifestyle factors and risk of hypertension. *J Am Soc Hypertens.* (2012) 6:284–90. doi: 10.1016/j.jash.2012.06.002

19. You Y, Teng W, Wang J, Ma G, Ma A, Wang J, et al. Hypertension and physical activity in middle-aged and older adults in china. *Sci Rep.* (2018) 8:16098. doi: 10.1038/s41598-018-34617-y

20. Pavey TG, Peeters G, Bauman AE, Brown WJ. Does vigorous physical activity provide additional benefits beyond those of moderate? *Med Sci Sports Exerc.* (2013) 45:1948–55. doi: 10.1249/MSS.0b013e3182940b91

21. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc.* (2003) 35:1381–95. doi: 10.1249/01.MSS.0000078924.61453.FB

22. Physical AGAC. *Physical Activity Guidelines Advisory Committee Report, 2008.* Washington, DC: US Department of Health and Human Services (2008).

23. Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. *CMAJ.* (2006) 174:801–9. doi: 10.1503/cmaj.051351

24. Kenney MJ, Seals DR. Postexercise hypotension. *Key features, mechanisms, and clinical significance Hypertension.* (1993) 22:653–64. doi: 10.1161/01.HYP.22.5.653

25. Sharman JE, La Gerche A, Coombes JS. Exercise and cardiovascular risk in patients with hypertension. *Am J Hypertens.* (2015) 28:147–58. doi: 10.1093/ajh/hpu191

26. Whelton PK, Carey RM, Aronow WS, Casey DJ, Collins KJ, Dennison HC, et al. 2017 acc/aha/aapa/abc/acpm/ags/apha/ash/aspc/nma/pcna guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the american college of cardiology/american heart association

task force on clinical practice guidelines. *J Am Coll Cardiol.* (2018) 71:e127–248. doi: 10.1016/j.jacc.2017.11.006

27. 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

28. Taylor-Tolbert NS, Dengel DR, Brown MD, McCole SD, Pratley RE, Ferrell RE, et al. Ambulatory blood pressure after acute exercise in older men with essential hypertension. *Am J Hypertens.* (2000) 13:44–51. doi: 10.1016/S0895-7061(99)00141-7

29. Smith L, Lee JA, Mun J, Pakpahan R, Imm KR, Izadi S, et al. Levels and patterns of self-reported and objectively-measured free-living physical activity among prostate cancer survivors: a prospective cohort study. *Cancer-Am Cancer Soc.* (2019) 125:798–806. doi: 10.1002/cncr.31857

30. Prince SA, Adamo KB, Hamel ME, Hardt J, Connor GS, Tremblay MA, et al. Comparison of direct versus self-report measures for assessing physical activity in adults: a systematic review. *Int J Behav Nutr Phys Act.* (2008) 5:56. doi: 10.1186/1479-5868-5-56

31. Füzéki E, Engeroff T, Banzer W. Health benefits of light-intensity physical activity: a systematic review of accelerometer data of the national health and nutrition examination survey (nhanes). *Sports Med.* (2017) 47:1769–93. doi: 10.1007/s40279-017-0724-0

32. Bakker EA, Sui X, Brellenthin AG, Lee DC. Physical activity and fitness for the prevention of hypertension. *Curr Opin Cardiol.* (2018) 33:394–401. doi: 10.1097/HCO.0000000000000526

33. Castro I, Waclawovsky G, Marcadenti A. Nutrition and physical activity on hypertension: implication of current evidence and guidelines. *Curr Hypertens Rev.* (2015) 11:91–9. doi: 10.2174/1573402111666150429170302

34. Gambardella J, Morelli MB, Wang XJ, Santulli G. Pathophysiological mechanisms underlying the beneficial effects of physical activity in hypertension. *J Clin Hypertens.* (2020) 22:291–5. doi: 10.1111/jch.13804

35. Di Francescomarino S, Sciartilli A, Di Valerio V, Di Baldassarre A, Gallina S. The effect of physical exercise on endothelial function. *Sports Med.* (2009) 39:797–812. doi: 10.2165/11317750-000000000-00000

36. Wang R, Bishwajit G, Zhou Y, Wu X, Feng D, Tang S, et al. Intensity, frequency, duration, and volume of physical activity and its association with risk of depression in middle- and older-aged chinese: evidence from the china health and retirement longitudinal study, 2015. *PLoS ONE.* (2019) 14:e221430. doi: 10.1371/journal.pone.0221430

37. Casey DP, Ranadive SM, Joyner MJ. Aging is associated with altered vasodilator kinetics in dynamically contracting muscle: role of nitric oxide. *J Appl Physiol.* (1985) 119: 232–41. doi: 10.1152/japplphysiol.00787.2014

38. Rolland Y, Lauwers-Cances V, Cristini C, Abellan VKG, Janssen I, Morley JE, et al. Difficulties with physical function associated with obesity, sarcopenia, and sarcopenic-obesity in community-dwelling elderly women: the epidos (epidemiologie de l'osteoporose) study. *Am J Clin Nutr.* (2009) 89:1895–900. doi: 10.3945/ajcn.2008.26950

39. Macfarlane DJ, Lee CC, Ho EY, Chan KL, Chan DT. Reliability and validity of the Chinese version of ipaq (short, last 7 days). *J Sci Med Sport.* (2007) 10:45–51. doi: 10.1016/j.jsams.2006.05.003

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 29 September 2022
DOI 10.3389/fpubh.2022.1005260

Check for updates

OPEN ACCESS

EDITED BY
Bojan Masanovic,
University of Montenegro, Montenegro

REVIEWED BY
Kamal Jyoti Maji,
Georgia Institute of Technology,
United States
Borko Katanic,
University of Montenegro, Montenegro

*CORRESPONDENCE
Yuantao Hao
haoyt@mail.sysu.edu.cn
Guoyou Qin
gyqin@fudan.edu.cn
Yongfu Yu
yu@fudan.edu.cn

†These authors share first authorship

SPECIALTY SECTION
This article was submitted to
Aging and Public Health,
a section of the journal
Frontiers in Public Health

RECEIVED 28 July 2022
ACCEPTED 31 August 2022
PUBLISHED 29 September 2022

CITATION
Yang Y, Xu H, Liu X, Li J, Liew Z, Liu X, Huang C, Zhu J, Zhang J, Chen L, Hao Y, Qin G and Yu Y (2022) Joint association of smoking and physical activity with mortality in elderly hypertensive patients: A Chinese population-based cohort study in 2007–2018.
Front. Public Health 10:1005260.
doi: 10.3389/fpubh.2022.1005260

Joint association of smoking and physical activity with mortality in elderly hypertensive patients: A Chinese population-based cohort study in 2007–2018

Yating Yang[1†], Huilin Xu[2†], Xiaoqin Liu[3], Jiong Li[4,5], Zeyan Liew[6], Xing Liu[7], Chen Huang[1], Jingjing Zhu[1], Jinling Zhang[2], Linli Chen[2], Yuantao Hao[8]*, Guoyou Qin[9]* and Yongfu Yu[1]*

[1]Department of Biostatistics, School of Public Health, The Key Laboratory of Public Health Safety of Ministry of Education, Fudan University, Shanghai, China, [2]Shanghai Minhang Center for Disease Control and Prevention, Shanghai, China, [3]NCRR-National Centre for Register-Based Research, Aarhus University, Aarhus, Denmark, [4]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark, [5]Department of Clinical Epidemiology, Aarhus University, Aarhus, Denmark, [6]Department of Environmental Health Sciences, Yale School of Public Health, New Haven, CT, United States, [7]Department of Epidemiology, School of Public Health, The Key Laboratory of Public Health Safety of Ministry of Education, Fudan University, Shanghai, China, [8]Department of Medical Statistics and Epidemiology, School of Public Health, Sun Yat-sen University, Guangzhou, China, [9]Shanghai Institute of Infectious Disease and Biosecurity, Shanghai, China

Background: Although associations of physical activity and smoking with mortality have been well-established, the joint impact of physical activity and smoking on premature mortality among elderly hypertensive population was still unclear. This study aimed to assess association of physical activity, smoking, and their interaction with all-cause and cardiovascular disease (CVD) mortality risk in elderly hypertensive patients.

Methods: We included 125,978 Chinese hypertensive patients aged 60–85 years [mean (SD) age, 70.5 (6.9) years] who had records in electronic health information system of Minhang District of Shanghai, China in 2007–2015. Cox regression was used to estimate individual and joint association of smoking and physical activity on all-cause and CVD mortality. Interactions were measured both additively and multiplicatively. Additive interaction was evaluated by relative excess risk due to interaction (RERI), attributable proportion due to interaction (AP) and synergy index (S).

Results: Among 125,978 elderly hypertensive patients (median age 70.1), 28,250 deaths from all causes and 13,164 deaths from CVD were observed during the follow-up up to 11 years. There was an additive interaction between smoking and physical inactivity [RERI: all-cause 0.19 (95% CI: 0.04–0.34), CVD 0.28 (0.06–0.50); AP: all-cause 0.09 (0.02–0.16), CVD 0.14 (0.04–0.23); S: all-cause 1.21 (1.04–1.42), CVD 1.36 (1.06–1.75)], while the concurrence of both risk factors was associated with more than 2-fold risk of death [hazard ratio (HR): all-cause 2.10 (1.99–2.21), CVD 2.19 (2.02–2.38)].

Conclusion: Our study suggested that smoking and physical inactivity together may have amplified association on premature death compared to the sum of their individual associations, highlighting the importance of improving behavioral factors in combination and promoting a comprehensive healthy lifestyle in hypertensive elderly.

KEYWORDS

hypertension, cardiovascular disease, all-cause mortality, physical activity, smoking, interaction, elderly

Introduction

Worldwide, there were 703 million people aged 65 years and above in 2019, comprising 9% of total population (1); by 2050, those numbers are expected to rise to 20% (1.6 billion) (2). Among the elderly, hypertension is the leading cause of premature death and cardiovascular disease (CVD) globally (3). Approximately 31.1% of adults worldwide live with hypertension, and 9.4 million people die from hypertension and complications every year (4). While hypertension is more prevalent among the elderly (5, 6), its treatment and control have been suboptimal (3). For example, in China, the prevalence of hypertension in people over 65 years old is as high as 58%, while only half of them receive antihypertensive medication treatment and the control rate is less than one-fifth (7). With the increasing life expectancy and aging trend of the population (1), the burden of disease from hypertension is an alarming issue (8).

Smoking and physical inactivity are modifiable risk factors of CVD and premature death (9–11). Evidence reveals that even low-intensity tobacco use can be harmful to health (12). Multiple studies from China (13, 14), Japan (15), and South Korea (16) have shown that smoking may greatly increase the risk of premature death in hypertensive patients due to the synergistic effect between smoking and elevated blood pressure. In contrast, higher levels of physical activity can reduce the risk of all-cause mortality and CVD events in hypertensive patients (17, 18). Previous studies have established that the elderly and patients with various chronic diseases can obtain substantial health benefits through increasing physical activities (19–22).

Although relationship between smoking, physical activity and mortality has been well-established, the interaction of smoking and physical activity on mortality remains unclear. A good understanding of the interaction is important to identify target groups for interventions and to implement primary prevention strategies. Several studies have investigated the comprehensive influence of multiple health risk factors on health (23–27). However, most of these studies (24, 26) mainly focused on the association of the co-exposure of smoking and physical inactivity with adverse health outcomes, but failed to provide sufficient quantitative measures of interaction to explore the joint association in detail. Whether physical activity moderates the effect of smoking on mortality risk in the elderly hypertensive population has never been evaluated. Therefore, using data from a large-scale prospective cohort in China, our study aimed to explore the joint association of smoking and physical exercise with all-cause mortality and CVD mortality in elderly hypertensive patients. This research is very important in order to clarify whether there is an additional benefit of simultaneous interventions for smoking and lack of exercise.

Methods

Data source and study population

Shanghai Electronic Health Records Management System (EHR) holds information on electronic health records for Shanghai residents. Each patient has a unique personal identification number in this system. All institutions, including secondary and tertiary hospitals and primary healthcare centers, use EHR system to record clinical activities, regular follow-ups of primary health care, and collect information on physical examinations, chronic disease management and medication treatments (28, 29).

Since 2007, Minghang district of Shanghai has initiated primary care management for patients with hypertension (30). According to International Practical Guidelines for Hypertension (31), hypertension is defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg, or taking antihypertensive drugs. All patients diagnosed with hypertension are included in the primary care management. According to the standard operating procedures (SOPs) of EHR system, patients were required to have at least one physical examination every 6 months (28, 29).

Data collection, recording, and uploading were carried out following pre-established SOPs. According to the standardized information collection manual, primary medical staff was uniformly trained every year, and special supervisors were regularly assigned for supervision. To evaluate internal effectiveness of this registration system, a mid-term evaluation was conducted from February 1, 2008 to May 30, 2009. We

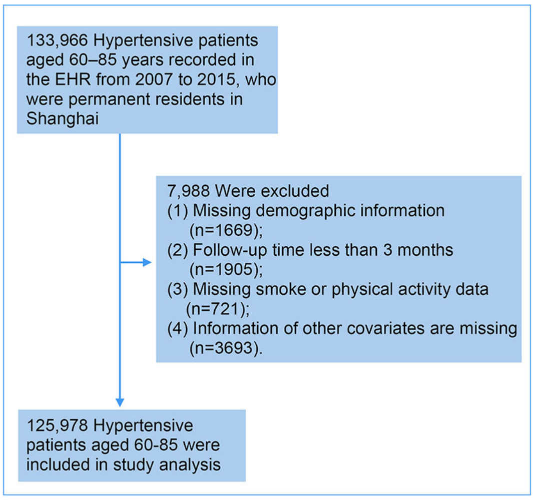

FIGURE 1
Study population. EHR system denotes the electronic health information system.

randomly selected 1,700 hypertensive patients from EHR system, provided them with free physical examination and clinical consultation, and arranged 10 senior physicians to re-evaluate the patients. In the end, a total of 1,459 patients completed the reassessment. The consistent rates of diagnosis of hypertension, stroke, diabetes, left ventricular hypertrophy, atherosclerotic plaque and retinal artery stenosis were 0.97, 0.96, 0.93, 0.96, 0.79, and 0.83, respectively.

This study included all 133,966 hypertensive patients aged 60–85 years recorded in EHR from 2007 to 2015, who were permanent residents in Shanghai. Exclusion criteria were as follows: (1) Missing demographic information ($n = 1669$); (2) Follow-up time <3 months ($n = 1905$); (3) Missing smoke or physical activity data ($n = 721$); (4) Information of other covariates are missing ($n = 3693$). After exclusion, this study included 125,978 (94.0%) hypertensive patients aged 60–85 years [mean (SD) age, 70.5 (6.9) years] (Figure 1).

Exposures

Self-reported smoking status and physical activity were obtained in face-to-face interviews. Smoking status was categorized into never-smoking and smoking. Never-smokers were defined as life-long non-smokers. Smokers included those who self-reported smoking regularly, occasionally and quit smoking at baseline.

Physical exercise was categorized into three groups (regular exercise, occasional exercise, and never exercise) (32). Regular exercise was defined as ≥150 min of moderate-intensity activities or ≥75 min of high-intensity activities per week. To be more specific, moderate-intensity activities referred to physical activities between 3 and 6 times the resting intensity, also equivalent to 50–60% of individual's physical capacity; high-intensity activities referred to physical activities more than six times the resting intensity, relative to 70–80% of individual's physical capacity. This definition of regular exercise was consistent with exercise intensity recommended by World Health Organization (WHO), which is applicable to the elderly (32). The exercise below this intensity was defined as occasional exercise.

Outcomes

The outcomes of interest were all-cause mortality and CVD mortality. The primary cause of death was reported according to International Classification of Diseases, 10th Revision (ICD-10) (33), the corresponding code for cardiovascular disease was I00-I99. All death information has been verified by death documents provided by Minhang District Center for Disease Control and Prevention in Shanghai.

The follow-up in our study ended on 31 December 2018. The overall survival was defined as the time period between the day of patients firstly recorded until the day of outcome of interest, updating once every 3 months. The patient was censored on the date of the last follow-up in EHR.

Covariates

Potential confounders were determined according to variable relationships shown in directed acyclic graph based on previous research (Supplementary Figure 1). We included gender, age, alcohol drinking (never drinking, occasional drinking, regular drinking defined as at least twice drinks per week for more than a year) (34), body mass index (BMI, calculated by weight in kilograms divided by the square of height in meters), diabetes (fasting blood glucose ≥7.0 mmol/L or 2-h blood glucose ≥11.1 mmol/L), classification of hypertension (grade 1 hypertension: SBP140-159 or DBP90-99, grade 2 hypertension: SBP160-179 or DBP100-109, grade 3 hypertension:SBP ≥ 180 or DBP ≥ 110) (31), family history of CVD (no, yes), family history of diabetes (no, yes), family history of hypertension (no, yes), and family history of stroke (no, yes).

Statistical analysis

Basic characteristics of population according to different levels of smoking and physical activity were compared by chi-square test for categorical variables, and one-way analysis of variance or Kruskal-Wallis test for continuous variables where appropriate. Cumulative incidence of CVD mortality by smoking and exercise was estimated in the presence of competing risk, treating non-cardiovascular deaths as competing events (34, 35). Cumulative incidence of all-cause mortality was also presented.

Cox proportional hazards regression was used to estimate the individual and joint association of smoking and physical exercise on the risk of all-cause and CVD mortality. The proportional hazards assumption was evaluated by log-minus-log plots (35, 36), and the curves were approximately parallel as shown in Supplementary Figure 2.

We measured interactions on both additive and multiplicative scales. The coefficient of product term (physical exercise*smoking) in Cox regression could reflect the multiplicative interaction, which measures the relative change of risk (37). Three indicators were used to evaluate the additive interaction of smoking and never exercising, which measures the absolute change of risk: (1) Relative excess risk due to interaction (RERI), (2) attributable proportion due to interaction (AP), (3) synergy index (S), defined as follow (38);

$$RERI = HR_{11} - HR_{10} - HR_{01} + 1$$

$$AP = \frac{RERI}{HR_{11}}$$

$$S = \frac{HR_{11} - 1}{(HR_{10} - 1) + (HR_{01} - 1)}$$

Here HR_{11} represented the hazard ratio of people who smoke and never exercise, HR_{10} for people who smoke and exercise regularly, and HR_{01} for people who never smoke and never exercise. There was an additive interaction if RERI and AP were unequal to 0, or S was unequal to 1.

Stratified analysis was also presented to see whether the association of smoking with mortality modified by physical activity. Considering sex differences in smoking, the joint association of smoking and physical exercise were estimated by gender. And we calculated the joint association stratified by age to gain more specific information in elderly population. We also conducted interaction analyses using sex-stratified Cox regression model with age as time scale (39). Moreover, we excluded people with diabetes and family history of chronic diseases to assess if the relations were sensitive to comorbid chronic diseases and genetic factors. All analyses were two-sided test with a significant level of 0.05, performed by SAS 9.4 and Stata 16. Three measures of additive interaction were computing by SAS programs provided by Li and Chambless (40).

Results

Basic characteristics and mortality follow-up

Of 125,978 elderly hypertensive patients, the median age was 70.1 years old, smoking rate was 16.7%, and women accounted for 53.3%. Compared with never smokers, smokers were more likely to be male, younger, drink regularly, have more severe stage of hypertension and have family history of chronic diseases. Compared with those who never exercised, those who exercised regularly were more likely to be male, younger, have comorbid diabetes, have grade 3 hypertension and family history of chronic diseases (Table 1).

During the 1,004,801 person-years of follow-up (median follow-up: 8.9 years, interquartile range: 5.8–10.6 years), 28,250 deaths from all causes and 13,164 deaths from CVD were observed. Overall, people with lower intensity of physical activity had a higher mortality rate (Table 3). Cumulative incidence estimation according to smoke and exercise showed similar results (Figure 2).

Individual associations of smoking and physical activity

Table 2 presented the independent associations of smoking and physical activity on mortality risk. Higher levels of physical activity and never smoking were associated with reduced risk of death. Compared with never exercise, regular exercise was associated with lower risk of all-cause mortality by 36% (HR: 0.64, 95% CI: 0.62–0.66) and CVD mortality by 40% (HR: 0.60, 95% CI: 0.57–0.63). Compared with smokers, non-smokers had lower hazard ratios for all-cause death (HR: 0.73, 95%CI: 0.71–0.76) and CVD death (HR: 0.77, 95% CI: 0.73–0.82).

Joint associations of smoking and physical activity

Table 3 shows the joint association of smoking and physical activity. In both smokers and non-smokers, lower exercise levels were associated with higher risk of death, but the strength of this adverse association was stronger among smokers. Taking both regular exercise and non-smoking as reference group, risk of death increased as concurrent exposures to smoking and lacking exercise increased. Smokers who never exercised had greatest risk for mortality (HR for All-cause: 2.10, 95% CI: 1.99–2.21; HR for CVD: 2.19, 95% CI: 2.02–2.38), but increasing physical activity levels might counteract some of these extra risks. Similar patterns were observed for all-cause mortality and CVD mortality by different combinations of smoking and physical activity (Table 3). We found a significant additive interaction between smoking and never exercise, with RERI, AP, and S being 0.29 (95% CI: 0.10–0.49), 0.13 (0.05–0.22) and 1.33 (1.10–1.61) for CVD mortality, and 0.20 (0.08–0.33), 0.10 (0.04–0.15) and 1.23 (1.08–1.39) for all-cause mortality, respectively. However, the multiplicative interaction was not statistically significant (all-cause: 1.00, 0.96–1.04; CVD: 0.97, 0.91–1.03).

TABLE 1 Characteristics of participants according to physical activity and smoking (n = 125,978)[a].

Variables	Total	Physical activity			Smoke	
		Never (N = 39,350)	Occasional (N = 54,120)	Regular (N = 32,508)	No (N = 104,955)	Yes[b] (N = 21,023)
Gender						
Male	58,891 (46.7)	16,528 (42.0)	25,835 (47.7)	16,528 (50.8)	38,612 (36.8)	20,279 (96.5)
Female	67,087 (53.3)	22,822 (58.0)	28,285 (52.3)	15,980 (49.2)	66,343 (63.2)	744 (3.5)
Age (median, IQR[c]), years	70.1 (11.8)	72.0 (12.6)	70.1 (11.7)	69.9 (10.6)	70.7 (11.9)	67.3 (10.6)
60–69	62,356 (49.5)	16,794 (42.7)	28,596 (52.8)	16,966 (52.2)	49,509 (47.2)	12,847 (61.1)
70–79	49,305 (39.1)	16,240 (41.3)	19,972 (36.9)	13,093 (40.3)	42,447 (40.4)	6,858 (32.6)
≥80	14,317 (11.4)	6,316 (16.1)	5,552 (10.3)	2,449 (7.5)	12,999 (12.4)	1,318 (6.3)
BMI (median, IQR[c]), kg/m^2	23.7 (3.8)	23.8 (4.1)	24.0 (3.8)	24.0 (3.7)	23.9 (3.9)	23.9 (3.7)
Underweight (<18.5 kg/m^2)	4,098 (3.3)	1,634 (4.2)	1,611 (3.0)	853 (2.6)	3,465 (3.3)	633 (3.0)
Normal (18.5–24.9 kg/m^2)	80,784 (64.1)	25,245 (64.2)	34,702 (64.1)	20,837 (64.1)	67,341 (64.2)	13,443 (63.9)
Overweight (25–29.9 kg/m^2)	36,773 (29.2)	10,983 (27.9)	15,991 (29.5)	9,799 (30.1)	30,387 (29.0)	6,386 (30.4)
Obesity (≥30 kg/m^2)	4,323 (3.4)	1,488 (3.8)	1,816 (3.4)	1,019 (3.1)	3,762 (3.6)	561 (2.7)
Comorbid diabetes	26,009 (20.6)	8,118 (20.6)	10,980 (20.3)	6,911 (21.3)	22,210 (21.2)	3,799 (18.1)
Alcohol drinking						
Never	104,572 (83.0)	34,318 (87.2)	43,761 (80.9)	26,493 (81.5)	95,049 (90.6)	9,523 (45.3)
Occasional	14,872 (11.8)	3,093 (7.9)	7,890 (14.6)	3,889 (12.0)	8,086 (7.7)	6,786 (32.3)
Regular	6,534 (5.2)	1,939 (4.9)	2,469 (4.6)	2,126 (6.5)	1,820 (1.7)	4,714 (22.4)
Classification of Hypertension						
Grade 1 hypertension	64,219 (51.0)	19,958 (50.7)	28,026 (51.8)	16,235 (49.9)	54,582 (52.0)	9,637 (45.8)
Grade 2 hypertension	42,909 (34.1)	13,329 (33.9)	18,582 (34.3)	10,998 (33.8)	35,275 (33.6)	7,634 (36.3)
Grade 3 hypertension	18,850 (15.0)	6,063 (15.4)	7,512 (13.9)	5,275 (16.2)	15,098 (14.4)	3,752 (17.8)
Family history of CVD						
No	123,118 (97.7)	38,510 (97.9)	53,023 (98.0)	31,585 (97.2)	102,624 (97.8)	20,494 (97.5)
Yes	2,860 (2.3)	840 (2.1)	1,097 (2.0)	923 (2.8)	2,331 (2.2)	529 (2.5)
Family history of diabetes						
No	120,830 (95.9)	37,880 (96.3)	51,920 (95.9)	31,030 (95.5)	100,811 (96.1)	20,019 (95.2)
Yes	5,148 (4.1)	1,470 (3.7)	2,200 (4.1)	1,478 (4.5)	4,144 (3.9)	1,004 (4.8)
Family history of hypertension						
No	83,006 (65.9)	27,215 (69.2)	35,636 (65.8)	20,155 (62.0)	70,314 (67.0)	12,692 (60.4)
Yes	42,972 (34.1)	12,135 (30.8)	18,484 (34.2)	12,353 (38.0)	34,641 (33.0)	8,331 (39.6)
Family history of stroke						
No	123,415 (98.0)	38,569 (98.0)	53,130 (98.2)	31,716 (97.6)	103,010 (98.1)	20,405 (97.1)
Yes	2,563 (2.0)	781 (2.0)	990 (1.8)	792 (2.4)	1,945 (1.9)	618 (2.9)

[a]Values are n (%) unless explained otherwise; CVD, cardiovascular disease.
The chi-square test was used to compare categorical variables and the Kruskal-Wallis test was used to compare continuous variables, and the P-values were <0.01 between all groups, except BMI for smoker and non-smoker (P = 0.68).
[b]Smoking, including quitting.
[c]IQR, interquartile range calculated by Q3-Q1.

Stratified analyses

Non-smokers had lower mortality risk than smokers among different levels of physical activity, and this beneficial association became stronger in people who exercised regularly (Supplementary Table 1). People who had higher intensity of exercise were associated with lower mortality risk than people who never exercised despite varying levels of smoking (Supplementary Table 2).

TABLE 2 The hazard ratios for the independent associations of smoking and physical activity on mortality risk[a].

	Person-years of follow-up	All-cause mortality			CVD mortality		
		Deaths	Rate /1,000 person-years	HR[b] (95% CI)	Deaths	Rate /1,000 person-years	HR[b] (95% CI)
Physical activity							
Never	317,050	12,041	37.98	1.00	5,993	18.90	1.00
Occasional	405,809	10,085	24.85	0.76 (0.74, 0.78)	4,457	10.98	0.70 (0.67, 0.73)
Regular	281,942	6,124	21.72	0.64 (0.62, 0.66)	2,714	9.63	0.60 (0.57, 0.63)
Smoke							
Yes (including quitting)	164,805	5,281	32.04	1.00	2,102	12.75	1.00
No	839,997	22,969	27.34	0.73 (0.71, 0.76)	11,062	13.17	0.77 (0.73, 0.82)

[a]CI, confidence interval; CVD, cardiovascular disease.
[b]Adjusted for age, gender, alcohol drinking, BMI, comorbid diabetes, classification of hypertension, family history of CVD, family history of diabetes, family history of hypertension, family history of stroke, and mutually for either smoking or physical activity; the product term (physical activity * smoke) was not statistically significant in the models, so it was not included in the independent effect estimates.

TABLE 3 Joint association of smoking and physical activity with mortality risk[a].

Measurements		Number	Person-years of follow-up (average person-years)	All-cause mortality		CVD mortality	
				Deaths (Rate /1,000 person-years)	Hazard ratio (95% CI)	Deaths (Rate /1,000 person-years)	Hazard ratio (95% CI)
Joint association							
Never smoke	Regular exercise	26,719	233,231 (8.7)	4,875 (20.90)	1.00	2,240 (9.60)	1.00
	Occasional exercise	45,151	339,442 (7.5)	8,133 (23.96)	1.17 (1.13, 1.21)	3,734 (11.00)	1.16 (1.10, 1.22)
	Never exercise	33,085	267,324 (8.1)	9,961 (37.26)	1.55 (1.50, 1.61)	5,088 (19.03)	1.65 (1.57, 1.74)
Smoke (include quitting)	Regular exercise	5,789	48,712 (8.4)	1,249 (25.64)	1.34 (1.25, 1.43)	474 (9.73)	1.24 (1.12, 1.38)
	Occasional exercise	8,969	66,367 (7.4)	1,952 (29.41)	1.64 (1.55, 1.73)	723 (10.89)	1.49 (1.36, 1.63)
	Never exercise	6,265	49,726 (7.9)	2,080 (41.83)	2.10 (1.99, 2.21)	905 (18.20)	2.19 (2.02, 2.38)
Interaction on additive scale[b]					**Estimates (95% CI)**		**Estimates (95% CI)**
RERI					0.20 (0.08, 0.33)		0.29 (0.10, 0.49)
AP					0.10 (0.04, 0.15)		0.13 (0.05, 0.22)
S					1.23 (1.08, 1.39)		1.33 (1.10, 1.61)
***P*-value**					0.001		0.003
Interaction on multiplicative scale					**Estimates (95% CI)**		**Estimates (95% CI)**
Physical activity * Smoke					1.00 (0.96, 1.04)		0.97 (0.91, 1.03)
***P*-value**					0.96		0.28

[a]Models adjusted for age, gender, alcohol drinking, BMI, comorbid diabetes, classification of hypertension, family history of CVD, family history of diabetes, family history of hypertension, family history of stroke, and the product term (physical activity * smoke).
[b]RERI, relative excess risk due to interaction; AP, attributable proportion due to interaction; S, synergy index; Additive interactions exist if RERI and AP are unequal to 0, or S is unequal to 1.

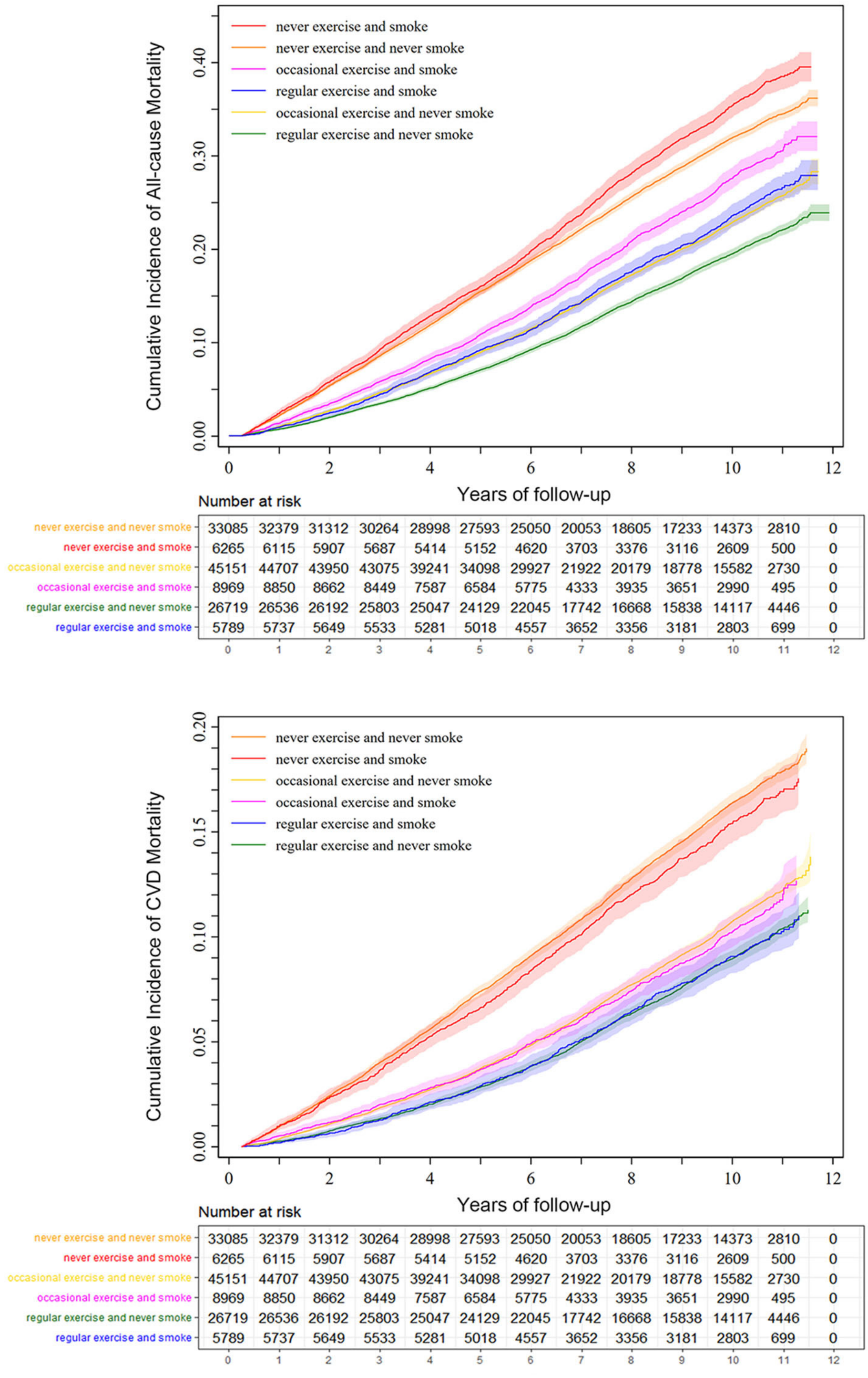

FIGURE 2
Cumulative incidence and corresponding 95% CI of all-cause and CVD mortality by smoke and exercise. Estimation of CVD mortality accounted for competing risk treating non-cardiovascular deaths as competing events.

Due to the large gender differences in smoking rates (34.44% in males and 1.11% in females), we calculated joint associations of smoking and exercise according to different genders. In men and women, the pattern of combined effects was consistent with that in entire population, but estimates were greater in men (Table 4). Results in different age groups were also similar. The joint association of physical activity and smoking on mortality were also found in individuals aged 80 years and above (Supplementary Table 3).

Sensitivity analyses

The results of interaction analyses using sex-stratified Cox regression model with age as time scale were similar to the primary analyses (Supplementary Table 4). Analyses excluding people with diabetes and family history of chronic diseases did not change the results (Supplementary Table 5).

Discussion

We found that regular exercise and never smoking were associated with lower risk of all-cause mortality and CVD mortality in an elderly hypertensive population. There was an additive interaction between smoking and physical inactivity, with the concurrence of both risk factors was associated with more than 2-fold risk of death [HR: all-cause 2.10 (1.99–2.21), CVD 2.19 (2.02–2.38)]. The estimates were more pronounced in men than in women. Smokers who never exercised had the greatest risk for mortality among all exposure groups, but increasing physical activity levels might counteract some of the extra risks. Although multiplicative interaction was not significant, we found a tendency that the strength of beneficial association of non-smoking became stronger among regular exerciser in stratified analyses.

Additive interaction measures the absolute change of risk, while multiplicative interaction measures the relative change of risk. Additive interaction has more public health significance and is more related to biological interaction (41–43). When health resources are limited, it is recommended to make decisions based on additive interaction to maximize the benefits of intervention (41–43).

Most of the available studies, yet not all, supported a joint association of smoking and physical activity with mortality. In US adults, combined effect of smoking and physical inactivity could significantly advance death by at least 2.4 years, which was consistent with our study (24). Similarly, a cohort study from Finland showed that risk of death was higher among inactive smokers (HR: 3.27, 95% CI: 2.05–5.22), compared with vigorously active non-smokers (26). A study among white-collar workers in the UK showed a lower incidence of coronary heart disease among non-smokers who engage in vigorous physical activity (4.2%) compared with smokers reporting no activity (11.5%) (44). However, study by Rehm et al. (45) indicated no interaction between smoking and exercise, but their calculated indicators of interaction were insufficient, using only the Mantel-Haenszel test ($p > 0.1$); the study by O'Donovan et al. (46) measured additive and multiplicative interactions between physical activity and smoking in-depth based on surveillance data of UK households and found a tendency of additive interaction, but the results were statistically insignificant. Our study show that smoking and physical inactivity interact on an additive scale. From the perspective of public health, this means that prevention of either smoking or physical inactivity not only reduces the risk of mortality by eliminating the independent effect of this factor, but also prevents cases caused by the interaction of these two factors. Health care providers should ensure that recommendation to promote physical activity and long-term non-smoking are addressed as part of routine care. If one already had poor behavior habits, early change of these habits could be salutary (47).

However, tobacco control in China faced substantial barriers due to low willingness of smoking cessation (48). China is the largest consumer of tobacco worldwide. In 2018, China Adult Tobacco Survey Report showed that smoking rate in China was 26.6%, and the rate among men was 50.5% (49). At present, smokers' willingness to quit smoking in China (16.1%) (49) was much lower than those in other middle and high-income countries (Canada 81.1%, Australia 75.6%, the UK 65.3%, the US 75.1%) (50). Based on the findings of our study, we can invest more efforts in promoting physical activity as a way to reduce mortality risk among smokers.

The following mechanisms may underlie the interaction between smoking and physical activity: (1) Smoking may increase the risk of CVD and premature deaths by elevating blood lipid and oxidative stress levels, while exercise may help reduce post-prandial oxidative stress in smokers by increasing the activity of endogenous antioxidant enzymes and by improving clearance of blood triglyceride and glucose (51). (2) Increased level of physical activity may help alleviate the withdrawal symptoms in smokers and increase the success rate of quitting (52, 53). Quitting smoking would cause weight gain, which can reduce some people's motivation to quit, especially women. And exercise can reduce weight gain (54, 55), activity restriction, pain, depression, and anxiety after quitting (56). (3) Smoking may affect lung function and have a negative impact on exercise capacity (57).

The main strength of this study is the large representative study sample that including all hypertensive patients aged over 60 years in Minhang District, Shanghai. In Shanghai, individuals aged over 35 years would be asked to measure blood pressure at their first medical appointment, which means we can identify majority of hypertensive patients (58). No previous study has examined the interaction between smoking and physical activity in-depth in hypertensive population or aging population, and this study provides research evidence on these issues using prospective data.

This study also has some limitations. Firstly, data of smoking and physical activity were obtained based on register system

TABLE 4 The joint association of smoking and physical activity on mortality stratified by gender[a].

Joint association of different exposure combinations		Male ($n = 99,034$)		Female ($n = 113,348$)	
		Deaths (rate/1,000 person-years)	HR (95% CI)	Deaths (rate/1,000 person-years)	HR (95% CI)
All-cause mortality					
Never smoke	Regular exercise	2,365 (25.43)	1.00	2,510 (17.90)	1.00
	Occasional exercise	3,616 (29.16)	1.20 (1.14, 1.26)	4,517 (20.97)	1.12 (1.07, 1.18)
	Never exercise	3,737 (46.41)	1.69 (1.60, 1.77)	6,224 (33.32)	1.44 (1.37, 1.51)
Smoke (including quitting)	Regular exercise	1,210 (25.65)	1.37 (1.28, 1.47)	39 (25.45)	1.27 (0.92, 1.75)
	Occasional exercise	1,895 (29.50)	1.69 (1.58, 1.79)	57 (26.65)	1.27 (0.98, 1.66)
	Never exercise	1,986 (41.62)	2.16 (2.03, 2.30)	94 (46.90)	1.78 (1.45, 2.19)
CVD mortality					
Never smoke	Regular exercise	1,000 (10.75)	1.00	1,240 (8.84)	1.00
	Occasional exercise	1,544 (12.45)	1.23 (1.13, 1.33)	2,190 (10.17)	1.10 (1.02, 1.17)
	Never exercise	1,781 (22.12)	1.89 (1.75, 2.04)	3,307 (17.70)	1.47 (1.38, 1.57)
Smoke (including quitting)	Regular exercise	452 (9.58)	1.29 (1.15, 1.45)	22 (14.36)	1.41 (0.92, 2.17)
	Occasional exercise	697 (10.85)	1.57 (1.42, 1.74)	26 (12.16)	1.12 (0.76, 1.66)
	Never exercise	859 (18.00)	2.34 (2.13, 2.57)	46 (22.95)	1.67 (1.24, 2.25)

[a]Models adjusted for age, alcohol drinking, BMI, comorbid diabetes, classification of hypertension, family history of CVD, family history of diabetes, family history of hypertension, family history of stroke, and the product term (physical activity * smoke).

thus the intensity and duration of exposures might be crude, and we only measured exposures at baseline while they can change over time; however, such misclassification may have biased the associations toward null, which means we may have underestimated the individual and joint associations of smoking and physical activity. Secondly, the measuring of smoking and physical activity was self-reported, which may be subject to recall bias. However, we classified them as dichotomous or trichotomous variables, which may reduce recall bias to some extent. Thirdly, this study was unable to control for education background and all comorbidities that could be confounders, some diseases may limit exercise ability and also be risk factors for death, such as heart failure and stroke. But we controlled for family history of chronic diseases including CVD and stroke, and sensitivity analyses excluding people with diabetes and family history of chronic diseases yielded similar results. Future studies could quantitatively measure the exposures and regularly monitor their changes to obtain more accurate estimates. Subsequent studies can monitor the physical activity level using an accelerometer and define the smoke level with a more adequate classification. It is also a suggestion to see if there are differences between different types of physical activities.

Conclusion and clinical implications

Our study suggested that smoking and physical inactivity together may have amplified association on death compared to their independent associations, highlighting the importance of improving behavioral factors in combination. In the elderly hypertensive population, smokers who never exercised had the greatest risk for mortality among all exposure groups, but increasing physical activity levels might counteract some of the extra risks. Clinically, physicians should be aware of this increased risk among smokers who never exercised. Health care providers should ensure that recommendation to promote physical activity and long-term non-smoking are addressed as part of routine care, which may help to prevent cases caused by the interplay of these two factors. Government should promote primary prevention strategies that improve behavioral factors in combination and promoting a comprehensive healthy lifestyle in hypertensive elderly. And government could invest more efforts in promoting physical activity as a way to reduce mortality risk among smokers when tobacco control faced substantial barriers.

Data availability statement

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

Ethics statement

The studies involving human participants were reviewed and approved by the Institutional Review Board of Center for Disease Control and Prevention in Minhang District, Shanghai (No: EC-P-2019-009). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

YYu, GQ, and HX: had full access to all of the data in the study, take responsibility for the integrity of the data, and the accuracy of the data analysis. YYu, YH, and GQ: study concept and design and study supervision. YYa: drafting of the manuscript. YYu, JL, XiaL, and ZL: critical revision of the manuscript for important intellectual content. YYa, HX, YH, GQ, and YYu: statistical analysis. YYu, JL, GQ, YX, and XinL: obtained funding. HX, YH, GQ, YYu, and JL: administrative, technical, or material support. All authors acquisition, analysis, or interpretation of data. All authors contributed to the article and approved the submitted version.

Funding

This study was supported by a grant from Shanghai Rising-Star Program (21QA1401300) to YYu, a grant from Shanghai Municipal Natural Science Foundation (22ZR1414900) to YYu, grants from the Independent Research Fund Denmark (DFF-6110- 00019B, DFF-9039-00010B, and DFF-1030-00012B) to JL, a grant from the Nordic Cancer Union (R275-A15770) to JL, a grant from the Karen Elise Jensens Fond (2016) to JL, a grant from Novo Nordisk Foundation (NNF18OC0052029) to JL, grants from the National Natural Science Foundation of China (82073570 and 11871164) to GQ, Shanghai Municipal Science and Technology Major Project (ZD2021CY001) to GQ, Three-year Action Program of Shanghai Municipality for Strengthening the Construction of Public Health System (GWV-10.1-XK05) Big Data and Artificial Intelligence Application to GQ, Shanghai Municipal Nature Science Foundation (19ZR1445900), Min hang district key disciplines in public health (MGWXK01) and Health Consortium Foundation of Fudan University and Minhang District Health Committee (2019FM02) to HX. XiaL is supported by the European Union's Horizon 2020 Research and Innovation Programme under the Marie Sklodowska-Curie grant agreement No. 891079. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflict of interest

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

Publisher's note

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.2022.1005260/full#supplementary-material

References

1. United Nations. *World Population Ageing Report*. United Nations (2019). Available online at: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2019-Report.pdf (accessed June 15, 2020).

2. World Health Organization. *Global Report on Ageism*. (2021). Available online at: https://www.who.int/publications/i/item/9789240016866 (accessed March 18, 2021).

3. Nguyen TN, Chow CK. Global and national high blood pressure burden and control. *Lancet.* (2021) 1688:3. doi: 10.1016/S0140-6736(21)01688-3

4. Zhou B, Carrillo-Larco RM, Danaei G, Riley LM, Paciorek CJ, Stevens GA, et al. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet.* (2021) 398:957–80. doi: 10.1016/S0140-6736(21)01330-1

5. NCD Risk Factor Collaboration. Long-term and recent trends in hypertension awareness, treatment, and control in 12 high-income countries: an analysis of 123 nationally representative surveys. *Lancet.* (2019) 394:639–51. doi: 10.1016/S0140-6736(19)31145-6

6. Geldsetzer P, Manne-Goehler J, Marcus ME, Ebert C, Zhumadilov Z, Wesseh CS, et al. The state of hypertension care in 44 low-income and middle-income countries: a cross-sectional study of nationally representative individual-level data from 1·1 million adults. *Lancet.* (2019) 394:652–62. doi: 10.1016/S0140-6736(19)30955-9

7. Wang Z, Chen Z, Zhang L, Wang X, Hao G, Zhang Z, et al. Status of hypertension in China: results from the China hypertension survey, 2012–2015. *Circulation.* (2018) 137:2344–56. doi: 10.1161/CIRCULATIONAHA.117.032380

8. Fried LP, Rowe JW. Health in aging - past, present, and future. *N Engl J Med.* (2020) 383:1293–6. doi: 10.1056/NEJMp2016814

9. Colin Mathers GS, Mascarenhas M. *Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks*. Geneva: World Health Organization (2016).

10. Lee DH, Nam JY, Kwon S, Keum N, Lee JT, Shin MJ, et al. Lifestyle risk score and mortality in Korean adults: a population-based cohort study. *Sci Rep.* (2020) 10:10260. doi: 10.1038/s41598-020-66742-y

11. Yang Q, Cogswell ME, Flanders WD, Hong Y, Zhang Z, Loustalot F, et al. Trends in cardiovascular health metrics and associations with all-cause and CVD mortality among US adults. *J Am Med Assoc.* (2012) 307:1273–83. doi: 10.1001/jama.2012.339

12. Inoue-Choi, L, Reyes-Guzman C, Hartge P, Caporaso N, Freedman ND. Association of long-term, low-intensity smoking with all-cause and cause-specific mortality in the National Institutes of Health-AARP diet and health study. *J Am Med Assoc Intern Med.* (2017) 177:87–95. doi: 10.1001/jamainternmed.2016.7511

13. Tan J, Zhang X, Wang W, Yin P, Guo X, Zhou M. Smoking, blood pressure, and cardiovascular disease mortality in a large cohort of Chinese men with 15 years follow-up. *Int J Environ Res Public Health.* (2018) 15:51026. doi: 10.3390/ijerph15051026

14. Ge Z, Hao Y, Cao J, Li J, Chen J, Huang J, et al. Does cigarette smoking exacerbate the effect of blood pressure on the risk of cardiovascular and all-cause mortality among hypertensive patients? *J Hypertens.* (2012) 30:2307–13. doi: 10.1097/HJH.0b013e328359aa1f

15. Hozawa A, Okamura T, Murakami Y, Kadowaki T, Nakamura K, Hayakawa T, et al. Joint impact of smoking and hypertension on cardiovascular disease and all-cause mortality in Japan: NIPPON DATA80, a 19-year follow-up. *Hypertens Res.* (2007) 30:1169–75. doi: 10.1291/hypres.30.1169

16. Lim SJ, Gombojav B, Jee SH, Nam CM, Ohrr H. Gender-specific combined effects of smoking and hypertension on cardiovascular disease mortality in elderly Koreans: the Kangwha Cohort Study. *Maturitas.* (2012) 73:331–6. doi: 10.1016/j.maturitas.2012.09.002

17. Joseph G, Marott JL, Torp-Pedersen C, Biering-Sørensen T, Nielsen G, Christensen AE, et al. Dose-response association between level of physical activity and mortality in normal, elevated, and high blood pressure. *Hypertension.* (2019) 74:1307–15. doi: 10.1161/HYPERTENSIONAHA.119.13786

18. Pescatello LS, Buchner DM, Jakicic JM, Powell KE, Kraus WE, Bloodgood B, et al. Physical activity to prevent and treat hypertension: a systematic review. *Med Sci Sports Exerc.* (2019) 51:1314–23. doi: 10.1249/MSS.0000000000001943

19. Lakoski SG, Eves ND, Douglas PS, Jones LW. Exercise rehabilitation in patients with cancer. *Nat Rev Clin Oncol.* (2012) 9:288–96. doi: 10.1038/nrclinonc.2012.27

20. Shortreed SM, Peeters A, Forbes AB. Estimating the effect of long-term physical activity on cardiovascular disease and mortality: evidence from the Framingham Heart Study. *Heart.* (2013) 99:649–54. doi: 10.1136/heartjnl-2012-303461

21. Yang YJ. An overview of current physical activity recommendations in primary care. *Korean J Fam Med.* (2019) 40:135–42. doi: 10.4082/kjfm.19.0038

22. Sherrington C, Fairhall N, Kwok W, Wallbank G, Tiedemann A, Michaleff ZA, et al. Evidence on physical activity and falls prevention for people aged 65+ years: systematic review to inform the WHO guidelines on physical activity and sedentary behaviour. *Int J Behav Nutr Phys Act.* (2020) 17:144. doi: 10.1186/s12966-020-01041-3

23. Paffenbarger RS, Hyde RT, Wing AL, Hsieh CC. Physical activity, all-cause mortality, and longevity of college alumni. *N Engl J Med.* (1986) 314:605–13. doi: 10.1056/NEJM198603063141003

24. Borrell LN. The effects of smoking and physical inactivity on advancing mortality in adults US. *Ann Epidemiol.* (2014) 24:484–7. doi: 10.1016/j.annepidem.2014.02.016

25. Holme A, Anderssen SA. Physical activity, smoking and mortality among men who participated in the Oslo studies of 1972 and 2000. *Tidsskr Nor Laegeforen.* (2014) 134:1743–8. doi: 10.4045/tidsskr.14.0073

26. Lallukka T, Lahti J, Lahelma E, Rahkonen O. The contribution of smoking to mortality during working age at different levels of leisure-time physical activity. *Eur J Public Health.* (2016) 26:826–30. doi: 10.1093/eurpub/ckw065

27. Lacombe JM, Armstrong EG, Wright FL, Foster C. The impact of physical activity and an additional behavioural risk factor on cardiovascular disease, cancer and all-cause mortality: a systematic review. *BMC public health.* (2019) 19:900. doi: 10.1186/s12889-019-7030-8

28. Wang Y, Wang Y, Qain Y, Zhang J, Tang X, Sun J, et al. Association of body mass index with cause specific deaths in Chinese elderly hypertensive patients: Minhang community study. *PLoS ONE.* (2013) 8:e71223. doi: 10.1371/journal.pone.0071223

29. Yu JM, Kong QY, Schoenhagen P, Shen T, He YS, Wang JW, et al. The prognostic value of long-term visit-to-visit blood pressure variability on stroke in real-world practice: a dynamic cohort study in a large representative sample of Chinese hypertensive population. *Int J Cardiol.* (2014) 177:995–1000. doi: 10.1016/j.ijcard.2014.09.149

30. Shanghai Municipal Health Commission. *Guidelines for Prevention and treatment of Hypertension in Shanghai Communities (Trial)*. Shanghai: Shanghai Municipal Health Commission (2004).

31. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of hypertension global hypertension practice guidelines. *Hypertension.* (2020) 75:1334–57. doi: 10.1161/HYPERTENSIONAHA.120.15026

32. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med.* (2020) 54:1451–62. doi: 10.1136/bjsports-2020-102955

33. *World Health Organization, International Classification of Diseases, Tenth Revision (ICD-10)*. World Health Organization. Available online at: https://www.who.int/classifications/classification-of-diseases

34. Zhu J, Liu X, Zhang J, Li J, Chen L, Huang C, et al. Time-varying association between body mass index and all-cause mortality in patients with hypertension. *Int J Obes.* (2022) 46:316–24. doi: 10.1038/s41366-021-00994-0

35. Hess KR. Graphical methods for assessing violations of the proportional hazards assumption in Cox regression. *Stat Med.* (1995) 14:1707–23. doi: 10.1002/sim.4780141510

36. George B, Seals S, Aban I. Survival analysis and regression models. *J Nucl Cardiol.* (2014) 21:686–94. doi: 10.1007/s12350-014-9908-2

37. Andersson T, Alfredsson L, Källberg H, Zdravkovic S, Ahlbom A. Calculating measures of biological interaction. *Eur J Epidemiol.* (2005) 20:575–9. doi: 10.1007/s10654-005-7835-x

38. VanderWeele TJ, Knol MJ. A tutorial on interaction. *Epidemiolog Methods.* (2014) 3:5. doi: 10.1515/em-2013-0005

39. Allison PD. *Survival Analysis Using SAS®: A Practical Guide*. 2nd ed. Cary, NC: SAS Institute Inc. (2010).

40. Li R, Chambless L. Test for additive interaction in proportional hazards models. *Ann Epidemiol.* (2007) 17:227–36. doi: 10.1016/j.annepidem.2006.10.009

41. Blot WJ, Day NE. Synergism and interaction: are they equivalent? *Am J Epidemiol.* (1979) 110:99–100. doi: 10.1093/oxfordjournals.aje.a112793

42. Rothman KJ, Greenland S, Walker AM. Concepts of interaction. *Am J Epidemiol.* (1980) 112:467–70. doi: 10.1093/oxfordjournals.aje.a113015

43. Saracci R. Interaction and synergism. *Am J Epidemiol.* (1980) 112:465–6. doi: 10.1093/oxfordjournals.aje.a113014

44. Morris JN, Everitt MG, Pollard R, Chave SP, Semmence AM. Vigorous exercise in leisure-time: protection against coronary heart disease. *Lancet.* (1980) 2:1207–10. doi: 10.1016/S0140-6736(80)92476-9

45. Rehm J, Fichter MM, Elton M. Effects on mortality of alcohol consumption, smoking, physical activity, and close personal relationships. *Addiction.* (1993) 88:101–12. doi: 10.1111/j.1360-0443.1993.tb02767.x

46. O'Donovan G, Hamer M, Stamatakis E. Relationships between exercise, smoking habit and mortality in more than 100,000 adults. *Int J Cancer.* (2017) 140:1819–27. doi: 10.1002/ijc.30611

47. Robsahm TE, Heir T, Sandvik L, Prestgaard E, Tretli S, Erikssen JE, et al. Changes in midlife fitness, body mass index, and smoking influence cancer incidence and mortality: a prospective cohort study in men. *Cancer Med.* (2019) 8:4875–82. doi: 10.1002/cam4.2383

48. Zhou X, Nonnemaker J, Sherrill B, Gilsenan AW, Coste F, West R. Attempts to quit smoking and relapse: factors associated with success or failure from the ATTEMPT cohort study. *Addict Behav.* (2009) 34:365–73. doi: 10.1016/j.addbeh.2008.11.013

49. Tobacco Control Office. *Results of 2018 China Adult Tobacco Survey Released: Smoking Prevalence Among 15 Years and Older Tends to Decline*. Chinese Center

for Disease Control and Prevention. (2018). Available online at: http://www.chinacdc.cn/yw_9324/201905/t20190530_202932.html (accessed May 30, 2019).

50. Hyland A, Laux FL, Higbee C, Hastings G, Ross H, Chaloupka FJ, et al. Cigarette purchase patterns in four countries and the relationship with cessation: findings from the International Tobacco Control (ITC) Four Country Survey. *Tob Control.* (2006) 15(Suppl.3):iii59–64. doi: 10.1136/tc.2005.012203

51. Bloomer RJ, Fisher-Wellman K. The role of exercise in minimizing postprandial oxidative stress in cigarette smokers. *Nicotine Tob Res.* (2009) 11:3–11. doi: 10.1093/ntr/ntn005

52. Nakagata T, Fukao K, Kobayashi H, Katamoto S, Naito H. The effects of transdermal nicotine patches on the cardiorespiratory and lactate responses during exercise from light to moderate intensity: implications for exercise prescription during smoking cessation. *Medicina.* (2019) 55:70348. doi: 10.3390/medicina55070348

53. Jonsdottir D, Jonsdottir H. Does physical exercise in addition to a multicomponent smoking cessation program increase abstinence rate and suppress weight gain? An intervention study. *Scand J Caring Sci.* (2001) 15:275–82. doi: 10.1046/j.1471-6712.2001.00039.x

54. Jain P, Danaei G, Manson JE, Robins JM, Hernán MA. Weight gain after smoking cessation and lifestyle strategies to reduce it. *Epidemiology.* (2020) 31:7–14. doi: 10.1097/EDE.0000000000001106

55. Luo J, Manson JE, Hendryx M, Shadyab AH, Johnson KC, Dinh PC, et al. Physical activity and weight gain after smoking cessation in postmenopausal women. *Menopause.* (2019) 26:16–23. doi: 10.1097/GME.0000000000001168

56. Nduaguba SO, Ford KH, Rascati K. The role of physical activity in the association between smoking status and quality of life. *Nicotine Tob Res.* (2019) 21:1065–71. doi: 10.1093/ntr/nty052

57. Linke SE, Rutledge T, Johnson BD, Olson MB, Bittner V, Cornell CE, et al. The joint impact of smoking and exercise capacity on clinical outcomes among women with suspected myocardial ischemia: the WISE study. *J Womens Health.* (2009) 18:443–50. doi: 10.1089/jwh.2008.1023

58. Shanghai Municipal Commission of Health and Family Planning. *Shanghai Community Health Management Work Standards - Integrated Prevention and Treatment of Chronic Diseases (2017 Edition)*. Shanghai: Shanghai Municipal Commission of Health and Family Planning (2017).

frontiers | Frontiers in Public Health

TYPE Systematic Review
PUBLISHED 14 October 2022
DOI 10.3389/fpubh.2022.1032076

Check for updates

OPEN ACCESS

EDITED BY
Stevo Popovic,
University of Montenegro, Montenegro

REVIEWED BY
Predrag R. Bozic,
Serbian Institute of Sport and Sports Medicine (SISSM), Serbia
Dragan Cvejić,
University of Novi Sad, Serbia
Aleksandra Aleksić Veljković,
University of Nis, Serbia

*CORRESPONDENCE
Špela Bogataj
spela.bogataj@kclj.si

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 30 August 2022
ACCEPTED 27 September 2022
PUBLISHED 14 October 2022

CITATION
Bogataj Š, Mesarič KK, Pajek M, Petrušič T and Pajek J (2022) Physical exercise and cognitive training interventions to improve cognition in hemodialysis patients: A systematic review.
Front. Public Health 10:1032076.
doi: 10.3389/fpubh.2022.1032076

Physical exercise and cognitive training interventions to improve cognition in hemodialysis patients: A systematic review

Špela Bogataj[1]*, Katja Kurnik Mesarič[1], Maja Pajek[2], Tanja Petrušič[3] and Jernej Pajek[1]

[1]Department of Nephrology, University Medical Centre Ljubljanag, Ljubljana, Slovenia, [2]Faculty of Sport, University of Ljubljana, Ljubljana, Slovenia, [3]Faculty of Education, University of Ljubljana, Ljubljana, Slovenia

Introduction: Patients with chronic kidney disease treated with hemodialysis (HD) have lower cognitive abilities compared to the age-matched healthy population. Recently, physical exercise and cognitive training have been presented as possible interventions to improve cognitive abilities both in the general population and in patients with chronic diseases. To date, there is no general overview of the current knowledge on how these interventions affect cognitive abilities in HD patients and what tests are used to measure these effects.

Methods: Three electronic databases were searched for randomized controlled studies of physical exercise or cognitive training interventions that examined effects on cognitive abilities/performance in HD patients.

Results: Six articles were included. All included studies used physical exercise as an intervention, with one study also including tablet-based cognitive training. Four studies included an intradialytic approach and two included a home-based intervention. Intervention lasted. A significant intervention effect was observed in three studies compared with the control condition.

Conclusion: The present review suggests that physical exercise might improve or at least not worsen cognitive performance in HD patients, whereas the effect of cognitive training has not yet been adequately studied. There is a need for more sensitive and specific cognitive tests to adequately measure the effects of interventions in the HD population.

KEYWORDS

cognitive performance, hemodialysis, physical exercise, cognitive training, cognitive tests, intervention

10.3389/fpubh.2022.1032076

Introduction

It is well-documented that cognitive deficits cause progression toward dementia (1, 2). This phenomenon is even more pronounced in clinical populations (3). An example of a vulnerable population with an increased incidence of cognitive impairment is patients with kidney disease treated with hemodialysis (HD). The cognitive decline in HD patients is not only the result of underlying and concomitant diseases but can also be attributed to their changed lifestyle after starting HD. These patients have to travel to a dialysis center every other day, where they spend 4–5 h in a sedentary position during a HD procedure. Many reports a post-dialysis burnout and fatigue lasting for up to 24 h post-dialysis (4). As a result, these patients are less physically active and activate their mental functions to a lesser extent. Moreover, in HD patients, diabetes, a common chronic kidney disease (CKD) comorbidity, was significantly associated with larger cognitive impairment (5). HD treatment itself also contributes to a higher risk of developing dementia by causing ischemic stunning of the brain (6). In addition, dementia risk factors such as obesity, depression, and social isolation are common in the HD population.

It was found that only 13% of HD patients have a normal cognitive function (7). Moreover, clinicians usually fail to recognize declining cognitive performance in these patients; therefore, cognitive impairment is critically underestimated and not appropriately treated (8). It has been reported that <5% of all patients with kidney disease with cognitive impairment have been evaluated or received a medical diagnosis (9). Measurement of cognitive function is not currently part of the physical examination and medical history of CKD patients.

Lately, non-pharmacological interventions have been introduced as possible approaches to mitigate cognitive decline and dementia (3). Studies that examined the effect of exercise interventions on cognitive performance showed conflicting results. A systematic review of exercise intervention studies on cognition in older adults did not provide sufficient evidence that exercise affects cognitive performance (10). Another systematic review concluded that physical activity could delay the progression of cognitive decline in the elderly (11). In a recent study, the authors reported the results of a 6-month aerobic exercise intervention in older adults (>60 years) on cognitive function. Compared to control subjects, participants in the training group showed broad improvement in cognitive abilities, including processing speed, episodic memory, executive functions, and updating (12).

In addition to physical activity, cognitive training programs to improve general and specific cognitive domains are being increasingly used in research on cognitive decline. A meta-analysis of 17 controlled interventional trials of computer-assisted cognitive training in subjects with mild cognitive impairment showed a moderate effect on general cognition (13). In community-dwelling older adults, the ACTIVE trial demonstrated long-term retention of a benefit of 10–14 weeks' cognitive training with significant improvement in cognitive abilities and maintenance of functional status after a 10-year period (14).

Despite the fact that there is a plethora of research on physical and cognitive interventions, most of the focus has been on the general population. There is little research addressing the clinical population. In addition, there is no systematic review of the effect of physical exercise and cognitive training that focuses on patients with CKD undergoing HD. Therefore, the aim of this systematic review was to examine the effects of non-pharmacological interventions in the form of cognitive and physical exercise training on different domains of cognitive performance.

Materials and methods

The review methods and reporting were performed according to the preferred reporting items in systematic review and meta-analyses (PRISMA) guidelines (15).

Eligibility criteria

The PICOS search tool (participant, intervention, comparison, outcome, and study design) was used to determine keywords (Table 1).

Studies were included in the systematic review if they met the following criteria: (a) randomized controlled trials, (b) published in academic journals, (c) written in English, (d) with participants on hemodialysis and (e) studies that included physical exercise or cognitive training interventions with (f) outcome of cognitive performance. Studies were excluded if study population were CKD patients without kidney replacement therapy or patients on peritoneal dialysis, animal studies, and individual case studies.

TABLE 1 "PICOS" items (participants, intervention, comparisons, outcomes, study designs) used to select keywords.

PICOS item	Detail
Participants	Hemodialysis patients
Interventions	Physical exercise training or/and cognitive training
Comparisons	Active or inactive control group
Outcomes	Cognitive performance
Study designs	RCTs

RCT, randomized controlled trial.

Search strategy

To identify potentially relevant studies, we performed a comprehensive literature search in electronic databases including PsycInfo, PubMed and MEDLINE (Ovid) from the database's inception to the final update in August 2022. Medical subject heading (mesh) terms were used, if available, for a qualitative search of potential studies. Search strategies utilized a combination of key words to represent definitions of hemodialysis, cognitive functioning, physical activity interventions and cognitive training. Terms were combined using the "AND" and "OR" Boolean operator (for the full list of search phrases and terms, see Table 2). To increase the likeliness of including all relevant trials, a backward and forward search were performed by screening the citations and references list of the included studies. A flow diagram of the search is presented in Figure 1.

Study selection and data collection procedure

Articles from the above databases were checked for duplicates using EndNote X9. Subsequently, all articles were

TABLE 2 Search strategy.

Literature search	
PsycInfo	Hemodialysis OR haemodialysis AND cognition OR cognitive function OR cognitive performance OR cognitive abilities OR cognitive ability
	Hemodialysis OR haemodialysis AND cognition OR cognitive function OR cognitive performance OR cognitive abilities OR cognitive ability AND intervention
	Hemodialysis OR haemodialysis AND cognitive training
	Hemodialysis OR haemodialysis AND physical activity OR exercise OR fitness OR physical exercise
	Hemodialysis OR haemodialysis AND physical activity OR exercise OR fitness OR physical exercise AND intervention
	Hemodialysis OR haemodialysis AND cognitive intervention
	Renal dialysis AND cognition OR cognitive function OR cognitive performance OR cognitive abilities OR cognitive ability AND intervention
	Renal dialysis AND cognition OR cognitive function OR cognitive performance OR cognitive abilities OR cognitive ability AND intervention AND physical activity OR exercise OR fitness OR physical exercise
	Renal dialysis AND cognition OR cognitive function OR cognitive performance OR cognitive abilities OR cognitive ability
	Renal dialysis AND physical activity OR exercise OR fitness OR physical exercise AND intervention
	Renal dialysis AND cognitive training
Filters	English, academic journals
PubMed	Hemodialysis AND cognition [MeSH]
	Hemodialysis [MeSH] AND cognitive training
	Hemodialysis [MeSH] AND physical activity intervention and cognition [MeSH]
	Hemodialysis [MeSH] AND and exercise [MeSH] AND cognition [MeSH]
	Renal dialysis [MeSH] AND cognition AND intervention
	Renal dialysis [MeSH] AND physical activity AND cognition AND intervention
	Renal dialysis [MeSH] AND cognitive training
	Renal dialysis [MeSH] AND exercise [MeSH]
Filters	English, randomized controlled trials
Medline (OVID)	Renal dialysis AND cognition AND exercise
	Renal dialysis AND cognitive training
	Renal dialysis AND cognitive training OR physical exercise intervention
	Hemodialysis OR renal dialysis AND cognitive training
	Renal dialysis AND physical acitivity intervention OR fitnes intervention OR physical excercise intervention
	Renal dialysis AND cognitive intervention
	Renal dialysis AND cognitive intervention OR physical excercise intervention
	Renal dialysis AND cognit*
Filters	English, academic journals, expand term finder

*Wildcard that finds variant spellings of words.

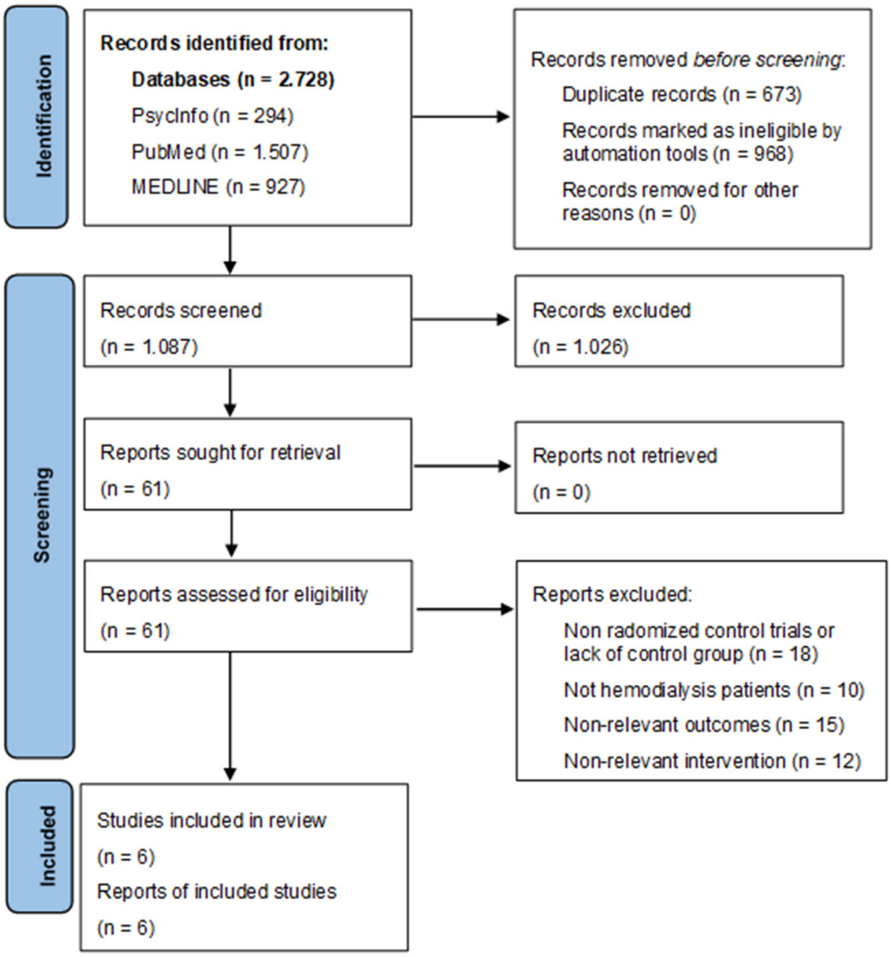

FIGURE 1
PRISMA flow diagram.

screened using the Rayyan app (16). In the app, two reviewers (ŠB and KKM) independently reviewed the titles and abstracts of each article in a blinded manner. The decision to include an article was made at the research team meeting. Articles that met the inclusion criteria underwent quality assessment.

Risk of bias assessment

The quality of the included studies was evaluated using the revised Cochrane Collaboration's risk of bias tool (17). The following biases were evaluated: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, bias in selection of the reported result and overall bias. Risk of bias was assessed as low, some concerns or high for each domain and for overall bias.

Results

Study selection

The flow of studies through the review process is reported in Figure 1. Automation tools used in databases were language (English), type of publication (Academic journals) and if possible study type (randomized controlled trial). Duplicate records were removed once the search strategy outputs were combined. Titles and abstracts were screened to identify studies that administered physical activity interventions or cognitive training/interventions to promote cognitive functioning. Full-texts of these articles were read to see whether full inclusion criteria were met. All studies that met inclusion criteria were again screened to determined eligibility for the systematic literature review.

Quality assessment

The bias risks are presented using a risk of bias summary in Figure 2. In the aspects of measurement of outcome, two of the studies were assessed as high risk (18, 19), in the aspects of randomization process three of six included studies were assessed with some concerns (18–20). Three of all included studies were assessed as low risk on all domains and overall (21–23).

Study characteristics

The six included studies were published between 2015 and 2021. They included a total of 466 HD patients. Two hundred fourteen patients received a physical exercise intervention and seven patients received a cognitive training intervention. The control group, which received standard treatment or stretching exercises, consisted of 245 HD patients. The average age of participants in the included studies ranged from 48 to 75 years. The youngest patients were in the exercise group of the study by McAdams-DeMarco et al. (20), and the oldest were in the control group of the study by Baggetta et al. (18). Two studies did not report the frequency of exercise. The remaining physical activity studies reported that exercise was performed three times per week. The duration of the intervention ranged from 12 to 24 weeks. The characteristics of the included studies are shown in Table 3.

Two included studies examined the effect of a 6-month home-based walking program on self-reported cognitive function as measured by KDQOL-SF (18, 19). In one study, there was a significant increase in cognitive function (19) and in the other study the control group experienced a decline while an experimental group preserved self-reported cognitive function in older dialysis patients (>65 years) (18). An intradialytic exercise program in the form of stretching exercises and cycling significantly improved cognitive performance as measured by the MMSE in the experimental group compared to the standard care control group (23). Contraindicatory, intradialytic resistance exercise (22) and chair stand exercise program (21) showed no significant effect on cognitive ability as measured by MoCA and 3MS. Only one included pilot study examined the effects of cognitive training (20) with 20 HD patients randomly assigned to a cognitive training group (brain games on tablet computers, $n = 7$), an intradialytic cycling group ($n = 6$), or to standard treatment group ($n = 7$). The intervention lasted 3 months and showed a decline in executive functions and psychomotor speed in the control group, whereas the decline was not observed in either the cycling or cognitive training groups.

Regarding the duration of the intervention, in two studies (20, 21), the 12-week intervention did not result in significant improvement in selected cognitive domains. In the remaining studies, the intervention was delivered for 16 weeks or longer and showed either significant improvement (19, 23) or maintenance of cognitive performance compared to the control group (18, 22).

Cognitive performance/ability was assessed using various validated cognitive tests/questionnaires: Modified Mini-Mental State (3MS), Trail-Making Test A and B (TMTA and TMTB), Kidney Disease Quality of Life Short Form (KDQOL-SF), Montreal Cognitive Assessment (MoCA), and Mini-Mental State Examination (MMSE). Brief description of used tests and questionnaires is offered in Table 4.

The MoCA test is a cognitive screening test that has good sensitivity (76.7%) and specificity (78.6%) for assessing cognitive performance in HD patients (29). Another screening test, the MMSE, showed a sensitivity of 55.2% and specificity of 75% (29). The 3MS is a modified version of the MMSE, which showed a sensitivity of 88% and a specificity of 90% as a screening test for dementia in a study of elderly residents (30). In a study by Dobbs and Shergill (31) examining the predictive power of the TMT for

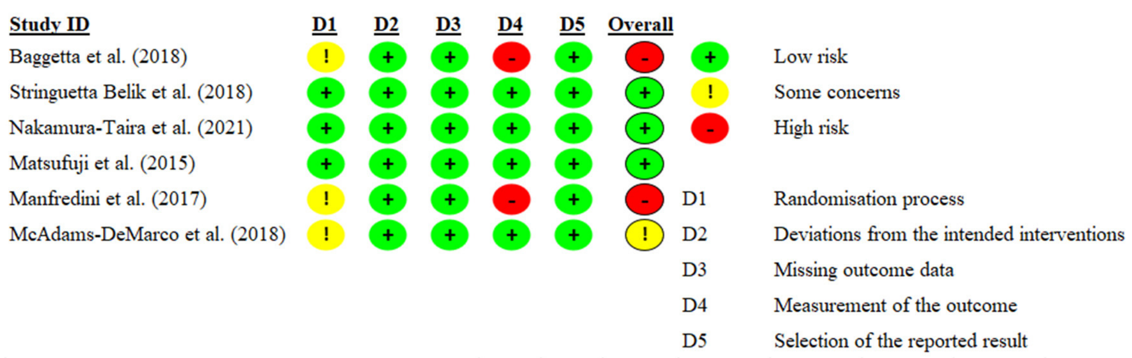

FIGURE 2
Risk of bias summary.

10.3389/fpubh.2022.1032076

TABLE 3 Characteristics of included studies.

Study	Sample size	Age (mean ± SD)	Intervention	Duration	Measures	Outcomes
McAdams-DeMarco et al. (20)	CT = 7 EX = 6 CON = 7	CT = 48.9 ± 12.2 EX = 48.0 ± 7.0 CON = 55.0 ± 9.7	CT = intradialytic cognitive training EX = intradialytic cycling CON = standard care	3x/week 12 weeks	3 MS TMTA TMTB	3 MS (score) mean change from baseline CT: −3.4 (9.2); $p = 0.24$; ES = −0.36 EX: 4.3 (5.4); $p = 0.17$; ES = +0.7 CON: −0.1 (7.0); $p = 0.96$; ES = −0.01 TMTA (s) mean change from baseline CT: −0.2 (14.7); $p = 0.98$; ES = −0.01 EX: −2.5 (9.3); $p = 0.77$; ES = −0.15 CON: 15.0 (25.8); $p = 0.055$; ES = +0.76 TMTB (s) mean change from baseline CT: 0.6 (29.1); $p = 0.97$; ES = +0.02 EX: −8.9 (24.4); $p = 0.63$; ES = −0.46 CON: 47.4 (45.7); $p = 0.006$; ES = +1.1
Manfredini et al. (19)	EX = 104 CON = 123	EX = 63 ± 13 CON = 64 ± 14	EX = walking exercise program CON = standard care	24 weeks	KDQOL-SF cognitive function	Change from baseline (range) EX: +0.3 (−3.2 to 3.8); $p = 0.87$; ES = +0.03 CON: −6.4 (−11.9 to −0.9); $p = 0.02$; ES = −0.44 Changes between groups (range) −6.7 (−13.2 to −0.2); p (EX vs. CON) = 0.04
Matsufuji et al. (21)	EX = 15 CON = 17	EX = 69 ± 11 CON = 69 ± 13	EX = chair stand exercise CON = stretch exercise	EX: 3x/week CON: 1x/week 12 weeks	3MS	Change from baseline (range) EX: 6 (0–17) CON: 2 (−5 to 12) Comparison between groups $p = 0.40$
Nakamura-Taira et al. (22)	EX = 21 CON = 21	EX = 74.9 ± 2.23 CON = 72.57 ± 2.26	EX = intradialytic resistance exercise CON = stretch exercise	3x/week 24 weeks	MoCA	Result at baseline and after 24 weeks EX: 18.45 ± 0.63 (baseline), 18.87 ± 0.71 (at 24 weeks); ES = +0.63 CON: 18.48 ± 0.77 (baseline), 18.09 ± 0.94 (at 24 weeks); ES = −0.45 Comparison between groups SMD = 0.86 95% CI = 0.23–1.5 ES = −0.13 $p > 0.05$
Stringuetta Belik et al. (23)	EX = 15 CON = 15	EX = 50.3 ± 17.24 CON = 57.8 ± 15.01	EX = intradialytic stretch exercises and cycling CON = standard care	3x/week 16 weeks	MMSE	Result at baseline and after 16 weeks

(Continued)

10.3389/fpubh.2022.1032076

TABLE 3 (Continued)

Study	Sample size	Age (mean ± SD)	Intervention	Duration	Measures	Outcomes
						EX: 24.0 ± 3.0 (baseline), 26.4 ± 2.92 (at 16 weeks); ES = +0.81; $p < 0.001$ CON: 22.4 ± 4.98 (baseline), 23.0 ± 5.09 (at 16 weeks); ES = +0.12; $p > 0.05$ Comparison between groups $p = 0.023$
Baggetta et al. (18)	EX = 53 CON = 62	EX = 73 ± 5 CON = 75 ± 6	EX = walking exercise program CON = standard care	24 weeks	KDQOL-SF cognitive function	Within group change EX: 0.8 (from −4.9 to 6.5); ES = +0.18; $p = 0.78$ CON: −9.6 (from −18.5 to −0.7); ES = −1.74; $p = 0.04$ Between-group difference in change (EX vs. CON) −10.4 (from −21.6 to 0.8); $p = 0.05$

CT, cognitive training group; EX, physical exercise group; CON, control group; 3MS, Modified Mini-Mental State; TMT, Trail-Making Test; KDQOL-SF, Kidney Disease Quality of Life Short Form; MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; ES, Cohens'd effect size; SMD, standardized mean difference; CI, confidence interval; p, statistical significance.

TABLE 4 Description of cognitive tests/questionnaires.

Test/questionnaire	Description
Trail-making test A and B (TMTA and TMTB)	TMT is a neuropsychological test that involves visual attention and task switching. It offers information about mental flexibility, visual search speed, speed of processing and executive functioning (24).
Kidney disease quality of life short form (KDQOL-SF)	KDQOL-SF offers disease specific quality of life measure for patients with end-stage renal disease. It includes generic and disease specific components. The scales of KDQOL-SF are: symptoms, effects of kidney disease, burden of kidney disease, work status, cognitive function, quality of social interaction, sexual function, sleep, social support, dialysis staff encouragement and patient satisfaction (25).
Montreal cognitive assessment (MoCA)	MoCA test is screening instrument for mild cognitive disfunction, and it offers information about cognitive domains of attention and concentration, executive functioning, memory, language, orientation, visuospatial abilities, conceptual thinking and orientation (26).
Mini-mental state examination (MMSE)	MMSE is a set of 11 tasks that can be used for assessing cognitive impairment (27). If offers a brief assessment of several cognitive domains: orientation, memory, attention, calculation, language and constructional ability.
Modified mini-mental state (3MS)	3MS is modified MMSE, it includes four additional items, and it extends scoring range. It can be used as a brief cognitive assessment or as a screening test. It offers a brief assessment of following cognitive domains: orientation, attention, concentration, calculation, language abilities, long-term and short-term memory, abstract thinking, and verbal fluency (28).

driving performance, the TMTA had a sensitivity of 77% and a specificity of 62%, while the TMTB had a sensitivity of 50% and a specificity of 88%. The cognitive domain of the KDQOL-SF had poor sensitivity (range, 28–36%) and modest specificity (range, 77–81%) for identifying poorer memory and executive function in the HD population (32).

Discussion

In the present review, we highlighted the effects of non-pharmacological interventions (physical exercise or cognitive training) on cognitive performance in HD patients. In addition, we presented and described the cognitive tests used in the included studies. The results of a limited number of studies show that physical exercise may significantly improve cognitive performance or at least mitigate cognitive decline in HD patients. Furthermore, there is insufficient evidence to conclude that cognitive training can attenuate cognitive decline in this population.

Lower cognitive functioning is often seen in HD patients (33–35). It has been documented that impaired cognitive abilities limit the ability to adhere to dialysis activities, make informed decisions, follow food and fluid restrictions, and are a risk factor for mortality in HD patients (36–39). Therefore, the recognition of poor cognitive function is crucial for the implementation of prevention and coping strategies to delay patients' cognitive decline. Furthermore, it is well-known that HD patients have poorer physical function compared to healthy individuals (40) and are mostly physically inactive (41), leading to a decreased quality of life (42). A growing number of randomized controlled trials of exercise training in the HD population show improvement in physical performance (43–46), dialysis symptoms (47), bone mineral density (48, 49), dialysis adequacy (50, 51), and quality of life (52). The highest adherence to physical exercise programs was observed in interventions performed during dialysis (53–55) and these interventions generally appear safe. Notwithstanding the positive effects of physical exercise mentioned above, randomized controlled trials investigating the effects on cognitive performance in HD patients are lacking. However, the limited number of studies included in this review suggests that patients may also benefit in this area.

There are several reasons for the positive association between physical activity and improved cognitive performance. Physical activity has been found to prevent cerebral atrophy or even increase hippocampal volume (56). Furthermore, a recent review found that up to 82% of total brain gray matter volume can be altered by physical activity (57). People in good physical condition can tolerate a higher neuropathological load without suffering cognitive impairment (58). The association between a low cognitive score and high risk or incidence of injury indicates a direct relationship between higher cognitive control and executive function (59, 60). Physical exercise may also have a positive effect on patients' cognitive performance by reducing inflammation and thus improving brain plasticity (61, 62). The results of the present review support the findings of the aforementioned studies in HD patients and contribute to the understanding of the relationship between physical exercise and cognitive performance in this population.

Cognitive training is another non-pharmacological intervention that has received attention in the scientific community. In healthy older adults, cognitive training prevented cognitive decline in executive functions, including working memory, abstracting ability, attentional control, inhibitory control, and verbal reasoning (63–65). Studies investigating cognitive training approaches to combat cognitive decline in HD patients are lacking.

This systematic review has its pitfalls, mainly related to the limitations of the included studies. Limitations include the small number of eligible studies, the small sample size of most included studies leading to low statistical power and possibly associated with potential imbalances in the study groups. The appropriateness of cognitive tests used to measure intervention effects is questionable. The instruments used in the included studies (3MS, MoCA, MMSE, KDQOL-SF) are predominantly screening tests to detect mild cognitive impairment, which are vulnerable to learning effects and may lack sensitivity and specificity (32, 66, 67). Therefore, the aforementioned tests are not the best option to detect the effects of the training interventions presented. Future studies should consider using more sensitive and specific tests instead of using tests that only measure global cognitive performance and are subject to the learning effect. It is proposed to develop a neurocognitive battery to systematically assess various cognitive abilities. Suggested cognitive tests with low learning effect, high sensitivity, validity, and reliability could be the Symbol Digit Modalities Test (SDMT), the Computerized Test of Attentional Performance (TAP), and the Trail Making Test (TMTA and TMTB) (24, 68, 69).

This is the first systematic review to demonstrate the effect of non-pharmacological interventions in the form of physical exercise and cognitive training in HD patients. It also provides insight into the instruments used to measure cognitive performance. These results from a small number of studies suggest that physical exercise training may have a positive effect on cognitive performance in HD patients. The effects of cognitive training or a combination of both approaches should be further investigated (70). Intra-dialysis period provides a unique opportunity to study these effects. Patients could use the time spent during the HD session to replace passive activities with activities that benefit their cognitive status. Research in nephrology has only begun to examine the short-term effects of exercise and cognitive training on cognition. Further studies are needed to replicate these findings and to investigate different strategies to maintain or improve cognitive function not only in HD patients but also in pre-dialysis CKD patients and in transplant recipients. In addition, long-term outcomes such as prevention of dementia should also be investigated. Furthermore, more sensitive and reliable instruments are needed to evaluate the effects of interventions on cognitive performance in this population.

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.

Author contributions

ŠB designed the search strategy. JP, KM, TP, and MP revised the design. Title and abstract screening was performed by ŠB and KM. Full text screening was performed by ŠB and JP. MP and TP performed data analysis. Quality assessment was performed by KM and ŠB. ŠB drafted the manuscript, which was revised by JP, KM, TP, and MP. All authors approved the final version of the manuscript.

Funding

The research is funded from ARRS postdoctoral research project Z3-3213 and ARRS research and infrastructure program P3-0323.

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.

References

1. Messier C, Gagnon M. Cognitive decline associated with dementia and type 2 diabetes: the interplay of risk factors. *Diabetologia.* (2009) 52:2471–4. doi: 10.1007/s00125-009-1533-2

2. Pal A, Pegwal N, Kaur S, Mehta N, Behari M, Sharma R. Deficit in specific cognitive domains associated with dementia in Parkinson's disease. *J Clin Neurosci.* (2018) 57:116–20. doi: 10.1016/j.jocn.2018.08.016

3. Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, et al. Dementia prevention, intervention, and care: 2020 report of the lancet commission. *Lancet.* (2020) 396:413–46. doi: 10.1016/S0140-6736(20)30367-6

4. Horigan AE. Fatigue in hemodialysis patients: a review of current knowledge. *J Pain Symptom Manage.* (2012) 44:715–24. doi: 10.1016/J.JPAINSYMMAN.2011.10.015

5. Cui L, Chen W, Yu X, Ju C. The relationship between cognitive function and having diabetes in patients treated with hemodialysis. *Int J Nurs Sci.* (2020) 7:60–5. doi: 10.1016/j.ijnss.2019.12.003

6. McIntyre CW. Haemodialysis-induced myocardial stunning in chronic kidney disease - a new aspect of cardiovascular disease. *Blood Purif.* (2010) 29:105–10. doi: 10.1159/000245634

7. Murray AM. Cognitive impairment in the aging dialysis and chronic kidney disease populations: an occult burden. *Adv Chronic Kidney Dis.* (2008) 15:123–32. doi: 10.1053/j.ackd.2008.01.010

8. Sehgal AR, Grey SF, DeOreo PB, Whitehouse PJ. Prevalence, recognition, and implications of mental impairment among hemodialysis patients. *Am J Kidney Dis.* (1997) 30:41–9. doi: 10.1016/S0272-6386(97)90563-1

9. Kurella M, Mapes D, Port FK, Chertow GM. Correlates and outcomes of dementia among dialysis patients: the dialysis outcomes and practice patterns study. *Nephrol Dialysis Transpl.* (2006) 21:2543–8. doi: 10.1093/ndt/gfl275

10. Snowden M, Steinman L, Mochan K, Grodstein F, Prohaska TR, Thurman DJ, et al. Effect of exercise on cognitive performance in community-dwelling older adults: Review of intervention trials and recommendations for public health practice and research. *J Am Geriatr Soc.* (2011) 59:704–16. doi: 10.1111/j.1532-5415.2011.03323.x

11. Carvalho A, Rea IM, Parimon T, Cusack BJ. Physical activity and cognitive function in individuals over 60 years of age: a systematic review. *Clin Interv Aging.* (2014) 9:661–82. doi: 10.2147/CIA.S55520

12. Jonasson LS, Nyberg L, Kramer AF, Lundquist A, Riklund K, Boraxbekk CJ. Aerobic exercise intervention, cognitive performance, and brain structure: results from the physical influences on brain in aging (PHIBRA) study. *Front Aging Neurosci.* (2017) 8:336. doi: 10.3389/fnagi.2016.00336

13. Hill NTM, Mowszowski L, Naismith SL, Chadwick VL, Valenzuela M, Lampit A. Computerized cognitive training in older adults with mild cognitive impairment or dementia: a systematic review and meta-analysis. *Am J Psychiatry.* (2017) 174:329–40. doi: 10.1176/appi.ajp.2016.16030360

14. Rebok GW, Ball K, Guey LT, Jones RN, Kim HY, King JW, et al. Ten-year effects of the advanced cognitive training for independent and vital elderly cognitive training trial on cognition and everyday functioning in older adults. *J Am Geriatr Soc.* (2014) 62:16–24. doi: 10.1111/jgs.12607

15. Page MJ, Mckenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* (2021) 372:n71. doi: 10.1136/bmj.n71

16. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev.* (2016) 5:1–10. doi: 10.1186/S13643-016-0384-4/FIGURES/6

17. Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. Assessing risk of bias in a randomized trial. *Cochrane Handbook Syst Rev Interv.* (2019) 205–28. doi: 10.1002/9781119536604.CH8

18. Baggetta R, D'Arrigo G, Torino C, Elhafeez SA, Manfredini F, Mallamaci F, et al. Effect of a home based, low intensity, physical exercise program in older adults dialysis patients: A secondary analysis of the EXCITE trial. *BMC Geriatr.* (2018) 18:248. doi: 10.1186/s12877-018-0938-5

19. Manfredini F, Mallamaci F, D'Arrigo G, Baggetta R, Bolignano D, Torino C, et al. Exercise in patients on dialysis: A multicenter, randomized clinical trial. *J Am Soc Nephrol.* (2017) 28:1259–68. doi: 10.1681/ASN.2016030378

20. McAdams-DeMarco MA, Konel J, Warsame F, Ying H, Fernández MG, Carlson MC, et al. Intradialytic cognitive and exercise training may preserve cognitive function. *Kidney Int Rep.* (2018) 3:81–8. doi: 10.1016/j.ekir.2017.08.006

21. Matsufuji S, Shoji T, Yano Y, Tsujimoto Y, Kishimoto H, Tabata T, et al. Effect of chair stand exercise on activity of daily living: a randomized controlled trial in hemodialysis patients. *J Renal Nutr.* (2015) 25:17–24. doi: 10.1053/J.JRN.2014.06.010

22. Nakamura-Taira N, Horikawa N, Oka F, Igarashi Y, Kobayashi S, Kato S, et al. Quasi-cluster randomized trial of a six-month low-intensity group-based resistance exercise for hemodialysis patients on depression and cognitive function: a 12-month follow-up. *Behav Med.* (2021) 2021:741–60. doi: 10.1080/21642850.2021.1966302

23. Stringuetta Belik F, Oliveirae Silva VR, Braga GP, Bazan R, Perez Vogt B, Costa Teixeira Caramori J, et al. Influence of intradialytic aerobic training in cerebral blood flow and cognitive function in patients with chronic kidney disease: a pilot randomized controlled trial. *Nephron.* (2018) 140:9–17. doi: 10.1159/000490005

24. Arnett JA, Labovitz SS. Effect of physical layout in performance of the trail making test. *Psychol Assess.* (1995) 7:220–1. doi: 10.1037/1040-3590.7.2.220

25. Hays R, Kallich J, Mapes D, Coons S, Amin N. *Kidney Disease Quality of Life Short Form (KDQOL-SF), version 1.3: A Manual for Use and Scoring.* (1997). Available online at: https://www.researchgate.net/profile/Ronald-Hays/publication/274568265_Kidney_Disease_Quality_of_Life_Short_Form_KDQOL-SF_Version_13_A_manual_for_use_and_scoring/links/

5cf56b524585153c3db18a19/Kidney-Disease-Quality-of-Life-Short-Form-KDQOL-SF-Version-13-A-manual-for-use-and-scoring.pdf (accessed August 25, 2022).

26. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc.* (2005) 53:695–9. doi: 10.1111/j.1532-5415.2005.53221.x

27. Pangman VC, Sloan J, Guse L. An examination of psychometric properties of the mini-mental state examination and the standardized mini-mental state examination: implications for clinical practice. *Appl Nurs Res.* (2000) 13:209–13. doi: 10.1053/APNR.2000.9231

28. Teng E, Chui CH. The modified mini-mental state examination (3MS). *J Consult Clin Psychol.* (1987) 48:314–8.

29. Tiffin-Richards FE, Costa AS, Holschbach B, Frank RD, Vassiliadou A, Krüger T, et al. The montreal cognitive assessment (MoCA) - a sensitive screening instrument for detecting cognitive impairment in chronic hemodialysis patients. *PLoS ONE.* (2014) 9:e106700. doi: 10.1371/JOURNAL.PONE.0106700

30. Bland RC, Newman SC. Mild dementia or cognitive impairment: the modified mini-mental state examination (3MS) as a screen for dementia. *Can J Psychiatry.* (2001) 46:506–10. doi: 10.1177/070674370104600604

31. Dobbs BM, Shergill SS. How effective is the trail making test (Parts A and B) in identifying cognitively impaired drivers? *Age Ageing.* (2013) 42:577–81. doi: 10.1093/AGEING/AFT073

32. Sorensen EP, Sarnak MJ, Tighiouart H, Scott T, Giang LM, Kirkpatrick B, et al. The kidney disease quality of life cognitive function subscale and cognitive performance in maintenance hemodialysis patients. *Am J Kidney Dis.* (2012) 60:417–26. doi: 10.1053/j.ajkd.2011.12.029

33. Elias MF, Elias PK, Seliger SL, Narsipur SS, Dore GA, Robbins MA. Chronic kidney disease, creatinine and cognitive functioning. *Nephrol Dial Transpl.* (2009) 24:2446–52. doi: 10.1093/ndt/gfp107

34. Drew DA, Weiner DE, Sarnak MJ. Cognitive impairment in CKD: pathophysiology, management, and prevention. *Am J Kidney Dis.* (2019) 74:782–90. doi: 10.1053/j.ajkd.2019.05.017

35. Ng CZ, Tang SC, Chan M, Tran BX, Ho CS, Tam WW, et al. A systematic review and meta-analysis of randomized controlled trials of cognitive behavioral therapy for hemodialysis patients with depression. *J Psychosom Res.* (2019) 126:109834. doi: 10.1016/j.jpsychores.2019.109834

36. Drew DA, Weiner DE, Tighiouart H, Scott T, Lou K, Kantor A, et al. Cognitive function and all-cause mortality in maintenance hemodialysis patients. *Am J Kidney Dis.* (2015) 65:303–11. doi: 10.1053/j.ajkd.2014.07.009

37. Alosaimi FD, Asiri M, Alsuwayt S, Alotaibi T, bin Mugren M, Almufarrih A, et al. Psychosocial predictors of nonadherence to medical management among patients on maintenance dialysis</div>. *Int J Nephrol Renovasc Dis.* (2016) 9:263–72. doi: 10.2147/IJNRD.S121548

38. Angermann S, Schier J, Baumann M, Steubl D, Hauser C, Lorenz G, et al. Cognitive impairment is associated with mortality in hemodialysis patients. *J Alzheimer's Dis.* (2018) 66:1529–37. doi: 10.3233/JAD-180767

39. Findlay MD, Dawson J, Dickie DA, Forbes KP, McGlynn D, Quinn T, et al. Investigating the relationship between cerebral blood flow and cognitive function in hemodialysis patients. *J Am Soc Nephrol.* (2019) 30:147–58. doi: 10.1681/ASN.2018050462

40. Bučar Pajek M, Pajek J. Characterization of deficits across the spectrum of motor abilities in dialysis patients and the impact of sarcopenic overweight and obesity. *Clin Nutr.* (2018) 37:870–7. doi: 10.1016/j.clnu.2017.03.008

41. Johansen KL, Chertow GM, Nga V, Mulligan K, Carey S, Schoenfeld PY, et al. Physical activity levels in patients on hemodialysis and healthy sedentary controls. *Kidney Int.* (2000) 57:2564–70. doi: 10.1046/j.1523-1755.2000.00116.x

42. Sietsema KE, Amato A, Adler SG, Brass EP. Exercise capacity as a predictor of survival among ambulatory patients with end-stage renal disease. *Kidney Int.* (2004) 65:719–24. doi: 10.1111/j.1523-1755.2004.00411.x

43. Segura-Ortí E, Kouidi E, Lisón JF. Effect of resistance exercise during hemodialysis on physical function and quality of life: randomized controlled trial. *Clin Nephrol.* (2009) 71:527–37. doi: 10.5414/cnp71527

44. Groussard C, Rouchon-Isnard M, Coutard C, Romain F, Malardé L, Lemoine-Morel S, et al. Beneficial effects of an intradialytic cycling training program in patients with end-stage kidney disease. *Appl Physiol Nutr Metabolism.* (2015) 40:550–6. doi: 10.1139/apnm-2014-0357

45. Frih B, Jaafar H, Mkacher W, Ben Salah Z, Hammami M, Frih A. The effect of interdialytic combined resistance and aerobic exercise training on health related outcomes in chronic hemodialysis patients: the tunisian randomized controlled study. *Front Physiol.* (2017) 8:288. doi: 10.3389/fphys.2017.00288

46. Bogataj Š, Pajek J, Buturović Ponikvar J, HadŽić V, Pajek M. Kinesiologist-guided functional exercise in addition to intradialytic cycling program in end-stage kidney disease patients: a randomised controlled trial. *Sci Rep.* (2020) 10:2564–70. doi: 10.1038/s41598-020-62709-1

47. Giannaki CD, Hadjigeorgiou GM, Karatzaferi C, Maridaki MD, Koutedakis Y, Founta P, et al. A single-blind randomized controlled trial to evaluate the effect of 6 months of progressive aerobic exercise training in patients with uraemic restless legs syndrome. *Nephrol Dial Transpl.* (2013) 28:2834–40. doi: 10.1093/ndt/gft288

48. Liao M-T, Liu W-C, Lin F-H, Huang C-F, Chen S-Y, Liu C-C, et al. Intradialytic aerobic cycling exercise alleviates inflammation and improves endothelial progenitor cell count and bone density in hemodialysis patients. *Medicine.* (2016) 95:e4134. doi: 10.1097/MD.0000000000004134

49. Marinho SM, Moraes C, Barbosa JE, dos SM, Carraro Eduardo JC, et al. Exercise training alters the bone mineral density of hemodialysis patients. *J Strength Cond Res.* (2016) 30:2918–23. doi: 10.1519/JSC.0000000000001374

50. Parsons TL, Toffelmire EB, King-VanVlack CE. The effect of an exercise program during hemodialysis on dialysis efficacy, blood pressure and quality of life in end-stage renal disease (ESRD) patients. *Clin Nephrol.* (2004) 61:261–74. doi: 10.5414/cnp61261

51. Bogataj Š, Pajek J, Buturović Ponikvar J, Pajek M. Functional training added to intradialytic cycling lowers low-density lipoprotein cholesterol and improves dialysis adequacy: a randomized controlled trial. *BMC Nephrol.* (2020) 21:352. doi: 10.1186/s12882-020-02021-2

52. Barcellos FC, Santos IS, Umpierre D, Bohlke M, Hallal PC. Effects of exercise in the whole spectrum of chronic kidney disease: a systematic review. *Clin Kidney J.* (2015) 8:753–65. doi: 10.1093/ckj/sfv099

53. Johansen KL. Exercise in the end-stage renal disease population. *J Am Soc Nephrol.* (2007) 18:1845–54. doi: 10.1681/ASN.2007010009

54. Sheng K, Zhang P, Chen L, Cheng J, Wu C, Chen J. Intradialytic exercise in hemodialysis patients: a systematic review and meta-analysis. *Am J Nephrol.* (2014) 40:478–90. doi: 10.1159/000368722

55. Bogataj Š, Pajek M, Buturović Ponikvar J, Pajek J. Outcome expectations for exercise and decisional balance questionnaires predict adherence and efficacy of exercise programs in dialysis patients. *Int J Environ Res Public Health.* (2020) 17:261–74. doi: 10.3390/ijerph17093175

56. Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, et al. Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci USA.* (2011) 108:3017–22. doi: 10.1073/pnas.1015950108

57. Batouli SAH, Saba V. At least eighty percent of brain grey matter is modifiable by physical activity: a review study. *Behav Brain Res.* (2017) 332:204–17. doi: 10.1016/j.bbr.2017.06.002

58. Wallace LMK, Theou O, Godin J, Andrew MK, Bennett DA, Rockwood K. Investigation of frailty as a moderator of the relationship between neuropathology and dementia in Alzheimer's disease: a cross-sectional analysis of data from the rush memory and aging project. *Lancet Neurol.* (2019) 18:177–84. doi: 10.1016/S1474-4422(18)30371-5

59. Wilkerson GB. Neurocognitive reaction time predicts lower extremity sprains and strains. *Int J Athletic Ther Train.* (2012) 17:4–9. doi: 10.1123/ijatt.17.6.4

60. Herman DC, Barth JC. Neuromuscular performance varies with baseline neurocognition: implications for anterior cruciate ligament injury risk and prevention. *Orthop J Sports Med.* (2015) 3:2325967115S0009. doi: 10.1177/2325967115S00095

61. Loprinzi PD, Herod SM, Cardinal BJ, Noakes TD. Physical activity and the brain: a review of this dynamic, bi-directional relationship. *Brain Res.* (2013) 1539:95–104. doi: 10.1016/J.BRAINRES.2013.10.004

62. Nascimento CMC, Pereira JR, Pires De Andrade L, Garuffi M, Ayan C, Kerr DS, et al. Physical exercise improves peripheral BDNF levels and cognitive functions in mild cognitive impairment elderly with different bdnf Val66Met genotypes. *J Alzheimers Dis.* (2015) 43:81–91. doi: 10.3233/JAD-140576

63. Mahncke HW, Connor BB, Appelman J, Ahsanuddin ON, Hardy JL, Wood RA, et al. Memory enhancement in healthy older adults using a brain plasticity-based training program: a randomized, controlled study. *Proc Natl Acad Sci USA.* (2006) 103:12523–8. doi: 10.1073/pnas.0605194103

64. Levine B, Stuss DT, Winocur G, Binns MA, Fahy L, Mandic M, et al. Cognitive rehabilitation in the elderly: effects on strategic behavior in relation to goal management. *J Int Neuropsychol Soc.* (2007) 13:143–52. doi: 10.1017/S1355617707070178

65. Anand R, Chapman SB, Rackley A, Keebler M, Zientz J, Hart J. Gist reasoning training in cognitively normal seniors. *Int J Geriatr Psychiatry.* (2011) 26:961–8. doi: 10.1002/GPS.2633

66. Dong Y, Sharma VK, Chan BPL, Venketasubramanian N, Teoh HL, Seet RCS, et al. The montreal cognitive assessment (MoCA) is superior to the mini-mental

state examination (MMSE) for the detection of vascular cognitive impairment after acute stroke. *J Neurol Sci.* (2010) 299:15–8. doi: 10.1016/j.jns.2010.08.051

67. Lee SH, Cho Aj, Min Y-K, Lee Y-K, Jung S. Comparison of the montreal cognitive assessment and the mini-mental state examination as screening tests in hemodialysis patients without symptoms. *Ren Fail.* (2018) 40:323–30. doi: 10.1080/0886022X.2018.1455589

68. Benedict RHB, Deluca J, Phillips G, LaRocca N, Hudson LD, Rudick R. Validity of the symbol digit modalities test as a cognition performance outcome measure for multiple sclerosis. *Multiple Sclerosis.* (2017) 23:721–33. doi: 10.1177/1352458517690821

69. Zimmermann P, Fimm B. *Test of Attentional Performance 2.3.1. Vera Fimm, Psychologische Testsysteme*. (2017). Available online at: https://www.psytest.de/index.php?page=TAP-2-2&hl=en_US (accessed February 1, 2021).

70. Bogataj Š, Trajković N, Pajek M, Pajek J. Effects of intradialytic cognitive and physical exercise training on cognitive and physical abilities in hemodialysis patients: study protocol for a randomized controlled trial. *Front Psychol.* (2022) 13:62. doi: 10.3389/FPSYG.2022.835486/BIBTEX

frontiers | Frontiers in Public Health

TYPE Systematic Review
PUBLISHED 19 October 2022
DOI 10.3389/fpubh.2022.1018460

Check for updates

OPEN ACCESS

EDITED BY
Bojan Masanovic,
University of Montenegro, Montenegro

REVIEWED BY
Amir Reza Moravejolahkami,
Isfahan University of Medical Sciences, Iran
Mihnea-Alexandru Găman,
Carol Davila University of Medicine and Pharmacy, Romania

*CORRESPONDENCE
Yang Yuan
yuanyangofficial@yeah.net
Jing-hong Liang
Liangjh78@mail2.sysu.edu.cn

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 13 August 2022
ACCEPTED 26 September 2022
PUBLISHED 19 October 2022

CITATION
Liang Z-d, Zhang M, Wang C-z, Yuan Y and Liang J-h (2022) Association between sedentary behavior, physical activity, and cardiovascular disease-related outcomes in adults—A meta-analysis and systematic review. *Front. Public Health* 10:1018460.
doi: 10.3389/fpubh.2022.1018460

Association between sedentary behavior, physical activity, and cardiovascular disease-related outcomes in adults—A meta-analysis and systematic review

Zhi-de Liang[1], Meng Zhang[2], Chuan-zhi Wang[3], Yang Yuan[1]* and Jing-hong Liang[4]*

[1]Cancer Institute of The Affiliated Hospital of Qingdao University and Qingdao Cancer Institute, Qingdao, China, [2]Postgraduate Department, Xi'an Physical Education University, Xi'an, China, [3]Department of Physical Education, College of Physical Education, Qingdao University, Qingdao, China, [4]Department of Maternal and Child Health, School of Public Health, Sun Yat-sen University, Guangzhou, China

Background: Sedentary behavior (SB) and physical activity (PA) are modifiable risk factors for cardiovascular disease (CVD); however, previous research on the effects of PA and SB on CVD has been relatively homogeneous. Our study investigated the association between PA, SB, and CVD-related outcomes.

Methods: A comprehensive search strategy was conducted in the MEDLINE, Embase, Cochrane Library, and Web of Science databases from their inception to September 2022. We identified eligible studies according to PICOS: the populations comprised healthy adults, the interventions or exposures were PA or SB, the outcomes were CVD-related outcomes, and the study designs were randomized controlled trials (RCTs) and longitudinal studies (LS). Outcomes were pooled using fixed or random effects models, and the quality of individual studies was assessed by the Cochrane Risk of Bias Instrument and the Newcastle Ottawa Scale.

Results: A total of 148 RCTs and 36 LS were included, comprising a total of 75,075 participants. The study quality was rated as low to moderate. We found an increased hazard ratio (HR) for CVD in the population with SB (HR = 1.34; 95% confidence interval [CI]: 1.26 to 1.43; $I^2 = 52.3\%$; $P_{heterogeneity} < 0.001$, random model) and a decreased HR for CVD in those who performed long-term PA (HR = 0.71; 95% CI: 0.66 to 0.77; $I^2 = 78.0\%$, $P_{heterogeneity} < 0.001$, random model). Long-term PA improved the lipid profiles in healthy adults; participants in this group exhibited increased high-density lipoprotein (weighted mean difference [WMD] = 2.38; 95% CI: 1.00 to 3.76; $I^2 = 84.7\%$; $P_{heterogeneity} < 0.001$, random model), decreased triglycerides (WMD = −7.27; 95% CI: −9.68 to −4.87; $I^2 = 0\%$, $P_{heterogeneity} = 0.670$, fixed model), and lower total-cholesterol (WMD = −6.84; 95% CI: −9.15 to −4.52; $I^2 = 38.4\%$, $P_{heterogeneity} < 0.001$, random model).

Conclusions: Long-term SB increases the risk of CVD in healthy adults, whereas PA reduces the risk of CVD and improves indicators associated with CVD. However, the ability of PA to improve blood lipids appeared to be limited. The detailed association of SB and PA on CVD needs to be further investigated in the future.

KEYWORDS

physical activity, meta-analysis, healthy adult, cardiovascular disease(s), sedentary behavior

Introduction

Cardiovascular disease (CVD) is a general term for a group of cardiovascular disorders, including coronary heart disease (CHD), heart failure (HF), aortic atherosclerosis, cerebrovascular disease, and peripheral artery disease (1). The advancement of medical technology and the dramatic improvement of the health environment have greatly reduced the mortality rate from infectious diseases and substantially increased life expectancy. In developed countries as well as some developing ones, chronic diseases, especially CVD, have become the leading cause of death (2). For example, in China, CVD accounts for 40% of deaths in the Chinese population (3), and the incidence of CVD increased by 14.7% between 1990 and 2016 (4).

The causes of CVD are multifactorial, and many CVD risk factors are not modifiable; these include age, gender, race, and family history of heart disease. However, other risk factors are modifiable; these include smoking, alcohol abuse, obesity, physical inactivity, a sedentary lifestyle, diet, hypertension, diabetes, and dyslipidemia (5, 6). Sedentary behavior (SB) is defined as spending waking hours in a sitting, reclined, or lying position and is characterized by low energy expenditure (≤1.5 metabolic equivalents for task [METs]) (5). Several studies have demonstrated that SB is a major modifiable risk factor for CVD (7–9), and sitting for more than 6 h per day is associated with an increased risk of 12 common chronic diseases. However, replacing sitting time with physical activity (PA) of varying intensities may reduce the risk of these chronic diseases (10). Therefore, PA has been proposed as an alternative strategy to improve quality of life and reduce the risk of CVD (11). The World Health Organization defines PA as "any physical movement produced by skeletal muscle that results in energy expenditure," and PA can be categorized into different types depending on the exercise mode, intensity, frequency, and duration (12). A meta-analysis comparing the effects of five types of PA on cardiometabolic health in people who were obese or overweight found that all types of PA played a key role in improving cardiometabolic health (13). Another meta-analysis demonstrated that PA reduced fatigue in patients with cancer and those who had received hematopoietic stem cell transplants (14). Other studies have revealed that PA reduces mortality, improves the quality of life of patients with CVD, and protects against damage at the early stages of myocardial infarction (15, 16).

Although previous studies have shown that PA can significantly improve the quality of life of patients with CVD (17, 18), research in this area is still insufficient. First, the results of previous studies on the association between CVD and PA are limited because they have focused primarily on cardiovascular mortality (CVM); few studies have investigated other CVD-related outcomes (19, 20). Therefore, the present study examined the effects of PA on all CVD outcomes to help fill the knowledge gap resulting from the one-sidedness of previous studies, and it aimed to elucidate the different effects of PA on CVM and other CVD outcomes. Second, several studies have found that PA reduces the risk of cardiovascular disease, but they did not distinguish between the age, region, and economic status of the participants (21). Third, the size and diversity of populations investigated in previous studies have been limited, including those with underlying diseases, and further research is needed to ensure that these findings are generalizable to healthy people (22). Fourth, CVD is a chronic disease that requires evidence not only from randomized controlled trials, but also from longitudinal studies, but previous studies have focused on only one of these (23, 24). Therefore, combining these two types of evidence can better analyze the association between PA, SB and CVD. Moreover, the number of published studies on the effects of SB and PA on CVD has increased significantly in recent years (25, 26). However, because of the increased volume of data, updated reviews are needed to provide more reliable evidence. Therefore, we conducted a comprehensive systematic review and meta-analysis of the literature to characterize and quantify the association between PA, SB, and CVD-related outcomes.

Methods

This meta-analysis was conducted following the recommendations of the Cochrane Collaboration Handbook (27) and the framework for meta-analysis of longitudinal studies in epidemiology (28). No ethical approval or patient consent was required because all analyses were performed using data from previous studies.

Search strategies and study selection

To identify publications on PA and SB in healthy adults, an exhaustive, strategic literature search of the MEDLINE, Embase, Cochrane Library, and Web of Science databases was conducted from their inception until September 2, 2022. The search strategy did not include any restrictions and consisted mainly of medical subject headings associated with keywords, free words, and Boolean operators. The detailed search strategy is described in the Appendix (p. 1); in brief, the following search terms were used: "cardiovascular disease," "sedentary behavior," "adults," "exercise," "training," "physical activity," "aerobic exercise," "triglyceride," "glucose," "lipoproteins," and "randomized controlled trial."

In addition, a recursive search for relevant publications was conducted by manually searching the bibliographic lists of similar reviews and large professional conferences. At least two investigators (ZM and LZ) performed the study selection and data extraction independently, and discrepancies that arose during the process were resolved by consulting a third investigator (YY). Title and abstract screening was used to eliminate duplicates, reviews, and irrelevant studies. Subsequently, potentially eligible studies were screened, and their full text was downloaded; those that could not be downloaded in full were excluded. The selected citations were independently cross-checked for completeness and accuracy by two investigators. All citations were managed and analyzed with EndNote X9 software (Thompson ISI Research Soft, Clarivate Analytics, Philadelphia, Philadelphia, USA).

Inclusion and exclusion criteria and data abstraction

Studies that met the following eligibility criteria were included.

Population

Participants were healthy adults aged 18 years or older; were physically independent; had no current cardiovascular or other significant medical conditions; had no history of medical conditions preventing them from participating in the exercise intervention; were not currently taking any medications; and had not engaged in regular PA in the past 1–2 years according to a physician report or self-report (obtained through a standard diagnostic interview).

Interventions and exposure

Studies on PA interventions in healthy adults were included. All participants received the PA intervention at least twice a week for at least 8 weeks, as recommended by the American College of Sports Medicine Guidelines (29). PA was defined as any type of body activity that resulted in energy expenditure (12). The specific breakdown of PA types was as follows (30, 31): (1) Aerobic exercise (AE), defined as exercise to improve cardiovascular health, including walking, running, and cycling. (2) Resistance exercise (RE), defined as exercise to increase muscle strength, such as using elastic bands and dumbbells. (3) Multicomponent exercise (ME), defined as a combination of at least two exercise types, such as AE, RE, and balance training; and (4) Mind–body exercise (MBE), defined as exercise to improve participants' physical and mental coordination through awareness exercises, such as Tai chi, yoga, and dance. In the interventions described above, PA was performed with and without supervision.

In addition, longitudinal studies on SB and PA in healthy adults were included to investigate the association between PA, SB, and CVD events (fatal or non-fatal). SB was defined as waking behavior characterized by low energy expenditure (≤1.5 METs) (5), including sitting or reclining at leisure, at work, in traffic, and at home. SB and PA time was obtained by a standardized questionnaire or self-report. If more than two PA or SB levels were present in a study, they were categorized into two groups—high PA or SB and low PA or SB—and the low PA or SB group was considered the reference category.

Comparators

The comparators included a non-exercise control group, a health education group, and a group that maintained their current lifestyle.

Outcomes

The primary outcomes of randomized controlled trials (RCTs) were lipid levels (triglycerides [TGs], total cholesterol [TC], high-density lipoprotein [HDL], and low-density lipoprotein [LDL]), and various clinical measures were used to assess changes in these metrics from baseline to endpoint. The secondary outcomes were other indicators related to CVD risk factors, namely body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), and blood glucose.

For longitudinal studies, any type of CVD incidence or mortality was selected as the primary outcome; this indicator was included in most studies and was considered an appropriate choice for acceptability.

Study design

Our study included all types of randomized controlled trials (RCTs), and to further explore the effect of SB and PA on CVD incidence, population-based longitudinal studies (including any type of prospective cohort or retrospective cohort study) were also included; no restrictions were placed on publication date, race, or region. Studies were excluded if (1) the study type was a systematic review, meta-analysis, or protocol; (2) the full text of the data analysis or data details were not available; or (3) the intervention method was a combination of PA and other methods.

Outcome measurement and quality assessment

The following key information was extracted: first author; year of publication; source; intervention or follow-up time; intervention dose; study type; sample size; and baseline characteristics of the participants, such as age and gender. If the baseline data were not available in the text, they were obtained by contacting the corresponding author.

The quality of the RCT was independently assessed by two reviewers (ZM and ZD) according to the Cochrane Risk of Bias tool (32), which consists of seven items: random sequence generation; allocation concealment; participant and personnel blinding; outcome assessment blinding; incomplete outcome data; selective reporting and other biases; and items judged as having high risk, low risk, and unclear risk.

All prospective and retrospective studies were evaluated by the Newcastle–Ottawa Scale (NOS), which consists of three main items: patient selection, comparability of the intervention and observation groups, and assessment of outcomes. Studies with NOS scores ≥7 were considered high-quality (33, 34). Two reviewers scored each study independently, and in cases of disagreement, a third reviewer reviewed their assessments.

Statistical analyses

A traditional paired meta-analysis was conducted for the trials that satisfied the inclusion criteria (27). For the results of continuous variables, baseline and terminal mean differences and standard deviation (SD) were extracted; if they were not provided, different methods were used to convert the data to a standard format (35, 36). If the study was a multi-arm RCT, all PA and control group data were extracted. A quantitative pooled analysis was performed according to a fixed-effects model (inverse variance), and forest plots were constructed to derive the weighted mean difference (WMD) and 95% confidence interval (CI); if heterogeneity existed, a random effects model was used (D-L heterogeneity approach) (27). Hazard ratios (HRs) and their 95% CIs were included as pooled effects for the longitudinal studies. Because such variables must be symmetric and follow a normal distribution, logarithmic transformation was performed, and a random effects model was then used to explain the effects of between-study heterogeneity (37).

The presence of heterogeneity was determined by examining the forest plots and I^2 statistics according to the latest version of the Cochrane Handbook (27). I^2 statistics were used to assess statistical heterogeneity, with estimates of 25, 50, and 75% indicating mild, moderate, and high heterogeneity, respectively; a P-value of < 0.1 was considered statistically significant (38, 39). Sensitivity analyses and a series of subgroup analyses were performed to identify the sources of heterogeneity by statistical methods, and the literature-by-deletion method was employed to analyze sensitivity. Funnel plots were used to check for publication bias, which mainly arises from publication bias, selective reporting, or other sources. Finally, Egger's tests were carried out to quantitatively evaluate whether the studies had publication bias, and $P < 0.05$ indicated the absence of publication bias (40). To explore the sources of heterogeneity and the relationships of primary outcomes in different conditions, a subgroup analysis was performed; variables of interest included the region (the U.S. vs. other countries; developed vs. developing countries), the intervention time or follow-up time (≤12 weeks vs. >12 weeks or ≤10 years vs. >10 years, respectively), age (≤60 years vs. >60 years), quality of the literature (NOS <7 vs. NOS ≥7), gender distribution (male ≥ female vs. male < female), sample size (≤10000 vs. >10000), CVD outcomes (fatal vs. non-fatal), year of publication (≤2015 vs. >2015; ≤2016 vs. >2016), SB vs. no SB, and PA type (AE, RE, ME, and MBE). The above analyses were performed in STATA software version 15.1 (Stata, Corp, College Station, Texas, USA).

Results

Study selection and characteristics of the included studies

We obtained 75,075 studies from the database and identified 42 studies through other sources; of these, 4,544 studies were excluded because of duplication, and 70,184 were excluded on the basis of their titles and abstracts. After full-text screening of the remaining 347 studies, a total of 163 publications were excluded for the following reasons: 37 studies did not meet the study type criteria; 56 studies did not have appropriate outcomes or did not provide data that could be analyzed; 46 studies included participants that did not satisfy the inclusion and exclusion criteria (patients with underlying diseases, younger than 18 years, or currently taking medication); and 24 studies included interventions other than PA. Ultimately, we included 184 studies, of which 148 were RCTs and 36 were longitudinal

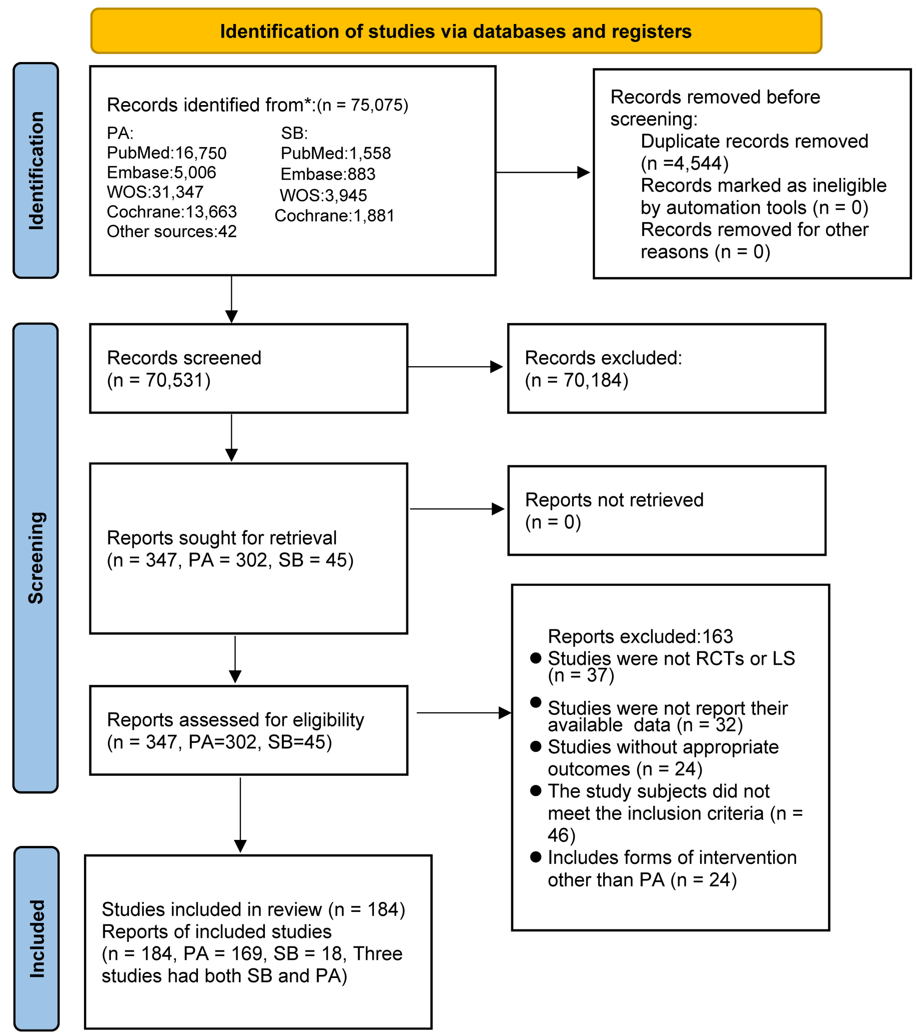

FIGURE 1
Literature review flowchart. LS, Longitudinal studies; PA, physical activity; RCT, randomized controlled trial; SB, sedentary behavior; WOS, web of science.

studies (Supplementary Table S1). Three longitudinal studies assessed both PA and SB. The study selection process is shown in Figure 1.

A total of 1,011,473 participants aged between 18 and 100 years old were recruited in the 184 included studies; 8,166 and 1,003,307 participants were included in the RCTs and the longitudinal studies, respectively. The proportion of male participants was lower than that of female participants (males in RCTs: 2,686 [32.9%]; males in longitudinal studies: 412,519 [41.1%]). The intervention duration in the RCTs ranged between 8 weeks and 24 months, and the mean follow-up time in the longitudinal studies was 11.4 years. Participants were mainly recruited in Europe (N = 61, 33.2%) and North America (N = 55, 31.5%). We extracted several indicators related to CVD risk from the RCTs, including BMI (N = 89), blood pressure (SBP: N = 65, DBP: N = 63), blood lipids (TGs: N = 76, TC: N = 79, HDL: N = 84, LDL: N = 78), and blood glucose (N = 65). The demographic characteristics of the included studies are summarized in Supplementary Table S1. Subgroup analyses of the main outcomes are shown in Table 1.

And the forest plots and funnel plots of all outcomes will be presented in the Appendix (p. 23–37).

Quality of the included studies

Of the 148 RCTs, 36 had a low risk of bias in random sequence generation, 17 had a low risk of selection bias, 18 had a low risk of performance bias, and 27 had a low risk of detection bias. Only six studies had a high risk of

TABLE 1 Outcomes and subgroup analysis based on indicators related to CVD.

Type of research and meta-analyses variables		Number of studies (included multi-arm study)	Number of participants		Weighted mean difference	Heterogeneity	
			Intervention	CG		I^2(%)	P
RCT							
Primary							
Lipids	TG	76	2,386	2,272	−7.27 (−9.68 to −4.87)	0	0.670
	TC	79	2,298	2,214	−6.84 (−9.15 to −4.52)	38.4	<0.001
	HDL	84	2,568	2,450	2.38 (1.00 to 3.76)	84.7	<0.001
	LDL	78	2,435	2,322	−5.80 (−8.04 to −3.57)	65.5	<0.001
Secondary outcomes							
Others	BMI	89	3,204	3,016	−0.36 (−0.43 to −0.30)	0	0.998
	SBP	65	1,820	1,680	−3.63 (−4.62 to −2.64)	58.0	<0.001
	DBP	63	1,759	1,614	−2.25 (−2.94 to −1.56)	51.3	<0.001
	GlU	65	1,743	1,670	−4.40 (−5.44 to −3.36)	86.5	<0.001
Subgroup analysis based on TG							
Region	Overall	76	2,386	2,272	−7.27 (−9.68 to −4.87)	0	0.670
	Developing countries	13	346	345	−13.83 (−19.88 to −7.79)	0	0.665
	Developed countries	63	2,040	1,927	−6.04 (−8.66 to −3.41)	0	0.727
Intervention time	Overall	76	2,386	2,272	−7.27 (−9.68 to −4.87)	0	0.670
	≤12weeks	41	1,026	944	−7.74 (−11.11 to −4.37)	12.1	0.228
	>12weeks	35	1,360	1,328	−6.79 (−10.23 to −3.35)	0	0.929
Published year	Overall	76	2,386	2,272	−7.27 (−9.68 to −4.87)	0	0.670
	≤2015	54	1,651	1,582	−9.30 (−12.46 to −6.15)	0	0.522
	>2015	22	735	690	−4.34 (−8.16 to −0.71)	0	0.884
Age	Overall	75	2,366	2,224	−7.31 (−9.72 to −4.90)	0	0.653
	≤60	54	1,782	1,596	−6.27 (−9.24 to −3.30)	0	0.928
	>60	21	584	628	−9.33 (−13.45 to −5.20)	30.4	0.076
Male to female ratio	Overall	72	2,264	1,982	−7.26 (−9.744 to −4.77)	0	0.555
	Female<male	51	1,685	1,483	−6.34 (−9.40 to −3.28)	0	0.495
	Male≥female	21	579	499	−9.03 (−13.29 to −4.78)	0	0.574
Sedentary	Overall	76	2,386	2,272	−7.27 (−9.68 to −4.87)	0	0.670
	Yes	45	1,472	1,438	−7.18 (−10.31 to −4.04)	0	0.918
	No/NR	31	914	834	−7.41 (−11.16 to −3.65)	17.8	0.163
Exercise type	Overall	76	2,386	2,272	−7.27 (−9.68 to −4.87)	0	0.670
	AE	55	1,550	1,455	−6.99 (−10.04 to −3.94)	0	0.525
	RE	16	314	303	−10.02 (−16.36 to −3.68)	0	0.823
	ME	16	499	491	−6.80 (−12.15 to −1.45)	10.6	0.332
	MBE	2	23	23	−3.40 (−16.84 to −10.04)	10.0	0.292
Subgroup analysis based on TC							
Region	Overall	79	2,298	2,214	−6.84 (−9.15 to −4.52)	38.4	<0.001
	Developing countries	15	385	382	−11.03 (−18.47 to −3.60)	64.0	<0.001
	Developed countries	64	1,913	1,832	−5.93 (−8.08 to −3.78)	19.3	<0.1
Intervention time	Overall	79	2,298	2,214	−6.84 (−9.15 to −4.52)	38.4	<0.001
	≤12weeks	43	1,054	971	−7.72 (−11.56 to −3.89)	45.7	<0.001
	>12weeks	36	1,244	1,243	−6.06 (−8.79 to −3.33)	27.0	<0.1
Published year	Overall	79	2,298	2,214	−6.84 (−9.15 to −4.52)	38.4	<0.001
	≤2015	56	1,720	1,681	−6.82 (−9.54 to −4.09)	38.0	<0.01
	>2015	33	578	533	−6.84 (−11.24 to −2.45)	39.2	<0.1

(Continued)

TABLE 1 (Continued)

Type of research and meta–analyses variables		Number of studies (included multi–arm study)	Number of participants		Weighted mean difference	Heterogeneity	
			Intervention	CG		I^2(%)	P
Age	Overall	77	2,269	2,188	−6.54 (−8.83 to −4.26)	36.8	<0.001
	≤60	54	1,641	1,509	−6.81 (−9.40 to −4.22)	31.9	<0.01
	>60	23	628	679	−6.56 (−11.41 to −1.70)	48.2	<0.01
Male to female ratio	Overall	75	2,067	1,915	−6.99 (−9.37 to −4.60)	37.6	<0.001
	Female<male	51	1,557	1,465	−6.52 (−9.49 to −3.55)	43.5	<0.001
	Male≥female	24	510	450	−8.47 (−12.38 to −4.56)	20.4	0.164
Sedentary	Overall	79	2,298	2,214	−6.84 (−9.15 to −4.52)	38.4	<0.001
	Yes	48	1,462	1,423	−5.05 (−7.92 to −2.19)	31.1	0.011
	No/NR	31	836	791	−9.31 (−12.96 to −5.67)	41.5	0.004
Exercise type	Overall	79	2,298	2,214	−6.84 (−9.15 to −4.52)	38.4	<0.001
	AE	58	1503	1417	−5.70 (−8.53 to −2.88)	35.4	<0.01
	RE	16	306	296	−8.77 (−16.51 to −1.04)	53.1	<0.01
	ME	17	466	478	−8.58 (−13.32 to −3.84)	34.5	<0.1
	MBE	2	23	23	−14.39 (−34.10 to 5.32)	62.4	0.103
Subgroup analysis based on HDL							
Region	Overall	84	2,568	2,450	2.38 (1.00 to 3.76)	84.7	<0.001
	Developing countries	18	406	406	2.34 (0.77 to 3.90)	27.3	0.117
	Developed countries	76	2,162	2,044	2.35 (0.68 to 4.01)	87.2	<0.001
Intervention time	Overall	84	2,568	2,450	2.38 (1.00 to 3.76)	84.7	<0.001
	≤12weeks	45	1,150	1,058	2.28 (−0.16 to 4.72)	89.3	<0.001
	>12weeks	39	1,418	1,392	2.43 (1.04 to 3.83)	70.4	<0.001
Published year	Overall	84	2,568	2,450	2.38 (1.00 to 3.76)	84.7	<0.001
	≤2015	60	1,790	1,715	2.83 (0.95 to 4.71)	88.0	<0.001
	>2015	24	778	735	0.95 (−0.18 to 2.08)	26.0	0.101
Age	Overall	83	2,548	2,433	2.34 (0.96 to 3.72)	84.6	<0.001
	≤60	59	1,898	1,731	2.07 (1.05 to 3.10)	56.6	<0.001
	>60	24	650	702	2.90 (−1.50 to 7.31)	94.7	<0.001
Male to female ratio	Overall	82	2,346	2,160	2.63(1.17 to 4.08)	85.2	<0.001
	Female<male	58	1,722	1,620	2.43 (0.37 to 4.49)	89.0	<0.001
	Male≥female	24	624	540	2.76 (1.53 to 3.98)	32.9	<0.100
Sedentary	Overall	84	2,568	2,450	2.38 (1.00 to 3.76)	84.7	<0.001
	Yes	47	1,515	1,474	1.17 (−0.75 to 3.09)	85.5	<0.001
	No/NR	37	1,053	976	3.84 (1.90 to 5.80)	82.1	<0.001
Exercise type	Overall	84	2,568	2,450	2.38 (1.00 to 3.76)	84.7	<0.001
	AE	61	1715	1590	2.71 (0.79 to 4.64)	88.6	<0.001
	RE	19	362	353	3.37 (1.09 to 5.66)	43.4	<0.1
	ME	18	468	484	0.49 (−2.06 to 3.04)	75.8	<0.001
	MBE	2	23	23	0.45 (−8.15 to 9.04)	55.9	0.132
Subgroup analysis based on LDL							
Region	Overall	78	2,435	2,322	−5.80 (−8.04 to −3.57)	65.5	<0.001
	Developing countries	14	354	357	−7.68 (−12.85 to −2.52)	58.8	<0.1
	Developed countries	64	2,081	1,965	−5.38 (−7.87 to −2.88)	66.9	<0.001
Intervention time	Overall	78	2,435	2,322	−5.80 (−8.04 to −3.57)	65.5	<0.001
	≤12weeks	39	1,003	921	−7.14 (−11.20 to −3.08)	77.1	<0.001
	>12weeks	39	1,432	1,401	−3.58 (−5.68 to −1.47)	31.6	<0.1

(Continued)

TABLE 1 (Continued)

Type of research and meta-analyses variables		Number of studies (included multi-arm study)	Number of participants		Weighted mean difference	Heterogeneity	
			Intervention	CG		I²(%)	P
Published year	Overall	78	2,435	2,322	−5.80 (−8.04 to −3.57)	65.5	<0.001
	≤2015	57	1,868	1,798	−4.75 (−7.33 to −2.16)	66.9	<0.001
	>2015	21	567	524	−8.94 (−13.47 to −4.41)	61.0	<0.001
Age	Overall	77	2,405	2,305	−5.72 (−7.95 to −3.49)	65.5	<0.001
	≤60	55	1,801	1,641	−3.71 (−5.44 to −1.98)	17.7	0.103
	>60	22	614	664	−8.25 (−14.06 to −2.44)	86.9	<0.001
Male to female ratio	Overall	74	2,213	2,032	−6.32 (−8.65 to −3.98)	67.1	<0.001
	Female<male	51	1,626	1,527	−6.44 (−9.37 to −3.51)	72.5	<0.001
	Male≥female	23	587	505	−5.73 (−9.43 to −2.02)	44.4	<0.01
Sedentary	Overall	78	2,435	2,322	−5.80 (−8.04 to −3.57)	65.5	<0.001
	Yes	47	1,518	1,475	−2.80 (−5.09 to −0.52)	35.1	<0.01
	No/NR	31	917	847	−9.06 (−12.81 to −5.31)	74.6	<0.001
Exercise type	Overall	78	2,435	2,322	−5.80 (−8.04 to −3.57)	65.5	<0.001
	AE	55	1,503	1,412	−3.93 (−6.31 to −1.54)	50.6	<0.001
	RE	17	330	320	−10.87 (−19.49 to −2.25)	83.2	<0.001
	ME	20	579	567	−4.47 (−7.04 to −1.90)	3.5	0.413
	MBE	2	23	23	−9.76 (−21.79 to 2.26)	0	0.336

Type of research and meta-analyses variables		Number of studies (included multi-arm study)	Number of participants		Hazard ratio	Heterogeneity	
			Exposure	REF		I²(%)	P
LS							
SB	HR	18	166,816	216,796	1.34 (1.26 to 1.43)	52.3	<0.01
PA	HR	21	239,479	380,216	0.71 (0.66 to 0.77)	78.0	<0.001
Subgroup analysis based on SB							
Region	Overall	18	166,816	216,796	1.34 (1.26 to 1.43)	52.3	<0.01
	United States	11	152,605	184,233	1.33 (1.25 to 1.42)	52.4	<0.01
	Others	7	14,211	32,563	1.42 (1.11 to 1.81)	60.0	<0.1
Published year	Overall	18	166,816	216,796	1.34 (1.26 to 1.43)	52.3	<0.01
	≤2016	13	135,478	187,115	1.32 (1.23 to 1.42)	59.8	<0.01
	>2016	5	31,338	29,681	1.44 (1.23 to1.68)	23.0	0.261
Follow-up time	Overall	18	166,816	216,796	1.34 (1.26 to 1.43)	52.3	<0.01
	≤10 years	12	125,900	173,235	1.32 (1.23 to 1.42)	47.4	<0.1
	>10 years	6	40,916	43,561	1.39 (1.23 to 1.59)	64.1	<0.1
Number of follow-up participants	Overall	17	166,816	216,796	1.34 (1.26 to 1.43)	55.1	<0.01
	≤10,000	9	9,817	11,497	1.56 (1.37 to 1.77)	21.2	0.255
	>10,000	8	156,999	205,299	1.28 (1.20 to 1.36)	49.1	<0.1
Disease type	Overall	18	166,816	216,796	1.34 (1.26 to 1.43)	52.3	<0.01
	CVM	7	90,730	94,255	1.32 (1.22 to 1.44)	36.5	0.126
	CVD	12	76,086	122,541	1.36 (1.24 to 1.50)	70.9	<0.01
Male to female ratio	Overall	16	165,944	215,954	1.34 (1.26 to 1.43)	55.1	<0.01
	Female<male	11	99,358	116,547	1.33 (1.22 to 1.44)	61.7	0.001
	Male≥female	5	66,586	99,407	1.37 (1.28 to 1.46)	0	0.575

(Continued)

TABLE 1 (Continued)

Type of research and meta–analyses variables		Number of studies (included multi–arm study)	Number of participants		Hazard ratio	Heterogeneity	
			Exposure	REF		I^2(%)	P
Quality of literature	Overall	17	166,816	216,796	1.34 (1.26 to 1.43)	52.3	<0.01
	<7	9	128,139	175,653	1.39 (1.29 to 1.49)	8.4	0.365
	≥7	8	38,677	44,143	1.30 (1.20 to 1.42)	58.9	<0.01
Subgroup analysis based on PA							
Region	Overall	21	239,479	380,216	0.71 (0.66 to 0.77)	78.0	<0.001
	United States	8	180,416	262,215	0.67 (0.58 to 0.78)	82.0	<0.001
	Others	13	59,063	118,001	0.75 (0.70 to 0.81)	55.0	<0.01
Published year	Overall	21	239,479	380,216	0.71 (0.66 to 0.77)	78.0	<0.001
	≤2016	10	56,980	72,557	0.70 (0.65 to 0.76)	0	0.683
	>2016	11	182,499	307,659	0.73 (0.65 to 0.82)	88.0	<0.001
Follow–up time	Overall	21	239,479	380,216	0.71 (0.66 to 0.77)	78.0	<0.001
	≤10 years	11	65,724	159,415	0.74 (0.68 to 0.80)	56.2	<0.1
	>10 years	10	173,755	220,801	0.69 (0.61 to 0.79)	83.2	<0.001
Number of follow–up participants	Overall	19	239,479	380,216	0.71 (0.66 to 0.77)	78.0	<0.001
	≤10,000	8	14,011	178,75	0.66 (0.56 to 0.79)	75.9	<0.001
	>10,000	11	225,468	362,341	0.78 (0.73 to 0.83)	51.9	<0.1
Disease type	Overall	21	239,479	380,216	0.71 (0.66 to 0.77)	78.0	<0.001
	CVM	11	188,625	266,336	0.72 (0.65 to 0.80)	54.4	<0.1
	CVD	10	50,854	76,256	0.71 (0.63 to 0.80)	85.8	<0.001
Male to female ratio	Overall	21	239,479	380,216	0.71 (0.66 to 0.77)	78.0	<0.001
	Female<male	13	210,071	231,408	0.71 (0.64 to 0.78)	81.7	<0.001
	Male≥female	4	29,408	38,799	0.81 (0.69 to 0.96)	61.7	<0.1
Quality of literature	Overall	21	239,479	380,216	0.71 (0.66 to 0.77)	78.0	<0.001
	<7	7	29,513	83,560	0.77 (0.70 to 0.86)	22.5	0.243
	≥7	14	209,966	296,656	0.70 (0.63 to 0.77)	84.1	<0.001

If studies reported with more than two categories of different SB, PA levels, they were converted into two groups, namely high-level SB, PA and low-level SB, PA while the later group was used as the reference category. Pool effect size: pooled WMDs (95% Confidence interval [CI]); pooled HRs(95% CI). BMI, Body mass index; CVD, Cardiovascular disease; CVM, Cardiovascular mortality; CG, Control Group; DBP, Diastolic blood pressure; HDL, High density lipoprotein; HR, Hazard Ratio; GlU, Glucose; LS, Longitudinal study; PA, Physical activity; REF, Reference; RCT, Randomized controlled trial; SBP, Systolic blood pressure; TG, Triglyceride; TC, Total cholesterol; LDL, Low density lipoprotein.

abrasion bias, and most studies had a low risk of reporting bias (143/148, 97.3%). The detailed assessment process is shown in Supplementary Figures S1, S2.

Of the 36 longitudinal studies, 29 received a score of 7 and were considered high-quality according to the NOS criteria; the detailed assessment process is shown in Supplementary Figure S3.

Primary outcomes

RCTs

Of the RCTs, 76 studies (4,658 participants) explored the effects of long-term PA on TGs, 79 studies (4,512 participants) described the effects of PA on TC, 84 studies (5,018 participants) investigated the effect of PA on HDL, and 78 studies (4,757 participants) described the effects of PA on LDL (Table 1). Most studies reported fasting lipids; only two studies (41, 42) reported non-fasting lipids. We pooled the WMD effect sizes according to a fixed model or a random model. The results showed that long-term PA significantly increased HDL levels ($P < 0.001$) and decreased TGs ($P < 0.001$), TC ($P < 0.001$), and LDL ($P < 0.001$). The pooled results for TG levels were as follows: WMD = −7.27; 95% CI: −9.68 to −4.87; I^2 = 0%, $P_{heterogeneity}$ = 0.670 (fixed model); TC: (WMD = −6.84; 95% CI: −9.15 to −4.52; I^2 = 38.4%, $P_{heterogeneity}$ < 0.001, random model); HDL: (WMD = 2.38; 95% CI: 1.00 to 3.76; I^2 = 84.7%; $P_{heterogeneity}$ < 0.001, random model); LDL: (WMD = −5.80; 95% CI: −8.04 to −3.57; I^2 = 65.5%, $P_{heterogeneity}$ < 0.001, random model). Among the four lipid indices, only the funnel plot for TC showed symmetry; the rest of the indices did not show symmetry (Supplementary Figures S17–S20). The Egger's test results were as follows: TGs, $P < 0.05$; TC, $P = 0.937$; HDL, $P = 0.240$; and LDL, $P < 0.05$.

To explore possible sources of heterogeneity, subgroup analyses of lipid outcomes were performed, grouping participants according to intervention time, region, age of participants, year of publication, male/female ratio, previous SB or no previous SB, and PA type. Some of the subgroup analyses were consistent; however, when studies were divided according to their male/female ratios, less heterogeneity was observed in the combined effect of long-term PA on TC in the studies with more males (WMD = −8.47; 95% CI: −2.38 to −4.56; I^2 = 20.4%, $P = 0.164$, random model). Similarly, when studies were divided according to the type of PA, less heterogeneity was observed in studies on the effect of ME on LDL (WMD = −4.47; 95% CI: −7.04 to −1.90; I^2 = 20.4%, $P = 0.164$, random model). In addition, PA was associated with a significant improvement in HDL only if participants were younger than 60 years old ($P < 0.001$), the intervention duration was longer than 12 weeks ($P < 0.01$), the study was conducted in people without previous SB habits, or the study assessed AE ($P < 0.01$) or RE ($P < 0.01$). The detailed subgroup analyses are presented in Table 1.

Longitudinal studies

Eighteen studies analyzed the effect of SB on CVD (Table 1). The results showed that people with SB had a significantly increased risk of CVD ($P < 0.001$), both fatal and non-fatal, with a pooled effect size (HR) of 1.34 (95% CI: 1.26 to 1.43) and relatively high heterogeneity (I^2 = 52.3%, $P_{heterogeneity} < 0.001$, random model). The funnel plot was asymmetric, and the publication bias was high ($P_{Egger's\ test} < 0.05$) (Supplementary Figure S22).

Twenty-one studies explored the effect of PA on CVD (Table 1). The results showed that long-term PA was associated with a significantly lower risk of CVD compared with low levels of PA ($P < 0.001$), with a pooled effect size (HR) of 0.71 (95% CI: 0.66 to 0.77) and high heterogeneity (I^2 = 78.0%, $P_{heterogeneity} < 0.001$, random model). The funnel plot was also asymmetric, showing potential publication bias ($P_{Egger's\ test} = 0.605$) (Supplementary Figure S23).

We performed subgroup analyses by dividing the studies according to several variables of interest (region, year of publication, male/female ratio, number of participants, follow-up time, quality of literature, and type of CVD), and some subsets of these subgroup analyses revealed sources of heterogeneity. For example, in the SB and CVD studies, heterogeneity was significantly lower in studies with population sizes under 10,000 (HR = 1.56; 95% CI: 1.37 to 1.77; I^2 = 21.2%, $P = 0.255$, random model) than in studies with population sizes greater than 10,000 (HR = 0.28; 95% CI:1.20 to 1.36; I^2 = 49.1%, $P = 0.033$, random model). Other sources of heterogeneity are detailed in Table 1.

Secondary outcomes

RCTs

BMI

According to the pooled combined effects of BMI using a fixed effects model, 89 RCTs (6,220 participants) revealed a significant effect regarding BMI reduction (WMD = −0.36; 95% CI: −0.43 to −0.30; I^2 = 0%, $P_{heterogeneity} = 0.998$, fixed model) (Table 1); however, the asymmetry of the funnel plot of BMI indicators suggested potential publication bias ($P_{Egger's\ test}$ = 0.051) (Supplementary Figure S14).

Blood pressure

A total of 65 RCTs (3,500 participants) explored the effects of PA on SBP, and 63 (3,373 participants) investigated the effects of PA on DBP (Table 1). The resting blood pressure in both sitting and supine positions was included. The combined effect showed a significant reduction in SBP (WMD = −3.63; 95% CI: −4.62 to −2.64; I^2 = 58.0%, $P_{heterogeneity} < 0.001$, random model) with some heterogeneity. DBP also decreased significantly by a small margin (WMD = −2.25; 95% CI: −2.94 to −1.56; I^2 = 51.3%, $P_{heterogeneity} < 0.001$, random model), and heterogeneity was observed. The forest plots for both indicators were asymmetric, and publication bias was detected (SBP: $P = 0.261$, DBP: $P < 0.001$) (Supplementary Figures S15, S16).

Blood glucose

A random effects model was used to pool glucose from 65 RCTs (3,413 participants) (Table 1), all of which required participants to fast for 8–14 h; the model revealed that PA was associated with a significant improvement in fasting glucose ($P < 0.001$) with high heterogeneity (WMD = −4.40; 95% CI: −5.44 to −3.36; I^2 = 86.5%; $P_{heterogeneity} < 0.001$, random model). The asymmetry of the forest plot suggested high publication bias ($P_{Egger's\ test}$ = 0.838) (Supplementary Figure S21).

Sensitivity analyses

Sensitivity analysis showed that all outcomes were stable for PA and SB.

Discussion

This is the first meta-analysis to combine randomized controlled trials and longitudinal studies to assess the association between SB, PA, and CVD. The analysis of 148 RCTs and 36 longitudinal studies indicated that long-term PA improved indicators related to CVD risk in healthy adults and directly reduced the risk of CVD. Conversely, long-term SB increased the risk of CVD in healthy people, regardless of the study region, the gender of participants, and follow-up time. In addition, long-term PA was not associated with a large improvement in HDL in studies on older adult populations, studies on previously sedentary populations, studies with short-term interventions, or studies that assessed ME.

SB has been identified as a risk factor for CVD in several previous studies (43, 44). Our meta-analysis confirmed the association between SB and CVD (HR:1.34; 95% CI: 1.26 to 1.43; $I^2 = 52.3$, $P < 0.01$; random model), suggesting a 34% increase in the risk of CVD (including non-fatal CHD, HF, and fatal myocardial infarction events) in people with frequent SB compared with those without SB. Evidence suggests that of the factors associated with all causes of CVD mortality, SB has the strongest association (8), and several other studies have reported strong, consistent results supporting this association. A prospective cohort study on 134,596 Americans found that the risk of death from CVD rose with increased sitting time, particularly while viewing television, and this finding was consistent across people of different weights, genders, and races; similar results were found in our study (45). A lack of PA due to SB leads to the decreased turnover of endogenous energy stores, myogenic glycogen, and intracellular lipids; in turn, these changes lead to skeletal muscle insulin resistance. When hyperinsulinism occurs, adipogenesis increases, promoting the production of very low-density lipoproteins and lower HDL levels in the liver. This results in the development of metabolic syndrome, which may contribute to the development of CVD. Similarly, steatosis may cause hyperglycemia, which not only causes diabetes but also potentially increases the risk of CVD (46, 47). In conclusion, the mechanisms through which SB causes CVD are complex and multifaceted.

We investigated the effects of long-term PA on CVD and several CVD risk indicators and found that long-term PA not only reduced the HR of CVD events (HR = 0.71; 95%CI: 0.66 to 0.77; $I^2 = 78.0\%$, $P_{heterogeneity} < 0.001$, random model) but also improved several CVD risk indicators. The cardioprotective effects of long-term PA have been confirmed by several studies. For example, an American cohort study that analyzed the effects of long-term PA in 88,140 adults found that the risk of CVD-specific death was 37 and 33% lower in participants who performed PA for 150–299 min and 1,500 min or more per week, respectively, compared with those who were inactive (48). Because of its large sample size, this study provides strong evidence supporting our meta-analysis results. For the mechanism by which PA reduces cardiovascular risk, one study suggests that PA improves cardiovascular health through the efficient use of energy-releasing raw materials (e.g., oxygen, fat, and glucose) and other resources, combined with autonomous skeletal muscle contraction that enhances metabolism and neural coordination (44). Furthermore, a large meta-analysis of RCTs showed that long-term PA significantly improved cardiopulmonary function and several CVD biomarkers (e.g., lipids) in healthy adults, which in turn reduced the incidence of CVD and improved cardiovascular health. To further explore the reasons for PA's effects on the risk of CVD, our study began by analyzing lipids because abnormalities in the lipoprotein–lipid profile account for 50% of the total risk of CVD (46); moreover, the assessment of lipid levels is the most common method to identify individuals at high risk of CVD (49). According to our study, long-term PA significantly reduced total TC, TGs, and LDL levels and significantly improved HDL levels. Other studies have shown that adults who engage in long-term PA have lower TC and LDL levels compared with those who are inactive (50, 51), these findings are consistent with our meta-analysis results. Furthermore, two longitudinal studies have demonstrated that TG levels are lower and HDL levels are higher in endurance athletes and in those with long-term aerobic training (52, 53). The more favorable lipid profiles in these populations may be due to an increase in lipoprotein lipase (LPL) mRNA, LPL mass, total LPL activity, and heparin-releasable LPL activity in the skeletal muscle after long-term PA (54). When the LPL concentration increases, the composition of lipoproteins changes *in vivo*, and apolipoprotein-E is redistributed. This change decreases plasma TG levels, LDL levels, and TC/HDL ratio and increases HDL concentrations (55, 56), thereby reducing the risk of CVD.

Furthermore, our study revealed significant improvements in BMI, blood pressure, and blood glucose in healthy adults who performed long-term PA, and these results have been widely confirmed. Several large RCTs have found that after more than 8 weeks of PA intervention, all participants had lower weight, blood pressure, and fasting glucose, and these effects were consistent for participants with different genders and weights as well as different types and intensities of PA (57–60). These improvements may be related to omentin-1, an adipokine that promotes insulin sensitivity; studies have shown that after long-term PA intervention, participants showed improvements in BMI, waist circumference, body fat, and blood glucose with a corresponding increase in their omentin-1 concentrations (61). Omentin-1 was present at lower concentrations in the obese population and was negatively correlated with BMI, fasting glucose, and blood pressure (62, 63). The concentration of omentin-1 in the body may have increased after the PA intervention, improving CVD-related outcomes.

In the subgroup analysis, we found that PA only significantly improved HDL when the intervention duration was longer than 12 weeks or the participants who were under 60 years of age. Shorter interventions may be insufficient to achieve observable improvements; moreover, the PA intensity may not reach the level needed for improvement in older adults because of their low exercise levels. In a previous study, a significant improvement in HDL was reported only after PA reached a certain intensity (64). We also observed a significant effect on HDL when people chose to perform AE or RE. Evidence shows that AE or RE alone can increase HDL levels (65), and the combination of AE and RE in ME can have the same effect (66); however, ME was not associated with significant changes in our study. This is likely because ME was mixed with other forms of exercise, such as balance exercises, and less evidence supports improvement in HDL with these forms of exercise; thus, the overall results may have been affected. Moreover, no significant differences were observed in terms of the effect of PA on HDL in the group with SB. This suggests that the beneficial effects of PA may be limited in people with SB; furthermore, a previous study showed that the effects of PA and SB were independent of each other (9). These findings warrant further investigation of the details of the interaction between PA and SB in future studies. In all other subgroup analyses, we obtained consistent results, indicating that the overall improvement in lipids levels was superior in participants who performed PA.

Our study has several implications in clinical practice and can provide guidance for practitioners. First, our findings support the American Heart Association (AHA) guidelines recommending long-term PA as a first-line treatment for improving dyslipidemia and reducing the risk of CVD (67). Therefore, 40 min of moderate to vigorous intensity aerobic exercise for three to four times per week is recommended to lower LDL and increase HDL (68). Second, our study found that PA also improved blood pressure levels, and according to the AHA guidelines, performing aerobic exercise three to four times a week for an average of 40 min per session for at least 12 weeks is a typical recommendation for improving blood pressure in adults (68). Third, according to our subgroup analysis, resistance training can also reduce the risk of CVD when performed at a recommended weekly training intensity of 500–1000 METs (69). In summary, patients should regularly engage in PA, and to maximize health benefits, they should perform at least 150 minutes of moderate-intensity aerobic exercise or 75 min of high-intensity aerobic exercise as well as two resistance training sessions per week (30).

Strengths and limitations

This study is the first to combine RCTs and longitudinal studies to examine the association between PA, SB, and CVD, contributing new medical evidence to the literature. We not only distinguished the population but also considered factors such as economic status, year of publication, and the number of participants, making this a more in-depth study than previous work. Because the volume of literature included in the previous meta-analysis was not very large, we collected studies from larger databases, resulting in a larger sample size meeting the inclusion criteria. The results of this study may provide more treatment options to policymakers, clinicians, and caregivers, and the findings may help guide decision-making and facilitate more in-depth research in the future.

The present study also has several limitations. First, the uneven quality of the literature on RCTs may have impacted the overall quality of the studies, and the high risk of outcome assessment blinding created some heterogeneity and imprecision in the study results. In addition, the inclusion of longitudinal studies and RCTs may have resulted in inconsistent results. Furthermore, we did not analyze certain confounding factors, such as diet, smoking, and obesity, because of inconsistencies in implementation criteria, dosing criteria, and rubrics, which may have contributed to limitations in the outcomes. Considering the above limitations, the study results should be interpreted with caution.

Conclusions

In conclusion, long-term SB increased the risk of CVD in healthy adults, whereas regular PA reduced the risk of CVD and improved indicators associated with CVD risk. However, improvement was limited in patients with SB, select ME and older age groups. Therefore, patients should be encouraged to limit their daily sitting time and increase their PA levels to reduce their risk of CVD. More detailed studies are needed to demonstrate and clarify the effects of PA and SB on CVD.

Data availability statement

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

Author contributions

Z-dL served as principal author and had full access to all the data in the study, takes responsibility for the accuracy of the data analysis, and the integrity of the data. Z-dL and MZ contributed to the conception, design, and drafting the manuscript. Z-dL, MZ, and C-zW contributed to data acquisition and interpretation. YY and J-hL contributed to revise of the article and final approval. All authors contributed to the article and approved the submitted version.

Funding

The work was supported by the National Natural Science Youth Foundation of China (No. 32000830) and the Special funding in China Postdoctoral Fund Station (No. 2021T140356).

Acknowledgments

We affirm that the work submitted for publication is original and has not been published other than as an abstract or preprint in any language or format and has not been submitted elsewhere for print or electronic publication consideration. We affirm that each person listed as authors participated in the Work in a substantive manner, in accordance with ICMJE authorship guidelines, and is prepared to take public responsibility for it. All authors consent to the investigation of any improprieties that may be alleged regarding the work. We appreciate the linguistic assistance provided by TopEdit (www.topeditsci.com) during the preparation of this manuscript.

Conflict of interest

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

Publisher's note

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.2022.1018460/full#supplementary-material

References

1. Olvera Lopez E, Ballard BD, Jan A. *Cardiovascular Disease*. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2022, StatPearls Publishing LLC. (2022).

2. Townsend N, Kazakiewicz D, Lucy Wright F, Timmis A, Huculeci R, Torbica A, et al. Epidemiology of cardiovascular disease in Europe. *Nature Rev Cardiol.* (2022) 19:133–43. doi: 10.1038/s41569-021-00607-3

3. Zhou M, Wang H, Zhu J, Chen W, Wang L, Liu S, et al. Cause-specific mortality for 240 causes in China during 1990–2013: a systematic subnational analysis for the Global Burden of Disease Study 2013. *Lancet.* (2016) 387:251–72. doi: 10.1016/S0140-6736(15)00551-6

4. Liu S, Li Y, Zeng X, Wang H, Yin P, Wang L, et al. Burden of cardiovascular diseases in China, 1990-2016: findings from the 2016 Global Burden of Disease Study. *JAMA Cardiol.* (2019) 4:342–52. doi: 10.1001/jamacardio.2019.0295

5. 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

6. Reiner Z, Catapano AL, De Backer G, Graham I, Taskinen MR, Wiklund O, et al. ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). *Eur Heart J.* (2011) 32:1769–818. doi: 10.1093/eurheartj/ehr158

7. Fletcher GF, Landolfo C, Niebauer J, Ozemek C, Arena R, Lavie CJ. Promoting physical activity and exercise: JACC health promotion series. *J Am Coll Cardiol.* (2018) 72:1622–39. doi: 10.1016/j.jacc.2018.08.2141

8. Katzmarzyk PT, Powell KE, Jakicic JM, Troiano RP, Piercy K, Tennant B. Sedentary behavior and health: update from the 2018 physical activity guidelines advisory committee. *Med Sci Sports Exerc.* (2019) 51:1227–41. doi: 10.1249/MSS.0000000000001935

9. Katzmarzyk PT, Church TS, Craig CL, Bouchard C. Sitting time and mortality from all causes, cardiovascular disease, and cancer. *Med Sci Sports Exerc.* (2009) 41:998–1005. doi: 10.1249/MSS.0b013e3181930355

10. Cao Z, Xu C, Zhang P, Wang Y. Associations of sedentary time and physical activity with adverse health conditions: outcome-wide analyses using isotemporal substitution model. *EClinicalMed.* (2022) 48:101424. doi: 10.1016/j.eclinm.2022.101424

11. Aune D, Schlesinger S, Leitzmann MF, Tonstad S, Norat T, Riboli E, et al. Physical activity and the risk of heart failure: a systematic review and dose-response meta-analysis of prospective studies. *Eur J Epidemiol.* (2021) 36:367–81. doi: 10.1007/s10654-020-00693-6

12. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep.* (1985) 100:126–31.

13. Batrakoulis A, Jamurtas AZ, Metsios GS, Perivoliotis K, Liguori G, Feito Y, et al. Comparative efficacy of 5 exercise types on cardiometabolic health in overweight and obese adults: a systematic review and network meta-analysis of 81 randomized controlled trials. *Circ Cardiovasc Qual Outcomes.* (2022) 15:e008243. doi: 10.1161/CIRCOUTCOMES.121.008243

14. Oberoi S, Robinson PD, Cataudella D, Culos-Reed SN, Davis H, Duong N, et al. Physical activity reduces fatigue in patients with cancer and hematopoietic stem cell transplant recipients: a systematic review and meta-analysis of randomized trials. *Crit Rev Oncol Hematol.* (2018) 122:52–9. doi: 10.1016/j.critrevonc.2017.12.011

15. Nordengen S, Andersen LB, Solbraa AK, Riiser A. Cycling is associated with a lower incidence of cardiovascular diseases and death: part 1 - systematic review of cohort studies with meta-analysis. *Br J Sports Med.* (2019) 53:870–8. doi: 10.1136/bjsports-2018-099099

16. Zhuo C, Zhao J, Chen M, Lu Y. Physical activity and risks of cardiovascular diseases: a mendelian randomization study. *Front Cardiovasc Med.* (2021) 8:722154. doi: 10.3389/fcvm.2021.722154

17. Caterini JE, Campisi ES, Cifra B. Physical activity promotion in pediatric congenital heart disease: are we running late? *Can J Cardiol.* (2020) 36:1406–16. doi: 10.1016/j.cjca.2020.07.003

18. Recchioni R, Marcheselli F, Antonicelli R, Mensà E, Lazzarini R, Procopio AD, et al. Epigenetic effects of physical activity in elderly patients with cardiovascular disease. *Exp Gerontol.* (2017) 100:17–27. doi: 10.1016/j.exger.2017.10.016

19. Cheng W, Zhang Z, Cheng W, Yang C, Diao L, Liu W. Associations of leisure-time physical activity with cardiovascular mortality: a systematic review and meta-analysis of 44 prospective cohort studies. *Eur J Prev Cardiol.* (2018) 25:1864–72. doi: 10.1177/2047487318795194

20. Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell KE, et al. Does physical activity attenuate, or even eliminate, the

detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *Lancet.* (2016) 388:1302–10. doi: 10.1016/S0140-6736(16)30370-1

21. Wahid A, Manek N, Nichols M, Kelly P, Foster C, Webster P, et al. Quantifying the association between physical activity and cardiovascular disease and diabetes: a systematic review and meta-analysis. *J Am Heart Assoc.* (2016) 5:e2495 doi: 10.1161/JAHA.115.002495

22. Lin X, Zhang X, Guo J, Roberts CK, McKenzie S, Wu WC, et al. Effects of exercise training on cardiorespiratory fitness and biomarkers of cardiometabolic health: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc.* (2015) 4:e2014 doi: 10.1161/JAHA.115.002014

23. Patterson R, McNamara E, Tainio M, de Sá TH, Smith AD, Sharp SJ, et al. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: a systematic review and dose response meta-analysis. *Eur J Epidemiol.* (2018) 33:811–29. doi: 10.1007/s10654-018-0380-1

24. Oja P, Kelly P, Murtagh EM, Murphy MH, Foster C, Titze S. Effects of frequency, intensity, duration and volume of walking interventions on CVD risk factors: a systematic review and meta-regression analysis of randomised controlled trials among inactive healthy adults. *Br J Sports Med.* (2018) 52:769–75. doi: 10.1136/bjsports-2017-098558

25. Lee YK, Cho SY, Roh HT. Effects of 16 weeks of taekwondo training on the cerebral blood flow velocity, circulating neurotransmitters, and subjective well-being of obese postmenopausal women. *Int J Environ Res Public Health.* (2021) 18:e82010789. doi: 10.3390/ijerph182010789

26. Mu X, Yu K, Long P, Niu R, Li W, Chen H, et al. Leisure-time physical activity and risk of incident cardiovascular disease in Chinese retired adults. *Sci Rep.* (2021) 11:24202. doi: 10.1038/s41598-021-03475-6

27. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. *Cochrane Handbook for Systematic Reviews of Interventions.* New York: John Wiley & Sons (2019).

28. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA.* (2000) 283:2008–12. doi: 10.1001/jama.283.15.2008

29. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc.* (2011) 43:1334–59. doi: 10.1249/MSS.0b013e318213fefb

30. Services USDoHaH. *Physical Activity Guidelines for Americans.* 2nd edition. (2018). Available online at: https://health.gov/sites/default/files/2019-09/Physical_Activity_Guidelines_2nd_edition.pdf (accessed September, 2019).

31. Wang S, Yin H, Wang X, Jia Y, Wang C, Wang L, et al. Efficacy of different types of exercises on global cognition in adults with mild cognitive impairment: a network meta-analysis. *Aging Clin Exp Res.* (2019) 31:1391–400. doi: 10.1007/s40520-019-01142-5

32. Higgins JP. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.0. 2.* (2009). The Cochrane Collaboration. Available online at: https://training.cochrane.org/handbook/archive/v5.0.2/.

33. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol.* (2010) 25:603–5. doi: 10.1007/s10654-010-9491-z

34. Abou-Setta AM, Mousavi SS, Spooner C, Schouten JR, Pasichnyk D, Armijo-Olivo S, et al. *Newcastle-Ottawa Scale Assessment of Cohort Studies: Newcastle-Ottawa Scale Assessment of Cohort Studies.* Agency for Healthcare Research and Quality (US). (2012).

35. Hedges LV. Distribution theory for Glass's estimator of effect size and related estimators. *J Educat Statis.* (1981) 6:107–28. doi: 10.3102/10769986006002107

36. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol.* (2014) 14:135. doi: 10.1186/1471-2288-14-135

37. Borenstein M, Hedges LV, Higgins JP, Rothstein HR, A. basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods.* (2010) 1:97–111. doi: 10.1002/jrsm.12

38. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* (2002) 21:1539–58. doi: 10.1002/sim.1186

39. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *Bmj.* (2003) 327:557–60. doi: 10.1136/bmj.327.7414.557

40. Egger M, Juni P, Bartlett C, Holenstein F, Sterne J. How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study. *Health Technol Assess.* (2003) 7:1–76. doi: 10.3310/hta7010

41. Korshøj M, Ravn MH, Holtermann A, Hansen Å M, Krustrup P. Aerobic exercise reduces biomarkers related to cardiovascular risk among cleaners: effects of a worksite intervention RCT. *Int Arch Occup Environ Health.* (2016) 89:239–49. doi: 10.1007/s00420-015-1067-5

42. Dagistan Akgöz A, Gözüm S. Effectiveness of a nurse-led physical activity intervention to decrease cardiovascular disease risk in middle-aged adults: a pilot randomized controlled study. *J Vascular Nurs.* (2020) 38:140–8. doi: 10.1016/j.jvn.2020.05.002

43. Young DR, Hivert MF, Alhassan S, Camhi SM, Ferguson JF, Katzmarzyk PT, et al. Sedentary behavior and cardiovascular morbidity and mortality: a science advisory from the American Heart Association. *Circulation.* (2016) 134:e262–79. doi: 10.1161/CIR.0000000000000440

44. Powell KE, Paluch AE, Blair SN. Physical activity for health: What kind? How much? How intense? On top of what? *Annual Rev Public Health.* (2011) 32:349–65. doi: 10.1146/annurev-publhealth-031210-101151

45. Kim Y, Wilkens LR, Park SY, Goodman MT, Monroe KR, Kolonel LN. Association between various sedentary behaviours and all-cause, cardiovascular disease and cancer mortality: the Multiethnic Cohort Study. *Int J Epidemiol.* (2013) 42:1040–56. doi: 10.1093/ije/dyt108

46. Booth FW, Laye MJ, Lees SJ, Rector RS, Thyfault JP. Reduced physical activity and risk of chronic disease: the biology behind the consequences. *Eur J Appl Physiol.* (2008) 102:381–90. doi: 10.1007/s00421-007-0606-5

47. Leiter LA. From hyperglycemia to the risk of cardiovascular disease. *Rev Cardiovasc Med.* (2006) 7 (Suppl 2):S3–9. Available online at: https://www.imrpress.com/journal/RCM/7/S2/pii/1561344059777-518357461?utm_source=TrendMD&utm_medium=cpc&utm_campaign=Reviews_in_Cardiovascular_Medicine_TrendMD_0

48. Zhao M, Veeranki SP Li S, Steffen LM Xi B. Beneficial associations of low and large doses of leisure time physical activity with all-cause, cardiovascular disease and cancer mortality: a national cohort study of 88,140 US adults. *Br J Sports Med.* (2019) 53:1405–11. doi: 10.1136/bjsports-2018-099254

49. Arsenault BJ, Boekholdt SM, Kastelein JJ. Lipid parameters for measuring risk of cardiovascular disease. *Nature Rev Cardiol.* (2011) 8:197–206. doi: 10.1038/nrcardio.2010.223

50. Hartung GH, Foreyt JP, Mitchell RE, Vlasek I, Gotto AM. Jr. Relation of diet to high-density-lipoprotein cholesterol in middle-aged marathon runners, joggers, and inactive me. *New Eng J Med.* (1980) 302:357–61. doi: 10.1056/NEJM198002143020701

51. Nagay B, Zielinski T, Lawczynski L. [Dermal calcinosis treated surgically]. *Wiadomosci lekarskie.* (1977) 30:493–4.

52. Driskell JA, Wolinsky I. *Energy-Yielding Macronutrients and Energy Metabolism In Sports Nutrition.* Florida: CRC Press. (1999).

53. Durstine JL, Haskell WL. Effects of exercise training on plasma lipids and lipoproteins. *Exerc Sport Sci Rev.* (1994) 22:477–521. doi: 10.1249/00003677-199401000-00017

54. Hamilton MT, Etienne J, McClure WC, Pavey BS, Holloway AK. Role of local contractile activity and muscle fiber type on LPL regulation during exercise. *Am J Physiol.* (1998) 275:E1016–22. doi: 10.1152/ajpendo.1998.275.6.E1016

55. Liu MS, Jirik FR, LeBoeuf RC, Henderson H, Castellani LW, Lusis AJ, et al. Alteration of lipid profiles in plasma of transgenic mice expressing human lipoprotein lipase. *J Biol Chem.* (1994) 269:11417–24. doi: 10.1016/S0021-9258(19)78140-X

56. Oscai LB, Tsika RW, Essig DA. Exercise training has a heparin-like effect on lipoprotein lipase activity in muscle. *Can J Physiol Pharmacol.* (1992) 70:905–9. doi: 10.1139/y92-121

57. Trajković N, Sporiš G, Krističević T, Bogataj Š. Effects of small-sided recreational volleyball on health markers and physical fitness in middle-aged men. *Int J Environ Res Public Health.* (2020) 17:93021 doi: 10.3390/ijerph17093021

58. Connolly LJ, Scott S, Morencos CM, Fulford J, Jones AM, Knapp K, et al. Impact of a novel home-based exercise intervention on health indicators in inactive premenopausal women: a 12-week randomised controlled trial. *Eur J Appl Physiol.* (2020) 120:771–82. doi: 10.1007/s00421-020-04315-7

59. Chen N, Xia X, Qin L, Luo L, Han S, Wang G, et al. Effects of 8-week hatha yoga training on metabolic and inflammatory markers in healthy, female chinese subjects: a randomized clinical trial. *Biomed Res Int.* (2016) 2016:5387258. doi: 10.1155/2016/5387258

60. Dalleck LC, Allen BA, Hanson BA, Borresen EC, Erickson ME, De Lap SL. Dose-response relationship between moderate-intensity exercise duration and coronary heart disease risk factors in postmenopausal women. *J Women's Health. (2002).* (2009) 18:105–13 doi: 10.1089/jwh.2008.0790

61. Saremi A, Asghari M, Ghorbani A. Effects of aerobic training on serum omentin-1 and cardiometabolic risk factors in overweight and obese men. *J Sports Sci.* (2010) 28:993–8. doi: 10.1080/02640414.2010.484070

62. de Souza Batista CM, Yang RZ, Lee MJ, Glynn NM Yu DZ, Pray J, et al. Omentin plasma levels and gene expression are decreased in obesity. *Diabetes.* (2007) 56:1655–61. doi: 10.2337/db06-1506

63. Tan BK, Adya R, Farhatullah S, Lewandowski KC, O'Hare P, Lehnert H, et al. Omentin-1, a novel adipokine, is decreased in overweight insulin-resistant women with polycystic ovary syndrome: ex vivo and in vivo regulation of omentin-1 by insulin and glucose. *Diabetes.* (2008) 57:801–8. doi: 10.2337/db07-0990

64. Kokkinos PF, Holland JC, Narayan P, Colleran JA, Dotson CO, Papademetriou V. Miles run per week and high-density lipoprotein cholesterol levels in healthy, middle-aged men: a dose-response relationship. *Arch Intern Med.* (1995) 155:415–20. doi: 10.1001/archinte.1995.00430040091011

65. Potteiger JA, Claytor RP, Hulver MW, Hughes MR, Carper MJ, Richmond S, et al. Resistance exercise and aerobic exercise when paired with dietary energy restriction both reduce the clinical components of metabolic syndrome in previously physically inactive males. *Eur J Appl Physiol.* (2012) 112:2035–44. doi: 10.1007/s00421-011-2174-y

66. Woudberg NJ, Mendham AE, Katz AA, Goedecke JH, Lecour S. Exercise intervention alters HDL subclass distribution and function in obese women. *Lipids Health Dis.* (2018) 17:232. doi: 10.1186/s12944-018-0879-1

67. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol.* (2019) 73:e285–350. doi: 10.1016/j.jacc.2018.11.003

68. Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Houston Miller N, Hubbard VS, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* (2014) 63:2960–84 doi: 10.1161/01.cir.0000437740.48606.d1

69. Jeong SW, Kim SH, Kang SH, Kim HJ, Yoon CH, Youn TJ, et al. Mortality reduction with physical activity in patients with and without cardiovascular disease. *Eur Heart J.* (2019) 40:3547–55. doi: 10.1093/eurheartj/ehz564

frontiers | Frontiers in Public Health

TYPE Review
PUBLISHED 28 October 2022
DOI 10.3389/fpubh.2022.1024856

Check for updates

OPEN ACCESS

EDITED BY
Szabolcs Halasi,
University of Novi Sad, Serbia

REVIEWED BY
Antonino Bianco,
University of Palermo, Italy
Antonio Palma,
University of Palermo, Italy

*CORRESPONDENCE
Alex Rizzato
alex.rizzato@unipd.it

SPECIALTY SECTION
This article was submitted to Aging and Public Health, a section of the journal Frontiers in Public Health

RECEIVED 22 August 2022
ACCEPTED 05 October 2022
PUBLISHED 28 October 2022

CITATION
Rizzato A, Marcolin G and Paoli A (2022) Non-exercise activity thermogenesis in the workplace: The office is on fire. *Front. Public Health* 10:1024856. doi: 10.3389/fpubh.2022.1024856

Non-exercise activity thermogenesis in the workplace: The office is on fire

Alex Rizzato*, Giuseppe Marcolin and Antonio Paoli

Department of Biomedical Sciences, University of Padova, Padua, Italy

From the second half of the previous century, there has been a shift toward occupations largely composed of desk-based behaviors. This, inevitably, has led to a workload reduction and a consequent lower energy expenditure. On this point, small increments of the non-exercise activity thermogenesis (NEAT) could be the rationale to reach health benefits over a prolonged period. Different published researches suggest solutions to reverse sitting time and new alternative workstations have been thought to increase total physical activity. Therefore, the purpose of this narrative review is to summarize the current state of the research regarding the "NEAT approach" to weight-gain prevention in work environments. This review analyzes the main evidence regarding new alternative workstations such as standing, walking workstations, seated pedal, and gymnastic balls to replace a standard office chair.

KEYWORDS

energy expenditure, sedentary behavior, workplace, sitting, physical activity

Introduction

Historical background and epidemiological frame

Over the past 50 years, technological development and the making of ever-new labor-saving devices have reduced physical activity and, consequently, energy expenditure (EE) across many different domestic and working settings (1). The term sedentary etymologically refers to "remaining in one place" from Middle French *sédentaire* (1590s) and directly from Latin *sedentarius* "sitting, remaining in one place." Later recorded in the 1660s, Proto-Indo-European referred to persons, in the sense of "not in the habit of exercise." Nowadays, it refers to a specific group of activities that involves low levels of EE in the range of 1.0–1.5 Metabolic Equivalent of Task or MET (1 MET is defined as 3.5 $mlO_2/Kg/min$): for example, sitting during transfers (i.e., by train or car), tasks performed while working, and for leisure or in the domestic location (2). A growing amount of evidence contended that the increased tendency to a sedentary lifestyle plays a main role in the rise of multiple chronic diseases, including cardiovascular disease, Type 2 diabetes (3), and overweight and obesity (4). Regarding the latter, despite the rising problem awareness, the obesity epidemic is constantly growing and obesity rates are increasing worldwide. In 2016, more than 1.9 billion adults, 18 years and older, were overweight. Of these, over 650 million were obese. About 39% of adults aged 18 years and over were overweight in 2016 and 13% were obese (5). As recalled, since a sedentary lifestyle represents one of the main risk factors for developing chronic diseases, disablement, and frailty, reducing the time spent in sedentary activities is a population-wide goal for positive health outcomes. Twenty-five years ago, Prentice et al. (6) published a study about the secular trends in diet and physical activity and obesity in Britain after retrospectively analyzing data from 1950 to 1990. Evidence suggested that changes in the prevalence of obesity were not related to changes in total energy or fat intake. Conversely, indirect measures of physical inactivity (i.e., car ownership and hours of television watching) appeared to be more closely related to a change in body weight. More recently, an epidemiological study differentiated sedentary sitting time alone from sedentary TV-viewing time. High levels of moderate-intensity physical activity (i.e., about 60–75 min per day) seemed able to eliminate the increased death risk related to the sitting time alone, having instead a little influence on the increased risk of death related to TV-viewing time (7). Ekelund et al. (7) hypothesized two possible explanations regarding this association. The first theory is that TV-viewing mainly happens after dinner, and postprandial sedentary time may be detrimental to glucose and lipid metabolism. Moreover, behaviorally, TV-viewing is frequently accompanied by snacking or other eating habits possibly influenced by TV advertising. In addition to morbidity and early mortality, a sedentary lifestyle is "guilty" of a considerable economic burden. A world global analysis revealed that physical inactivity cost for healthcare systems was $53.8 billion in 2013, of which $31.2 billion was borne by the public sector, $12.9 billion by the private sector, and $9.7 billion by households (8). The recent COVID-19 pandemic has increased sedentary behaviors during the imposed lockdown periods across several populations, including children and patients with a variety of medical conditions (9). Thus, multiple interventions targeting sedentary behaviors have been studied; for instance, Gardiner et al. studied the efficacy of a face-to-face goal-setting consultation and one individually tailored mailing providing feedback on accelerometer-derived sedentary time in a group of older adults. They found a decreased sedentary time (– 3.2%), increased breaks in sedentary time per day (i.e., four), and an increased level of light (2.2%) to moderate to vigorous (1.0%) physical activity (10). Moreover, the amount of sitting time, prolonged or interrupted, is significantly associated with cardiovascular disease risk in adults over age 45 years (11). Larsen et al. showed that interrupting the sitting time every 20 min positively influenced systolic blood pressure, such as reducing all-cause mortality risk by 3–4% (11). In addition, regular breaks during prolonged sitting periods lowered postprandial glycemia in middle-aged adults without metabolic impairment (12). Indeed, humans expend energy also having routinary postures and performing daily-living movements (e.g., standing, walking, stair climbing, and many others). Thus, some daily non-exercise activities, also alternated with prolonged sitting, could considerably contribute to an increase in total daily energy expenditure. In this regard, the "Compendium of Physical Activities" continued to accumulate and categorize published reports of the EE in MET associated with different physical activities (13, 14).

Humans: Evolutionary active animals

Although sedentary behaviors encompass large sections of the population, evolutionary biology suggested that humans are not physiologically adapted to periods of prolonged inactivity. In industrialized countries, activities that require daily locomotion to man are often very low. Thus, nowadays, human energy expenditure is reasonably lower than in our Paleolithic ancestors (15). This evolutionary theory could also account for the increase in obesity prevalence rates worldwide. Hayes et al. found that the physical activity levels of humans living in the modern environment were much lower than that observed in free-ranging mammals, used as a model for primitive humans (16). Unfortunately, data on energy expenditure from physical activity in prior times are lacking and it is possible to lend support to this hypothesis only through estimations. Malina et al. (17) presented an estimated summary of physical activity levels (PALs) along our evolutionary past (Figure 1). Humans are biologically equipped to be physically active, however, cultural development allowed sedentary chances. Moreover, not only periods of prolonged inactivity but also how this inactivity time is spent is crucial in the burden of the sedentary lifestyle. Reduced energy expenditure deriving from decreased muscle activity is responsible for the increased health risk due to chair-seated postures (18). In this regard, Raichlen et al. studying the non-ambulatory time, observed that, with respect to the industrialized population, the Hazda (an African hunter-gatherer population) spent their resting time in "active" rest postures (19). Moreover, the authors showed that these postures require significantly higher energy levels for lower-limb muscle activation than chair sitting calculated through estimation in the percentage of walking (19). For instance, in the assisted squat posture, muscle activation of the soleus (right: 10.831; left: 10.883) was significantly higher compared to chair sitting (4.943). Again, the full squatting posture elicited higher levels of muscle activity compared with chair sitting for soleus (left: 8.395; right: 15.086 vs. left: 4.943; right: 5.754), vastus lateralis (left: 14.616; right: 29.800 vs. left: 5.927; right: 10.508), and tibialis anterior (33.239 vs. 3.742). Thus, despite the sedentary time in the Hadza population is not lower than in industrialized people, Hadzas showed low levels of biomarkers related to an increased risk of cardiovascular diseases (19).

NEAT, an important part of total daily energy expenditure

Levine (20) defined non-exercise activity thermogenesis (NEAT) as the physical activities other than volitional exercises, such as the activities of daily living, fidgeting, spontaneous muscle contraction, and maintaining posture when not recumbent. Together with resting energy

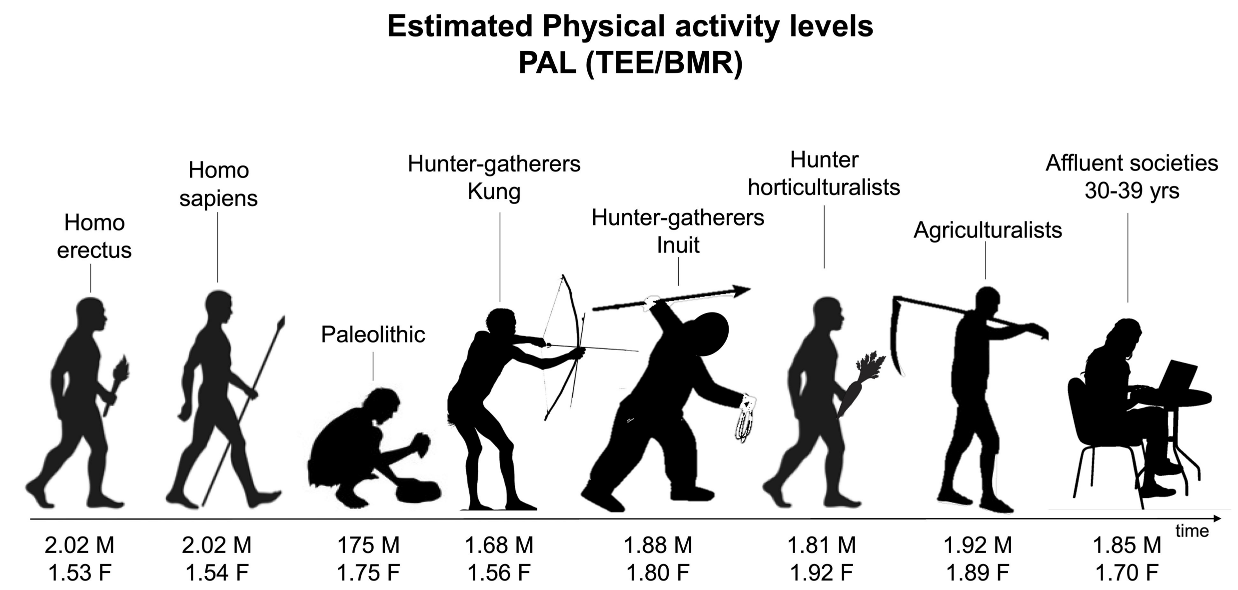

FIGURE 1
Estimated physical activity levels (PALs) for ancestors and modern populations. PAL = TEE/BMR (total energy expenditure/basal metabolic rate), see for details, Malina and Little (17).

expenditure, postprandial thermogenesis, and physical activity thermogenesis, NEAT composes the total daily EE. NEAT differentiates from physical activity and is defined as "any bodily movement produced by skeletal muscles that resulting in EE above the resting level," usually over 1.6 MET (21, 22). To better comprehend NEAT and its role in individuals with obesity, we can divide it into posture-related (e.g., standing, sitting, and lying) and movement-related thermogenesis (e.g., walking, occupation, and leisure time). In sedentary adults, EE deriving from NEAT helped to counteract weight gain during controlled overfeeding experiments (23). Von Loeffelholz (24) showed that NEAT could widely vary up to 2,000 kcal·day^{-1} between two individuals of similar size, lean body mass, and gender. The authors explained these differences with the interactions of several biological and environmental factors; indeed, it was given great importance to people's different occupations and leisure-time events. In a sedentary job, NEAT could range at a maximum of 700 kcal·day^{-1}, as average (24). These data confirmed those from Ravussin et al. (25), who used a human respiratory chamber to determine rates of EE over 24 h. They found that variability in the degree of spontaneous physical activity (range 100–800 kcal/d) could account for a large portion of daily EE (25). Among spontaneous movements or behaviors promoting NEAT, fidgeting has also been associated with weight loss across long periods of time (26). Fidgeting is defined as making continuous, small movements, typically with hands or feet, in a nervous or restless way, that is unnecessary to the ongoing task (27). These movements can occur while sitting or standing. An interesting study by Hagger-Johnson et al. (27) retrospectively examined the association between sitting time and mortality in almost 13,000 women from 1999 to 2002. They found that fidgeting minimizes the association between sitting time and mortality in the medium (5–6 h) and the high (7–17 h) fidgeting groups. Given the above, the employment of simple behaviors might contrast the negative consequences of time spent sitting, independently from the level of physical activity, hence, fidgeting appears to be sufficient to influence daily energy balance (28) with long-term health benefits, even to sedentary individuals. However, despite fidgeting representing a topic of interest for many researchers, measuring it with reliable markers is still an issue. When studying spontaneous physical activity, combining information from self-report and accelerometers (29, 30) together with the proper assessment of the subject's sitting position and specific limb movements appears to be necessary.

Levine suggested that the environmental factors promoting sedentary behavior affect differently obese and lean individuals; specifically, if subjects with obesity adopted the NEAT-enhanced behavior typical of their lean counterparts, they could expend an additional 350 kcal per day. With an unchanged energy intake, this could result in a weight loss of ∼15 kg over a year (31). On this point, small increments of NEAT could be the rationale to reach health benefits over a prolonged period. However, adults spend most of their days working (about one-third), and the work is surely becoming more sedentary (32). Understanding how much the occupational sedentary lifestyle count in reducing the total amount of time spent actively is the first step to directly program interventions in workplaces. Therefore, the purpose of this narrative review is to summarize the current state of the research regarding the “NEAT approach” to weight-gain prevention in work environments. Moreover, analyzing the variety of research strategies to increase NEAT at work, the review aims to point out questions, gaps, and openings.

Sedentary behaviors at work

From the second half of the previous century, there has been a shift toward occupations largely composed of desk-based behaviors. In the 1950s, Morris et al. already stated, “men in physically active jobs have a lower incidence of coronary (ischaemic) heart disease in middle-age than men in physically inactive jobs” (33). This trend has also been associated with population-level weight gain (34). Indeed, typical adult weight gain results from a daily positive energy balance of 15–50 kcal/day (35). This low amount of daily energy intake excess might not appear of clinical relevance and thus, its relevance for weight gain may be underestimated. The cumulative effect of very small daily weight gains is very likely to be a substantial contributor to the overall increase in body weight that frequently occurs during adulthood (36). Moreover, long periods of desk-based behavior have been linked to increased pain and musculoskeletal disorders. Specifically, Jensen et al. showed that jobs characterized by the highest level of repetitiveness (i.e., call center and data entry works) are associated with an increased rate of discomfort in the neck, shoulders, and upper extremities (37). In the scientific literature, several methods have been used to evaluate the level of physical activity at work, such as self-report (38), surveys (39), questionnaires (40), and motion sensors (41). For instance, Thorp et al. (42) conducted a study quantifying the sedentary working time using accelerometers in 193 employees. They concluded that working hours were mostly spent sedentary and that the working days were more sedentary and had less light-intensity activity than non-working days. However, a review proposed by Castillo-Retamal complained that there was a substantial inconsistency in assessing physical activity at work and that none of the studies considered the validity or reliability of these measures (22).

Strategies to increase NEAT at work

Technological development has addressed office ergonomics and, more in general, the environmental design toward a constant effort saving. This, inevitably, has led to a workload reduction and a consequent lower EE (43). Recently, different published researches suggest solutions to reverse increasing sitting time and encourage daily movement in the working scenario to reduce the risks connected to a sedentary lifestyle (20, 44, 45). New alternative workstations have been thought to increase total physical activity in sedentary workers and improve body composition (i.e., decreasing body fat) (46). The additional EE favored by alternative workstations should increase the NEAT and should be bearable for prolonged periods. However, dynamic workstations may carry limitations due to mental distraction that could affect work productivity or safety (45). For this reason, the design and engineering of alternative workstations should guarantee the normal execution of working tasks, indeed, workers risk finding themselves sitting on the fence between their NEAT increase and their working yield. For this reason, any modifications of the working scenario must carefully weigh the advantages and disadvantages of its ecological application. Following, we summarize the different methods to endorse EE in the working scenario. We reviewed the main evidence regarding new alternative workstations such as standing, walking workstations, seated pedal, and gymnastic balls to replace a standard office chair.

Standing workstation

It is well known that posture changes have chronic and acute relapses in many physiological variables such as metabolic rate, anti-gravitational muscle tone, and cardio-circulatory indexes (47–51). However, the actual query is when these changes, even significant, become relevant in terms of energy balance for weight gain prevention. On this topic, few controversial responses were observed. Indeed, some evidence demonstrated a greater EE while performing clerical work standing with respect to sitting (52). Speck et al. hypothesized that standing could increase the total daily EE over sitting by 384 kcal (i.e., 1,104 vs. 720 kcal). However, their experimental findings, using indirect calorimetry, demonstrated that full-time (8 h) standing workers did not gain the EE equivalent to an hour of daily moderate physical activity (53), while recommendations state that physical activity levels to prevent weight gain must be ≥1.6 times the basal metabolic rate (54). Again, Tudor-Locke et al. (55) strengthened the assumption that replacing sitting behaviors only with standing appears to be insufficient in terms of EE. Even though the focus should last on EE, other potential health benefits of standing than sitting position need to be acknowledged. For instance, Beers et al. found a significantly higher heart rate in standing than in seated posture during a word processing task (52). Thus, the standing posture could partially counterbalance the low physical activity associated with the seated position. An increased EE in the standing position due to higher muscle activation was also supposed. Available data showed higher muscle activation in the lumbopelvic region when maintaining erect postures compared to passive seated postures (56). Indeed, we demonstrated that anti-gravitational muscle tone increment in the standing posture is a major determinant of metabolic rate changes (57). In addition, Tikkanen et al. showed a higher thigh muscle activation during standing compared to sitting posture (58). However, possible disadvantages in maintaining a prolonged standing posture

10.3389/fpubh.2022.1024856

can occur. Epidemiological studies suggested that prolonged standing might be related to health problems such as venous insufficiency (59), decreased cognition or discomfort (60), and back pain (61). Occupational standing has been associated with elevated low back pain. Indeed, between 40 and 70% of the population who never had a low back injury are categorized as developing pain when exposed to a bout of static prolonged standing using self-reports (62, 63). On the other side, standing for >50% of a workday did not affect the pulse wave velocity of standing workers more than their seated counterparts, showing non-adverse effects on their arterial stiffness (64). Finally, subjective feeling of comfort, fatigue, and liking experienced during the standing posture is not a secondary topic (52) that can easily affect workers' productivity. Nowadays, there are no univocal guidelines to modulate sitting and standing times, as every person has dissimilar necessities and functional impairments (65). Thus, if sitting time can be harmful, standing time is not fully harmless.

Walking workstation

Among the activities recommended to increase NEAT, walking is one of the most feasible for almost all subjects. Thus, behavioral engineering and ergonomics studied different methods to increase walking, and consequently EE, in the workplace. For instance, many companies decided to remove e-mail or telephone for the correspondence between colleagues to stimulate walking or introduced a 10-min walking break during working hours. Straker et al. (43) well summarized the proposed solutions in three categories: equipment changes (e.g., walking to the printer on the second floor), task changes (e.g., workers do different working tasks in rotation), and organizational changes (e.g., information and sensitization activities for physical activity). Together with these NEAT-increasing solutions, walking workstations have also been developed through a treadmill placement at the workers' desk. The walking workstation consists of a setup that allows for walking slowly on a treadmill while working at a raised desk. In the late eighties, Edelson et al. already recommended walking on a treadmill to increase physical activity at work without a concurrent decrement in working performance (66). If activities with very low workloads, such as the aforementioned fidgeting, can increase by 20–40% EE over resting levels (28), walking can multiply basal EE (67). Indeed, Levine et al. estimated that walking at 1.6 km/h (e.g., quiet walking for shopping) doubles EE and that intentional walking at 3.2 to 4.8 km/h led to a doubling or tripling EE (68). Moreover, walking at 6.4 km/h has a MET level 5 times greater than sitting at rest (69). However, this topic deserves to be analyzed in a work context. Longitudinal studies investigated the long-term effects of a treadmill-desk program and showed a positive effect on anthropometry, body composition, blood lipids, and metabolic indexes (70–72). Walking workstations instead of standing workstations led to the greatest improvement in different physiological outcomes, including postprandial glucose and HDL cholesterol (73).

Besides, walking at a very slow speed of 1.7 km/h on a treadmill while working increased heart rate up to 15 bpm (74) and EE up to 119 kcal/h, as average (75) above the seated working condition. The reported walking EE is almost 2.7 times above the estimated EE in seated work (averaged at 72 kcal/h). For instance, full-time employment of treadmill workstations could utopianly lead to an EE of 4,800 kcal/day obviously without considering problems of tolerance, pleasure, or discomfort (55). It has been hypothesized that the daily use of a treadmill workstation for 2.5 h/day in subjects with obesity may lead to an estimated weight loss of 20 to 30 kg/year (75). However, Levine et al. (75) only prospectively estimated NEAT for weight loss starting from controlled research of short duration. Although the total daily amount of physical activity is positively affected by treadmill desks compared to standard chairs, the possible altered working performance is noteworthy to discuss. Research investigating this issue showed inconsistent results. More in detail, Thompson et al. (76) demonstrated that subjects using a walking workstation employed longer time in working tasks compared to sitting, while the accuracy in completing them remained unchanged. Conversely, other studies showed that exercising at moderate intensity had beneficial effects on task-speed solving, but not in its accuracy (77). Although the ideal walking velocity for letting the working performance unaffected is still under debate, results suggested 2.25 km/h for word processing tasks (78). Moreover, a systematic review suggested that a self-selected pace between 1.6 and 3.2 km/h is ideal for optimizing typing and mouse performance (73).

One of the issues related to walking workstations is that the continuous changes in the surrounding environments, acting forces, and sensory inputs could lead to a higher cognitive-motor interference due to increased information processing very similar to what occurs under dual-task conditions (79–81). Accordingly, Larson et al. (82) found no influence on executive and cognitive functions while working on a walking treadmill, even though fine motor skills and learning were negatively affected. These results were partially confirmed by Podrekar et al. (83) who showed a decreased working performance during walking activities, but not a worsening of cognitive functions (e.g., attention, learning, and memory). Thus, the hypothesis was that a higher familiarity with the device and its long-term employment and practice could have improved the worker's performance. Finally, since the several positive effects that walking workstations have demonstrated to produce on EE, additional studies are necessary to deepen the possible worsening of working performance and determine optimal walking speed. Moreover, although there is a relative abundance

TABLE 1 Summary of energy expenditure (kcal/min and Kcal/yr) derived from the employment of alternative workstations (i.e., seated, standing, seated pedal, and walking).

References	Workstation	EE (Kcal/min)	EE (Kcal/Yr)	Kg/Yr
Reiff et al. (107)	Seated	1.02	118483.20	16.93
Speck et al. (53)		1.30	151008.00	21.57
Swartz et al. (108)		1.46	169593.60	24.23
Carr et al. (86)		0.99	114998.40	16.43
Koepp et al. (84)		1.35	156816.00	22.40
Horswill et al. (45)		1.43	166108.80	23.73
Mean		1.26	146168.00	20.88
SD		0.20	23753.70	3.39
Reiff et al. (107)	Standing	1.36	157977.60	22.57
Straker et al. (74)		1.36	157977.60	22.57
Speck et al. (53)		1.29	149846.40	21.41
Cox et al. (109)		1.08	125452.80	17.92
Horswill et al. (45)		1.54	178886.40	25.56
Mean		1.33	154028.16	22.00
SD		0.17	19255.95	2.75
Carr et al. (86)	Seated Pedal	2.14	248582.40	35.51
Koepp et al. (84)		1.60	185856.00	26.55
Horswill et al. (45)		1.65	191664.00	27.38
Mean		1.80	208700.80	29.81
SD		0.30	34660.35	4.95
Levine et al. (75)	Walking	1.96	227673.60	32.52
Koepp et al. (71)		2.90	336864.00	48.12
Koepp et al. (84)		2.80	325248.00	46.46
Mean		2.55	296595.20	42.37
SD		0.52	59969.77	8.57

Moreover, considering that 1 kg of fat is approximately equivalent to 7,000 kcals, the kilograms of fat consumed over a year-long period are also reported.

of short-term evidence, longitudinal studies appear essential to strengthen the observed outcomes over the long-term application of walking workstations.

Seated pedal workstation

Standing or walking workstations force the employees to work in an unusual setting. Thus, an alternative method to defeat working sedentary behavior is to transform sitting into "active sitting" (84). The rationale is to promote NEAT while remaining in the most habitual seated position, averting an eventual decrease in working performance more likely in standing or walking workstations. Seated pedal workstations are easily manageable by workers who can alternate active pedaling to standard sitting, simply stopping leg movements (55). Peterman et al. (85) studied passive cycling (i.e., external motor moved subjects' legs) by considering how pedaling cadence (at 60 and 90 rpm) can influence EE and heart rate. During two-leg passive cycling, EE rates were significantly greater than rest for both 60 rpm (28%) and 90 rpm (49%). Heart rate showed no significant differences. Moreover, Carr et al. (86) showed that working at a seated active pedal workstation significantly increased EE (53.4%), heart rate (12%), and muscle activation of the biceps femoris (42.1%) and vastus lateralis (59.8%) over the sedentary workstation. The experimental trials were conducted at a pedaling cadence of 45 rpm, comparable to 2.25 km/h. Moreover, Horswill et al. (45) studied the HOVR device, a pendulum with two discs at the end that allows leg movement under the desk. When workers performed leg movements there was an increase in metabolic rate (by 17.6% and 7%) compared to sitting and standing, respectively. Studying the same HOVR device, Koepp et al. (84) found a significant increase (18%) in EE while using the under-the-table apparatus compared to the standard chair. However, the observed changes were much lower compared to a 1.6 km/h walking. Levine et al. found an increased EE in workers using an under-desk device for leg movement (98 ± 42 kcal/h) and a chair promoting fidgeting (89 ± 40 kcal/h) compared to the use of a standard chair (76 ± 31 kcal/h) (87).

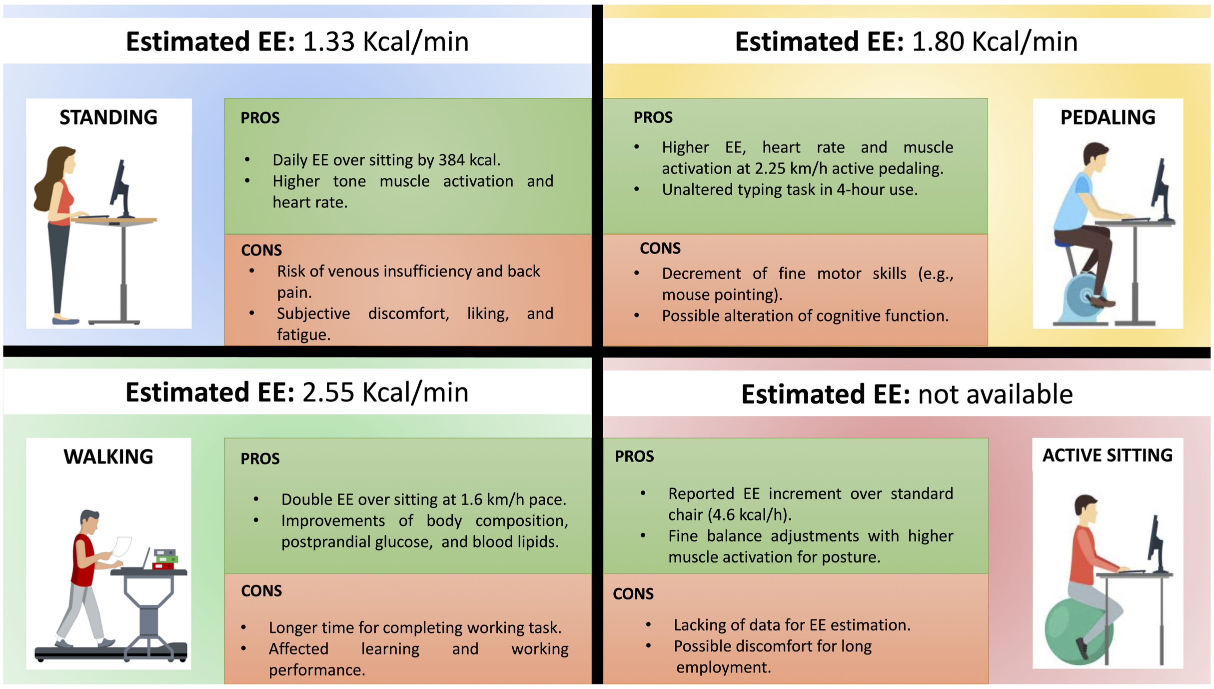

FIGURE 2
Alternative workstations. Summary of the main pros and cons of the standing, walking, pedaling, and gymball sitting workstations.

As before, the employment of pedal workstations cannot disregard the workers' tolerance and productivity. There was agreement among decrement of some finer motor tasks (i.e., mouse pointing, click time, and typing) using a pedal workstation compared to the standard chair. Besides, reported decrements in seated conditions (with or without pedaling) were surely lower than observed while walking (74). However, results were controversial on whether cognitive functions were altered (74) or not (86). Users' liking and perceptions on the choice of the most suitable workstation has certain effects on their working performance. Tardif et al. (88) tested users' experience through a questionnaire on using a pedal or a standing desk. They found a greater appreciation of the pedal desk over standing for its effective, useful, functional, convenient, and comfortable dimensions. During a standard 8-h working day, 97.6% of subjects reported that their typing proficiency could not be influenced by a 4-h employment of the pedal desk (89). Moreover, besides working productivity, the rates of compliance deserve attention. Indeed, a high number of hours and days of use are needed to improve health over long periods (90). On this point, even though workers reported the pedaling workstation as a feasible intervention, Carr et al. showed actual compliance of 61% over 20 days and 37.7% over 84 days (91). These studies suggest that workers may have used the devices primarily during work breaks and that further environmental modifications are necessary to encourage long-term use. Overall, findings from scientific literature globally suggested that seated pedal workstations offered a good balance between increased EE and affection for working performance. Indeed, it represents a tool to increase daily levels of NEAT, with a keen eye on work quality and workers' appreciation.

Gymnastic ball workstation

The employment of unstable devices such as gymnastic balls is a popular practice in athletic professional (92), recreational (93), and rehabilitation (94, 95) contexts. Several information channels frequently suggest gymnastic ball sitting (at work, home, libraries, and in many other environments), not always with scientific awareness (96). Indeed, gymnastic balls with respect to conventional chairs do not provide a stable base of support and thus may require a higher commitment to maintaining the body posture on top (97). Subjects are constantly constrained to find balance adjustments to maintain their posture (98). Thus, to preserve an adequate upright posture while sitting on the gymnastic ball, subjects should increase muscles' activation and experience increased heart rate, with a consequent higher metabolic rate (56, 99). In this regard, Haller (99) demonstrated that EE was significantly higher (5.6%) while sitting on a gymnastic ball than in a standard chair. These findings are very similar to those in a later study that found a higher EE (6%) when working on the gymnastic ball than while sitting on the standard chair. EE registered in subjects seated on the gymnastic ball was also very similar to that observed during the standing position (52). These EE increments produced an estimated additional net of 32 kcal/day when calculated over a full-time working day (55). As aforementioned, even though small, this extra amount of EE could successfully influence weight gain prevention (35). Although gymnastic ball application needs further insights to deepen its role on EE, other aspects of "active sitting" require to be acknowledged. For instance, gymnastic ball employment in workplaces could improve posture and muscle activation (100). However, controversial results can be found in the scientific literature.

Gregory et al. investigated trunk muscle activation and posture, comparing a standard office chair to a gymnastic ball. Among the registered muscles (i.e., thoracic and lumbar erector spinae, rectus abdominis, and external oblique), only the thoracic erector spinae was found to increase muscle activation (101). Similarly, Kingma et al. (102) found greater trunk motion (33%) and variation in lumbar electromyography activity (66%) in subjects seated on a gymnastic ball compared to an office chair. Conversely, other authors showed no difference in trunk muscle activation when users sat on a gymnastic ball compared to a stable stool (103). Even though some authors showed an increased self-perceived posture (100), long-term use of gymnastic balls could be unproductive if accompanied by discomfort (101–103). Other researchers suggested that trunk muscle strength could positively influence the experienced discomfort, often related to low back pain (104, 105). However, it is hard to infer if an increase in muscle strength could be due to the working employment of the gymnastic ball. Finally, workers can easily adopt gymnastic balls to obtain small behavioral changes and reduce sedentary negative behaviors. However, understanding whether the advantages of using a gymnastic ball may offset the disadvantages is still an open question, especially over long periods.

Conclusion

The NEAT approach in the workplace could contribute to consciously increasing activity in sedentary workers. Surely, structured exercise programs and an out-of-work active lifestyle represent the best solutions to counteract epidemic obesity. However, many people scarcely spent their leisure time doing physical activity due to other competing personal, domestic, and civic obligations. Indeed, as the working day takes up a large amount of the daytime, the application of alternative workstations will assist in the maintenance of a healthy weight. Theoretical frameworks suggested that NEAT is impacted by the environment (26). As such, using alternative workstations in an 8-h working day might be enough to slow down epidemic obesity. Moreover, Hill et al. showed that the median of the distribution of estimated energy accumulation is 15 kcal/day, and 90% of the population showed a surplus of 50 or fewer kcal/day. This means that an intervention that aims at reducing energy excess by 50 kcal/day could offset weight gain in about 90% of the population (106). Table 1 summarizes the EE (kcal/min) of the above-analyzed alternative workstations. As an assumption, considering that 1 kg of fat is equivalent to ∼7,000 kcals, the kilograms of fat consumed over a year are reported for each workstation. Thus, an increase in EE (Table 1) was estimated for standing (∼1.1 kg/yr), seated pedal (∼9 kg/yr), and walking (∼21.5 kg/yr) workstations over the standard seated position. We calculated these values through simplistic estimations considering 8 h of a working day, 22 working days in a month, and 11 working months in a year. Unfortunately, the only evidence about EE on the gymnastic ball workstation (52) makes hard the comparison with the other alternative workstations. As a result, considering the potential benefits associated with unstable devices (56, 99), this lack claims updated scientific evidence. The reported increment (4.1 Kcal/h) over the standard seated position is not sufficient to estimate EE over a year-long period (52). To date, the scientific literature deeply studying alternative workstations is still novel and fragmentary. About this, Figure 2 summarizes the pros and cons of new alternative workstations to point out their strengths and shortcomings. In conclusion, alternative workstations are ideally relevant opportunities for acting on the reduced EE related to sedentary works. However, proposals of NEAT approaches in the workplace must be optimized in compliance with worker's devices acceptance, and the safeguard of the working tasks.

Author contributions

AR, GM, and AP contributed to the literature review and classification. AR and AP wrote the first draft of the manuscript. GM and AP contributed to the manuscript revision and approved the submitted version. All authors contributed to the article and approved the submitted version.

Conflict of interest

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

The reviewer AB declared a past collaboration with the authors to the handling editor.

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.

References

1. Bowden S, Offer A. Household appliances and the use of time: the United States and Britain since the 1920s. *Econ Hist Rev.* (1994) 47:725. doi: 10.2307/2597714

2. Seale JL, Thorp JW, Conway JM, Rumpler W V, Haberman KJ. Energy expenditure and fluid production in hyperbaric He-O2 environments using doubly labeled water. *Undersea Hyperb Med.* (1994) 21:199–208.

3. Owen N, Salmon J, Koohsari MJ, Turrell G, Giles-Corti B. Sedentary behaviour and health: mapping environmental and social contexts to underpin chronic disease prevention. *Br J Sports Med.* (2014) 48:174–7. doi: 10.1136/bjsports-2013-093107

4. Manson JAE, Skerrett PJ, Greenland P, VanItallie TB. The escalating pandemics of obesity and sedentary lifestyle. A call to action for clinicians. *Arch Intern Med.* (2004) 164:249–58. doi: 10.1001/archinte.164.3.249

5. WHO. *Obesity and Overweight*. (2016). Available online at: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight (accessed January 28, 2022).

6. Prentice AM, Jebb SA. Obesity in Britain: gluttony or sloth? *BMJ.* (1995) 311:437–9. doi: 10.1136/bmj.311.7002.437

7. Ekelund U, Steene-Johannessen J, Brown WJ, Fagerland MW, Owen N, Powell KE, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *Lancet.* (2016) 388:1302–10. doi: 10.1016/S0140-6736(16)30370-1

8. Ding D, Lawson KD, Kolbe-Alexander TL, Finkelstein EA, Katzmarzyk PT, van Mechelen W, et al. The economic burden of physical inactivity: a global analysis of major non-communicable diseases. *Lancet.* (2016) 388:1311–24. doi: 10.1016/S0140-6736(16)30383-X

9. Stockwell S, Trott M, Tully M, Shin J, Barnett Y, Butler L, et al. Changes in physical activity and sedentary behaviours from before to during the COVID-19 pandemic lockdown: a systematic review. *BMJ Open Sport Exerc Med.* (2021) 7: e000960. doi: 10.1136/bmjsem-2020-000960

10. Gardiner PA, Eakin EG, Healy GN, Owen N. Feasibility of reducing older adults' sedentary time. *Am J Prev Med.* (2011) 41:174–7. doi: 10.1016/j.amepre.2011.03.020

11. Larsen RN, Kingwell BA, Sethi P, Cerin E, Owen N, Dunstan DW. Breaking up prolonged sitting reduces resting blood pressure in overweight/obese adults. *Nutr Metab Cardiovasc Dis.* (2014) 24:976–82. doi: 10.1016/j.numecd.2014.04.011

12. Brocklebank LA, Andrews RC, Page A, Falconer CL, Leary S, Cooper A. The acute effects of breaking up seated office work with standing or light-intensity walking on interstitial glucose concentration: a randomized crossover trial. *J Phys Act Health.* (2017) 14:617–25. doi: 10.1123/jpah.2016-0366

13. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR, Montoye HJ, Sallis JF, et al. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc.* (1993) 25:71–4. doi: 10.1249/00005768-199301000-00011

14. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR, Tudor-Locke C, et al. 2011 Compendium of physical activities: a second update of codes and MET values. *Med Sci Sports Exerc.* (2011) 43:1575–81. doi: 10.1249/MSS.0b013e31821ece12

15. Garland T, Schutz H, Chappell MA, Keeney BK, Meek TH, Copes LE, et al. The biological control of voluntary exercise, spontaneous physical activity and daily energy expenditure in relation to obesity: human and rodent perspectives. *J Exp Biol.* (2011) 214:206–29. doi: 10.1242/jeb.048397

16. Hayes M, Chustek M, Heshka S, Wang Z, Pietrobelli A, Heymsfield SB. Low physical activity levels of modern Homo sapiens among free-ranging mammals. *Int J Obes.* (2004) 29:151–156. doi: 10.1038/sj.ijo.0802842

17. Malina RM, Little BB. Physical activity: the present in the context of the past. *Am J Hum Biol.* (2008) 20:373–91. doi: 10.1002/ajhb.20772

18. Gao Y, Silvennoinen M, Pesola AJ, Kainulainen H, Cronin NJ, Finni T. Acute metabolic response, energy expenditure, and EMG activity in sitting and standing. *Med Sci Sports Exerc.* (2017) 49:1927–34. doi: 10.1249/MSS.0000000000001305

19. Raichlen DA, Pontzer H, Zderic TW, Harris JA, Mabulla AZP, Hamilton MT, et al. Sitting, squatting, and the evolutionary biology of human inactivity. *Proc Natl Acad Sci USA.* (2020) 117:7115–21. doi: 10.1073/pnas.1911868117

20. Levine JA, Eberhardt NL, Jensen MD. Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science (80-).* (1999) 283:212–4. doi: 10.1126/science.283.5399.212

21. Caspersen CJ, Powell KE, Christenson G. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Heal Rep.* (1985) 100:126–31.

22. Castillo-Retamal M, Hinckson EA. Measuring physical activity and sedentary behaviour at work: a review. *Work.* (2011) 40:345–3547. doi: 10.3233/WOR-2011-1246

23. Levine JA, Eberhardt NL, Jensen MD, Jensen M. Leptin responses to overfeeding: relationship with body fat and nonexercise activity thermogenesis. *J Clin Endocrinol Metab.* (1999) 84:2751–4. doi: 10.1210/jc.84.8.2751

24. von Loeffelholz C, Birkenfeld A. *The Role of Non-exercise Activity Thermogenesis in Human Obesity*. MDText.com, Inc. (2014). Available online at: https://www.ncbi.nlm.nih.gov/sites/books/NBK279077/ (accessed January 28, 2022).

25. Ravussin E, Lillioja S, Anderson TE, Christin L, Bogardus C. Determinants of 24-hour energy expenditure in man. Methods and results using a respiratory chamber. *J Clin Invest.* (1986) 78:1568–78. doi: 10.1172/JCI112749

26. Levine JA, Kotz CM. NEAT–non-exercise activity thermogenesis—egocentric & geocentric environmental factors vs. biological regulation. *Acta Physiol Scand.* (2005) 184:309–18. doi: 10.1111/j.1365-201X.2005.01467.x

27. Hagger-Johnson G, Gow AJ, Burley V, Greenwood D, Cade JE. Sitting time, fidgeting, and all-cause mortality in the UK women's cohort study. *Am J Prev Med.* (2016) 50:154–60. doi: 10.1016/j.amepre.2015.06.025

28. Levine JA, Schleusner SJ, Jensen MD. Energy expenditure of nonexercise activity. *Am J Clin Nutr.* (2000) 72:1451–4. doi: 10.1093/ajcn/72.6.1451

29. Sabia S, Van Hees VT, Shipley MJ, Trenell MI, Hagger-Johnson G, Elbaz A, et al. Association between questionnaire-and accelerometer-assessed physical activity: the role of sociodemographic factors. *Am J Epidemiol.* (2014) 179:781–90. doi: 10.1093/aje/kwt330

30. Scholes S, Coombs N, Pedisic Z, Mindell JS, Bauman A, Rowlands A V, et al. Age- and sex-specific criterion validity of the health survey for England physical activity and sedentary behavior assessment questionnaire as compared with accelerometry. *Am J Epidemiol.* (2014) 179:1493–502. doi: 10.1093/aje/kwu087

31. Levine JA, Lanningham-Foster LM, McCrady SK, Krizan AC, Olson LR, Kane PH, et al. Interindividual variation in posture allocation: possible role in human obesity. *Science.* (2005) 307:584–6. doi: 10.1126/science.1106561

32. Smith MJ, Conway FT, Karsh BT. Occupational stress in human computer interaction. *Ind Health.* (1999) 37:157–73. doi: 10.2486/indhealth.37.157

33. Saturday L, Morris JN, And DPH, Crawford MD. Coronary heart disease and physical activity of work. *Br Med J.* (1958) 2:1485. doi: 10.1136/bmj.2.5111.1485

34. Church TS, Thomas DM, Tudor-Locke C, Katzmarzyk PT, Earnest CP, Rodarte RQ, et al. Trends over 5 decades in US occupation-related physical activity and their associations with obesity. *PLoS ONE.* (2011) 6:e19657. doi: 10.1371/journal.pone.0019657

35. Hill JO, Wyatt HR, Peters JC. Energy balance and obesity. *Circulation.* (2012) 126:126–32. doi: 10.1161/CIRCULATIONAHA.111.087213

36. Yanovski JA, Yanovski SZ, Sovik KN, Nguyen TT, O'Neil PM, Sebring NG, et al. Prospective study of holiday weight gain. *N Engl J Med.* (2000) 342:861–7. doi: 10.1056/NEJM200003233421206

37. Jensen C, Finsen L, Søgaard K, Christensen H. Musculoskeletal symptoms and duration of computer and mouse use. *Int J Ind Ergon.* (2002) 30:265–75. doi: 10.1016/S0169-8141(02)00130-0

38. Sallis JF, Saelens BE. Assessment of physical activity by self-report: status, limitations, and future directions. *Res Q Exerc Sport.* (2000) 71:1–14. doi: 10.1080/02701367.2000.11082780

39. Guthold R, Stevens GA, Riley LM, Bull FC. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1·9 million participants. *Lancet Glob Heal.* (2018) 6:e1077–86. doi: 10.1016/S2214-109X(18)30357-7

40. Hidding LM, Chinapaw MJM, van Poppel MNM, Mokkink LB, Altenburg TM. An updated systematic review of childhood physical activity questionnaires. *Sport Med.* (2018) 48:2797–842. doi: 10.1007/s40279-018-0987-0

41. Voicu RA, Dobre C, Bajenaru L, Ciobanu RI. Human physical activity recognition using smartphone sensors. *Sensors.* (2019) 19:458. doi: 10.3390/s19030458

42. Thorp AA, Healy GN, Winkler E, Clark BK, Gardiner PA, Owen N, et al. Prolonged sedentary time and physical activity in workplace and non-work contexts: a cross-sectional study of office, customer service and call centre employees. *Int J Behav Nutr Phys Act.* (2012) 9:1–9 doi: 10.1186/1479-5868-9-128

43. Straker L, Mathiassen SE. Increased physical work loads in modern work—a necessity for better health and performance? *Ergonomics.* (2009) 52:1215–25. doi: 10.1080/00140130903039101

44. Levine JA. Health-chair reform: your chair: comfortable but deadly. *Diabetes.* (2010) 59:2715–6. doi: 10.2337/db10-1042

45. Horswill CA, Scott HM, Voorhees DM. Effect of a novel workstation device on promoting non-exercise activity thermogenesis (NEAT). *Work.* (2017) 58:447–54. doi: 10.3233/WOR-172640

46. Malaeb S, Perez-Leighton CE, Noble EE, Billington C. A "NEAT" approach to obesity prevention in the modern work environment. *Workplace Health Saf.* (2019) 67:102–10. doi: 10.1177/2165079918790980

47. Amorim PRS, Byrne NM, Hills AP. Combined effect of body position, apparatus and distraction on children's resting metabolic rate. *Int J Pediatr Obes.* (2007) 2:249–56. doi: 10.1080/17477160701453466

48. Chang AT, Boots RJ, Brown MG, Paratz JD, Hodges PW. Ventilatory changes following head-up tilt and standing in healthy subjects. *Eur J Appl Physiol.* (2005) 95:409–17. doi: 10.1007/s00421-005-0019-2

49. Jones AYM, Dean E. Body position change and its effect on hemodynamic and metabolic status. *Hear Lung J Acute Crit Care.* (2004) 33:281–90. doi: 10.1016/j.hrtlng.2004.04.004

50. Terkelsen KE, Clark AL, Hillis WS. Ventilatory response to erect and supine exercise. *Med Sci Sports Exerc.* (1999) 31:1429–32. doi: 10.1097/00005768-199910000-00011

51. Weissman C, Askanazi J, Rosenbaum SH, Hyman AI, Milic-Emili J, Kinney JM. The effects of posture on the metabolic and ventilatory response to low level steady state exercise. *Clin Sci.* (1986) 71:553–8. doi: 10.1042/cs0710553

52. Beers EA, Roemmich JN, Epstein LH, Horvath PJ. Increasing passive energy expenditure during clerical work. *Eur J Appl Physiol.* (2008) 103:353–60. doi: 10.1007/s00421-008-0713-y

53. Speck RM, Schmitz KH. Energy expenditure comparison: a pilot study of standing instead of sitting at work for obesity prevention. *Prev Med (Baltim).* (2011) 52:283–4. doi: 10.1016/j.ypmed.2011.02.002

54. Brooks GA, Butte NF, Rand WM, Flatt JP, Caballero B. Chronicle of the Institute of Medicine physical activity recommendation: how a physical activity recommendation came to be among dietary recommendations. *Am J Clin Nutr.* (2004) 79: 921S—30S. doi: 10.1093/ajcn/79.5.921S

55. Tudor-Locke C, Schuna JM, Frensham LJ, Proenca M. Changing the way we work: elevating energy expenditure with workstation alternatives. *Int J Obes.* (2014) 38:755–65. doi: 10.1038/ijo.2013.223

56. O'Sullivan PB, Grahamslaw KM, Kendell M, Lapenskie SC, Möller NE, Richards KV. The effect of different standing and sitting postures on trunk muscle activity in a pain-free population. *Spine.* (2002) 27:1238–44. doi: 10.1097/00007632-200206010-00019

57. Rubini A, Monte D, Catena V. Effects of the pneumoperitoneum and Trendelenburg position on respiratory mechanics in the rats by the end-inflation occlusion method. *Ann Thorac Med.* (2012) 7:205. doi: 10.4103/1817-1737.102168

58. Tikkanen O, Haakana P, Pesola AJ, Häkkinen K, Rantalainen T, Havu M, et al. Muscle activity and inactivity periods during normal daily life. *PLoS ONE.* (2013) 8:e52228. doi: 10.1371/journal.pone.0052228

59. Łastowiecka-Moras E. Standing and sitting postures at work and symptoms of venous insufficiency- results from questionnaires and a Doppler ultrasound study. *Int J Occup Saf Ergon.* (2021) 27:963–9. doi: 10.1080/10803548.2020.1834232

60. Baker R, Coenen P, Howie E, Lee J, Williamson A, Straker L, et al. detailed description of the short-term musculoskeletal and cognitive effects of prolonged standing for office computer work. *Ergonomics.* (2018) 61:877–90. doi: 10.1080/00140139.2017.1420825

61. Macfarlane GJ, Thomas E, Papageorgiou AC, Croft PR, Jayson MIV, Silman AJ. Employment and physical work activities as predictors of future low back pain. *Spine.* (1997) 22:1143–9. doi: 10.1097/00007632-199705150-00015

62. Marshall PWM, Patel H, Callaghan JP. Gluteus medius strength, endurance, and co-activation in the development of low back pain during prolonged standing. *Hum Mov Sci.* (2011) 30:63–73. doi: 10.1016/j.humov.2010.08.017

63. Gallagher KM, Campbell T, Callaghan JP. The influence of a seated break on prolonged standing induced low back pain development. *Ergonomics*. (2014) 57:555–562. doi: 10.1080/00140139.2014.893027

64. Greenlund IM, Suriano PE, Elmer SJ, Carter JR, Durocher JJ. Chronic standing desk use and arterial stiffness. *J Phys Act Heal.* (2019) 16:1022–8. doi: 10.1123/jpah.2018-0668

65. Mula A. Ergonomics and the standing desk. *Work.* (2018) 60:171–4. doi: 10.3233/WOR-182736

66. Edelson N, Danoffz J. Walking on an electric treadmill while performing VDT office work. *ACM Sigchi Bull.* (1989) 21:72–7. doi: 10.1145/67880.67890

67. Haymes EM, Byrnes WC. Walking and running energy expenditure estimated by caltrac and indirect calorimetry. *Med Sci Sports Exerc.* (1993) 25:1365–9. doi: 10.1249/00005768-199312000-00008

68. Levine JA. Non-exercise activity thermogenesis (NEAT). *Best Pract Res Clin Endocrinol Metab.* (2002) 16:679–702. doi: 10.1053/beem.2002.0227

69. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc.* (2000) 32:S498–504. doi: 10.1097/00005768-200009001-00009

70. John D, Thompson DL, Raynor H, Bielak K, Rider B, Bassett DR. Treadmill workstations: a worksite physical activity intervention in overweight and obese office workers. *J Phys Act Heal.* (2011) 8:1034–43. doi: 10.1123/jpah.8.8.1034

71. Koepp GA, Manohar CU, McCrady-Spitzer SK, Ben-Ner A, Hamann DJ, Runge CF, et al. Treadmill desks: a 1-year prospective trial. *Obesity.* (2013) 21:705–11. doi: 10.1002/oby.20121

72. Schuna JM, Swift DL, Hendrick CA, Duet MT, Johnson WD, Martin CK, et al. Evaluation of a workplace treadmill desk intervention: a randomized controlled trial. *J Occup Environ Med.* (2014) 56:1266–76. doi: 10.1097/JOM.0000000000000336

73. MacEwen BT, MacDonald DJ, Burr JF. A systematic review of standing and treadmill desks in the workplace. *Prev Med.* (2015) 70:50–8. doi: 10.1016/j.ypmed.2014.11.011

74. Straker L, Levine J, Campbell A. The effects of walking and cycling computer workstations on keyboard and mouse performance. *Hum Factors.* (2009) 51:831–44. doi: 10.1177/0018720810362079

75. Levine JA, Miller JM. The energy expenditure of using a "walk-and-work" desk for office workers with obesity. *Br J Sports Med.* (2007) 41:558–61. doi: 10.1136/bjsm.2006.032755

76. Thompson WG, Levine JA. Productivity of transcriptionists using a treadmill desk. *Work.* (2011) 40:473–7. doi: 10.3233/WOR-2011-1258

77. McMorris T, Hale BJ. Differential effects of differing intensities of acute exercise on speed and accuracy of cognition: a meta-analytical investigation. *Brain Cogn.* (2012) 80:338–51. doi: 10.1016/j.bandc.2012.09.001

78. Funk RE, Taylor ML, Creekmur CC, Ohlinger CM, Cox RH, Berg WP. Effect of walking speed on typing performance using an active workstation. *Percept Mot Skills.* (2012) 115:309–18. doi: 10.2466/06.23.26.PMS.115.4.309-318

79. Takakusaki K, Takahashi M, Obara K, Chiba R. Neural substrates involved in the control of posture. *Adv Robot.* (2017) 31:2–23. doi: 10.1080/01691864.2016.1252690

80. Ghai S, Ghai I, Effenberg AO. Effects of dual tasks and dual-task training on postural stability: a systematic review and meta-analysis. *Clin Interv Aging.* (2017) 12:557–77. doi: 10.2147/CIA.S125201

81. Rizzato A, Paoli A, Andretta M, Vidorin F, Marcolin G. Are static and dynamic postural balance assessments two sides of the same coin? A cross-sectional study in the older adults. *Front Physiol.* (2021) 12:939. doi: 10.3389/fphys.2021.681370

82. Larson MJ, LeCheminant JD, Carbine K, Hill KR, Christenson E, Masterson T, et al. Slow walking on a treadmill desk does not negatively affect executive abilities: an examination of cognitive control, conflict adaptation, response inhibition, and post-error slowing. *Front Psychol.* (2015) 6:723. doi: 10.3389/fpsyg.2015.00723

83. Podrekar N, Kozinc Ž, Šarabon N. The effects of cycle and treadmill desks on work performance and cognitive function in sedentary workers: a review and meta-analysis. *Work.* (2020) 65:537–45. doi: 10.3233/WOR-203108

84. Koepp GA, Moore G, Levine JA. An under-the-table leg-movement apparatus and changes in energy expenditure. *Front Physiol.* (2017) 8:318. doi: 10.3389/fphys.2017.00318

85. Peterman JE, Kram R, Byrnes WC. Factors affecting the increased energy expenditure during passive cycling. *Eur J Appl Physiol.* (2012) 112:3341–8. doi: 10.1007/s00421-012-2325-9

86. Carr LJ, Maeda H, Luther B, Rider P, Tucker SJ, Leonhard C. Acceptability and effects of a seated active workstation during sedentary work: a proof of concept study. *Int J Work Heal Manag.* (2014) 7:2–15. doi: 10.1108/IJWHM-03-2013-0008

87. Koepp GA, Moore GK, Levine JA. Chair-based fidgeting and energy expenditure. *BMJ Open Sport Exerc Med.* (2016) 2:e000152. doi: 10.1136/bmjsem-2016-000152

88. Tardif CB, Cantin M, Sénécal S, Léger PM, Labonté-Lemoyne É, Begon M, et al. Implementation of active workstations in university libraries—A comparison of portable pedal exercise machines and standing desks. *Int J Environ Res Public Health.* (2018) 15:1242. doi: 10.3390/ijerph15061242

89. Proença M, Schuna JM, Barreira T V, Hsia DS, Pitta F, Tudor-Locke C, et al. Worker acceptability of the Pennington Pedal Desk^{TM} occupational workstation alternative. *Work.* (2018) 60:499–506. doi: 10.3233/WOR-182753

90. Carr LJ, Leonhard C, Tucker S, Fethke N, Benzo R, Gerr F. Total worker health intervention increases activity of sedentary workers. *Am J Prev Med.* (2016) 50:9–17. doi: 10.1016/j.amepre.2015.06.022

91. Carr LJ, Karvinen K, Peavler M, Smith R, Cangelosi K. Multicomponent intervention to reduce daily sedentary time: a randomised controlled trial. *BMJ Open.* (2013) 3:e003261. doi: 10.1136/bmjopen-2013-003261

92. Reed CA, Ford KR, Myer GD, Hewett TE. The effects of isolated and integrated 'core stability' training on athletic performance measures. *Sport Med.* (2012) 42:697–706. doi: 10.1007/BF03262289

93. Marshall PW, Murphy BA. Core stability exercises on and off a Swiss ball. *Arch Phys Med Rehabil.* (2005) 86:242–9. doi: 10.1016/j.apmr.2004.05.004

94. Tsaklis P, Malliaropoulos N, Mendiguchia J, Korakakis V, Tsapralis K, Pyne D, et al. Muscle and intensity based hamstring exercise classification in elite female track and field athletes: implications for exercise selection during rehabilitation. Open access. *J Sport Med.* (2015) 6:209–17. doi: 10.2147/OAJSM.S79189

95. Marques J, Botelho S, Pereira LC, Lanza AH, Amorim CF, Palma P, et al. Pelvic floor muscle training program increases muscular contractility during first pregnancy and postpartum: electromyographic study. *Neurourol Urodyn.* (2013) 32:998–1003. doi: 10.1002/nau.22346

96. Lowe BD, Swanson NG, Hudock SD, Lotz WG. Unstable sitting in the workplace-are there physical activity benefits? *Am J Heal Promot.* (2015) 29:207–9. doi: 10.4278/ajhp.140331-CIT-127

97. Hildenbrand K, Noble L. Abdominal muscle activity while performing trunk-flexion exercises using the Ab Roller, ABslide, FitBall, and conventionally performed trunk curls. *J Athl Train.* (2004) 39:37–43.

98. Rizzato A, Paoli A, Marcolin G. Different gymnastic balls affect postural balance rather than core-muscle activation: a preliminary study. *Appl Sci.* (2021) 11:1337. doi: 10.3390/app11031337

99. Haller J, Roberts D, Freedson P. Increasing energy expenditure during sedentary activity. *Am College Sports Med Ann Meet.* (2006). 38:S367. doi: 10.1249/00005768-200605001-02430

100. Schult TM, Awosika ER, Schmunk SK, Hodgson MJ, Heymach BL, Parker CD. Sitting on stability balls: Biomechanics evaluation in a workplace setting. *J Occup Environ Hyg.* (2013) 10:55–63. doi: 10.1080/15459624.2012.748324

101. Gregory DE, Dunk NM, Callaghan JP. Stability ball vs. office chair: comparison of muscle activation and lumbar spine posture during prolonged sitting. *Hum Factors.* (2006) 48:142–53. doi: 10.1518/001872006776412243

102. Kingma I, van Dieën JH. Static and dynamic postural loadings during computer work in females: sitting on an office chair vs. sitting on an exercise ball. *Appl Ergon.* (2009) 40:199–205. doi: 10.1016/j.apergo.2008.04.004

103. McGill SM, Kavcic NS, Harvey E. Sitting on a chair or an exercise ball: Various perspectives to guide decision making. *Clin Biomech.* (2006) 21:353–60. doi: 10.1016/j.clinbiomech.2005.11.006

104. Ashmen KJ, Buz Swanik C, Lephart SM. Strength and flexibility characteristics of athletes with chronic low-back pain. *J Sport Rehabil.* (1996) 5:275–86. doi: 10.1123/jsr.5.4.275

105. Lee JH, Ooi Y, Nakamura K. Measurement of muscle strength of the trunk and the lower extremities in subjects with history of low back pain. *Spine.* (1995) 20:1994–1996. doi: 10.1097/00007632-199509150-00006

106. Hill JO, Wyatt HR, Reed GW, Peters JC. Obesity and the environment: where do we go from here? *Science.* (2003) 299:853–5. doi: 10.1126/science.1079857

107. Reiff C, Marlatt K, Dengel DR. Difference in caloric expenditure in sitting versus standing desks. *J Phys Act Health.* (2012) 9:1009-11. doi: 10.1123/jpah.9.7.1009

108. Swartz AM, Squires L, Strath SJ. Energy expenditure of interruptions to sedentary behavior. *Int J Behav Nutr Phys Act.* (2011) 8:69–75. doi: 10.1186/1479-5868-8-69

109. Cox RH, Guth J, Siekemeyer L, Kellems B, Brehm SB, Ohlinger CM. Metabolic cost and speech quality while using an active workstation. *J Phys Act Health.* (2011) 8:332–9. doi: 10.1123/jpah.8.3.332