



OPEN ACCESS

EDITED BY

Yufeng Zhang,
Tianjin Medical University, China

REVIEWED BY

Lin Wang,
Wuhan University of Technology, China
Liang Tan,
Gdansk University of Physical Education and
Sport, Poland

*CORRESPONDENCE

Xiaoqiang Wang
✉ wangxiaoqiang_001@126.com

[†]These authors have contributed equally to
this work

RECEIVED 20 March 2025

ACCEPTED 01 September 2025

PUBLISHED 15 September 2025

CITATION

Zhang W, Li X, He Q and Wang X (2025)
Effects of exercise on bone metabolism in
postmenopausal women: a systematic
review and meta-analysis of randomized
controlled trials.
Front. Endocrinol. 16:1597046.
doi: 10.3389/fendo.2025.1597046

COPYRIGHT

© 2025 Zhang, Li, He and Wang. This is an
open-access article distributed under the terms
of the [Creative Commons Attribution License](#)
(CC BY). The use, distribution or reproduction
in other forums is permitted, provided the
original author(s) and the copyright owner(s)
are credited and that the original publication
in this journal is cited, in accordance with
accepted academic practice. No use,
distribution or reproduction is permitted
which does not comply with these terms.

Effects of exercise on bone metabolism in postmenopausal women: a systematic review and meta-analysis of randomized controlled trials

Wenhua Zhang^{1†}, Xun Li^{2†}, Qiang He³ and Xiaoqiang Wang^{2*}

¹School of Graduate Education, Shandong Sport University, Jinan, Shandong, China, ²School of Sport and Health, Shandong Sport University, Jinan, Shandong, China, ³School of Physical Education, Shandong University, Jinan, Shandong, China

Objective: To assess the impact of exercise on bone metabolism in postmenopausal women through meta-analysis, and to offer evidence-based guidance for preventing and managing osteoporosis in this population.

Methods: We searched PubMed, Embase, and other databases using keywords such as “exercise,” “postmenopausal women,” and “bone metabolism” to identify randomized controlled trials published up to 2024 on the effect of exercise on bone metabolism in postmenopausal women. Studies were selected according to predefined inclusion and exclusion criteria. Data were analyzed using Review Manager 5.4 and Stata17. Study quality was assessed with the Cochrane risk-of-bias tool. Effect sizes were pooled as standardized mean differences (SMDs) with 95% confidence intervals (CIs), and heterogeneity was evaluated with the I^2 statistic. A fixed-effects model was used when $I^2 \leq 50\%$; otherwise, a random-effects model was applied. The overall evidence certainty was rated using the Grading of recommendations assessment, development, and evaluation (GRADE) system.

Results: A meta-analysis of 24 studies (1067 subjects total) showed that exercise significantly elevated the levels of alkaline phosphatase (ALP) (SMD = 0.49, 95% CI: 0.21–0.77, $P = 0.0006$), N-terminal propeptide of type I procollagen (P1NP) (SMD = 0.62, 95% CI: 0.24 to 1.01, $P = 0.002$) and osteocalcin (OC) (SMD = 0.21, 95% CI: 0.05 to 0.37, $P = 0.01$); exercise significantly reduced the levels of parathyroid hormone (PTH) (SMD = -0.51, 95% CI: -0.77 to -0.25, $P = 0.0001$) and type I collagen cross-linked C-terminal peptide (CTX) (SMD = -0.32, 95% CI: -0.51 to -0.12, $P = 0.001$). Subgroup analyses showed that aerobic exercise (SMD = -0.35, 95% CI: -0.65 to -0.06, $P = 0.02$) significantly reduced CTX levels, while both aerobic exercise (SMD = 0.23, 95% CI: 0.01 to 0.44, $P = 0.04$) and resistance exercise (SMD = 0.65, 95% CI: 0.10 to 1.20, $P = 0.02$) significantly increased OC levels. Exercise interventions lasting ≤ 6 months (SMD = -0.45, 95% CI: -0.72 to -0.18, $P = 0.001$) and sessions of ≤ 60 min (SMD = -0.48, 95% CI: -0.80 to -0.17, $P = 0.003$) both significantly reduced CTX levels, exercise interventions lasting ≤ 6 months (SMD = 0.35, 95% CI: 0.13 to 0.57, $P = 0.002$) and sessions of ≤ 60 min (SMD = 0.20, 95% CI: 0.01 to 0.39, $P = 0.04$) can significantly both increase OC levels.

Conclusion: Exercise significantly improves bone metabolism in postmenopausal women by reducing bone resorption and promoting bone formation. Aerobic exercise lowers CTX levels, while both aerobic and

resistance exercise increase OC levels. Short-term (≤ 6 months) and moderate-length (≤ 60 minutes/session) interventions are particularly effective. However, more high-quality randomized controlled trials are needed to confirm these benefits.

Systematic review registration: <https://www.crd.york.ac.uk/>, identifier CRD42024610810.

KEYWORDS

exercise, postmenopausal women, bone metabolism, osteoporosis, osteopenia, randomized controlled trial, meta-analysis

1 Introduction

Osteoporosis is a systemic metabolic bone disease whose main risk is fragility fracture and is recognized as a disease that seriously affects the public health of society (1). Numerous studies have confirmed that postmenopausal women are at high risk of developing osteoporosis, with approximately 200 million women worldwide suffering from osteoporosis after menopause. After menopause, there is destruction of the trabecular structure of the bone, which in turn leads to an increase in the brittleness of the bone and a decrease in the mechanical strength of the bone, which in turn increases the risk of fracture (2). With increasing age, decreased physical activity, insufficient calcium intake, decreased absorption, and decreased vitamin conversion can make bone calcium highly susceptible to absorption and migration (3). Therefore, it is of great practical significance to explore exercise to improve bone metabolism and prevent osteoporosis in postmenopausal women.

Previous studies have demonstrated that exercise improves bone metabolism in postmenopausal women, thereby effectively preventing and treating osteoporosis (4, 5). The effect of exercise on bone metabolism in postmenopausal women has been a hot research topic. Exercise can improve bone metabolism by stimulating the secretion of growth factors by bone cells, promoting blood circulation in the skeletal system, and accelerating the absorption and metabolism of nutrients (6). Additionally exercise can stimulate adaptive changes in the skeletal system by increasing muscle loading, increasing bone density and bone strength and thus improving bone health (7).

The effects of exercise on bone health in postmenopausal women have been reviewed with a focus on bone mineral density (BMD) (8–10), which is the most commonly used metric for assessing bone health and reflects a relatively static bone mass status (11). BMD does not fully reflect bone metabolism, and in order to overcome this limitation and to understand the dynamic response to bone remodeling with exercise, bone metabolism markers are therefore used as dynamic indicators to evaluate bone remodeling (11). In addition, as bone metabolism increases with age, the potential clinical application of these markers could

assess fracture risk and measure bone health in postmenopausal women (12). This article reviews the relevant studies on the changes in various bone metabolism indicators in postmenopausal women after various interventions such as aerobic exercise, resistance exercise, impact exercise, Tai Chi, whole-body vibration training, and combined exercise. Meta analysis is conducted on the outcome indicators to compare the effects of exercise on bone metabolism, providing a theoretical basis for postmenopausal women to exercise scientifically to prevent and treat osteoporotic fractures.

2 Materials and methods

2.1 Protocol and registration

This comprehensive systematic review and meta-analysis followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (13) (Supplementary Table S1). This study was registered with the PROSPERO platform under the registration number: CRD42024610810 (<https://www.crd.york.ac.uk/>).

2.2 Search strategy

The first author conducted the search from November 6 to 8, 2024. The databases Retrieved November 2024 by the first author. PubMed, Embase, Cochrane Library, Web of Science, Scopus and Google Scholar were searched. Randomized controlled trials (RCTs) on the effects of aerobic and resistance exercise on bone metabolism in middle-aged and elderly people were searched in each database. The search terms included “Exercise, physical exercise, postmenopausal women, osteoporosis, low bone mass, bone metabolism, randomized controlled trial”. To identify more potential studies, we manually searched gray literature, reference lists of identified studies, and relevant registration website (ClinicalTrials.gov) and consulted experts in this field. however, due to the lack of standardized peer-review processes and limited accessibility of detailed data, we decided to exclude gray literature

from our analysis. The full search strategies for all databases are shown in [Supplementary Table S2](#).

2.3 Inclusion and exclusion criteria for the studies

Inclusion criteria: Inclusion criteria: (i) Study type: RCTs on the effects of exercise on bone metabolism in middle-aged and older adults that have been published in various databases from the time of their construction to November 6, 2024. Only peer-reviewed articles published in English were included to ensure methodological quality and accessibility of data; (ii) Study subjects: postmenopausal women aged ≥ 45 years. In this study, “postmenopausal” was defined as a serum follicle-stimulating hormone (FSH) level >25 – 30 IU/L, natural amenorrhea for >12 months, or explicit mention in the literature that the participants were in the postmenopausal stage. (iii) Intervention: any form of physical exercise (which refers to the cultural activities in which participants are physically active through the importance of physical exercise with the purpose of strengthening their physical fitness and improving their health), and the intervention group was based on Physical exercise is the focus of the intervention group, and there is no requirement for the exercise mode and load volume. Control measures: the control group only carries out daily life or original physical exercise and does not receive additional exercise intervention. If the control group receives conventional treatment, the experimental group should adopt conventional treatment + exercise intervention at the same time. (iv) Out-come indicators: serum phosphorus, serum calcium, osteocalcin (OC), 25-hydroxyvitamin D (25(OH)D), alkaline phosphatase (ALP), parathyroid hormone (PTH), type I collagen carboxy-terminal peptide (CTX), N-terminal propeptide of type I procollagen (P1NP).

Exclusion criteria: (i) Duplicated published literature; (ii) Non-RCT; (iii) Study subjects were not postmenopausal women; (iv) Interventions did not meet the inclusion criteria and controls did not meet the inclusion criteria; and (v) Outcome metrics did not meet the outcome metrics associated with the inclusion criteria; (vi) Unpublished studies, conference abstracts, and grey literature were excluded due to the lack of complete methodological details and peer review, which may affect data reliability.

2.4 Literature screening and data extraction

The retrieved literature was imported into Endnote 20 software and duplicates were removed from it. Two researchers then screened the literature and extracted information based on established inclusion and exclusion criteria. If disagreements were encountered, they were discussed and resolved with a third researcher. Characteristics of included studies included authors, year of publication, country, sample size, and age ([Table 1](#)), and characteristics of included interventions included type of exercise, frequency of exercise, exercise period, duration of a single exercise

session, control exercise status, and outcome indicators ([Table 2](#)). Bone metabolism marker data were extracted as post-intervention mean and standard deviation (SD).

2.5 Risk of bias assessment

For RCTs and clinical controlled trials, the risk of bias was provided by the Review Manager 5.4 self-contained tool ([14](#)). Two researchers each assessed the risk of bias in the selected literature using the Cochrane Risk of Bias Assessment Tool. The assessment included randomized sequence generation, allocation concealment, blinding of investigators and subjects, blinded evaluation of study out-comes, completeness of outcome data, selective reporting and other biases. Each factor was assessed as high risk of bias, low risk of bias, or unknown risk of bias. Disagreements that arose during the assessment process were resolved through discussion.

2.6 Data analysis

Data were synthesized for the included outcome indicators using Review Manager 5.4 software and stata17 software. The outcome indicators of the studies included in this analysis were all continuous variables. Since all the incorporated studies were RCTs, the between-group differences at baseline should theoretically approach zero. Therefore, post-intervention values were used for the meta-analysis, and standardized mean differences (SMDs) with 95% confidence intervals (95% CIs) were selected as the effect measures for pooling the effect sizes. Statistical inferences were made through heterogeneity tests and statistical combined effect sizes. The heterogeneity test was evaluated using I^2 values. In the heterogeneity test, $P > 0.10$ indicated that the heterogeneity of the literature included in this study was negligible, and $P \leq 0.10$ indicated that the heterogeneity of the literature included in this study existed. $0 \leq I^2 \leq 25\%$ indicated that the heterogeneity was ignored, $25\% < I^2 \leq 50\%$ indicated that the inclusion of the literature existed in a mild degree, $50\% < I^2 \leq 75\%$ indicated that the inclusion of the study existed in a moderate degree, and $I^2 > 75\%$ indicated that the inclusion of the studies had high heterogeneity. Literature with moderate to high heterogeneity was analyzed using a random effects model, while literature with mild or negligible heterogeneity was analyzed using a fixed effects model.

2.7 Subgroup analysis

Subgroup analyses of OC and CTX were conducted according to exercise type, intervention period (≤ 6 months vs. > 6 months), and session duration (≤ 60 minutes vs. > 60 minutes). Due to the limited number of studies, subgroup analyses were not performed for other bone metabolism markers. In addition, because exercise intensity was inconsistently defined across trials (e.g., based on heart rate, load percentage, or perceived exertion) and only a few

TABLE 1 Research characteristics.

Author (Year)	Country and area	Subject type	Sample size (n)		Age		Bone status (diagnostic criteria, measurement sites, and measurement tools)
			EG	CG	EG	CG	
Hatori (16) (1993)	Japan	Post-menopausal women	9/12	12	MG: 58 ± 5 HG: 56 ± 4	58 ± 8	Healthy, no osteoporosis
Nelson (17) (1994)	United States of America	Post-menopausal women	20	18	61.4 ± 6.9	58.9 ± 8.1	Healthy, no osteoporosis
Iwamoto (18) (2001)	Japan	Post-menopausal women	8	20	65.3 ± 4.7	64.9 ± 5.7	Osteoporosis: BMD more than 30% below the young adult mean (in accordance with the Japanese diagnostic guidelines for osteoporosis) Measurement site: Lumbar spine (L2–L4) BMD Measurement tool: DXA
Ay (21) (2003)	Turkish	Post-menopausal women	23	23	54.28 ± 6.08	55.11 ± 5.32	Osteopenia or osteoporosis: BUA T-score ≤ -1 Measurement site: calcaneus Measurement tool: QUS
Wu (19) (2005)	Japan	Post-menopausal women	31	33	54.4 ± 2.9	53.8 ± 2.9	Healthy, no osteoporosis
Wu (20) (2006)	Japan	Post-menopausal women	31	33	54.4 ± 2.9	53.8 ± 2.9	Healthy, no osteoporosis
Shen (38) (2010)	United States of America	Post-menopausal women	44	42	58.3 ± 7.7	57.6 ± 7.5	Osteopenia: -2.5 < T-score < -1.0 Measurement sites: Lumbar spine or hip BMD Measurement tool: DXA
Tartibian (22) (2011)	Iran	Post-menopausal women	20	18	61.4 ± 6.9	58.9 ± 8.1	Healthy, no osteoporosis
Wayne (37) (2012)	United States of America	Post-menopausal women	43/26	43	58.8 ± 5.5/ 59.1 ± 4.9	60.4 ± 5.3	Osteopenia: -2.5 < T-score < -1.0 Measurement sites: lumbar spine (L1–L4), femoral neck, and total hip BMD Measurement tool: DXA
Bergström (23) (2012)	Sweden	Post-menopausal women	48	44	58.9 ± 4.3	59.6 ± 3.6	Osteopenia: -2.5 < T-score < -1.0 Measurement sites: hip or spine BMD Measurement tool: DXA
Baset (24) (2013)	Turkey	Post-menopausal women	11	12	SG: 55.9 ± 4.9 HIG: 55.6 ± 2.9	56.2 ± 4.0	Osteopenia: -2.5 < T-score < -1.0 Measurement sites: Lumbar spine (L1–L4) or femoral neck BMD Measurement tool: DXA
Mosti (25) (2013)	Norway	Post-menopausal women	8	8	61.9 ± 5.0	66.7 ± 7.4	Osteoporosis: T-score ≤ -2.5; Osteopenia: -2.5 < T-score < -1.0 Measurement sites: Lumbar spine (L1–L4), femoral neck, and total hip BMD Measurement tool: DXA
Roghani (26) (2013)	Iran	Post-menopausal women	8/9	10	45–65		Osteoporosis: T-score ≤ -2.5 Measurement sites: lumbar spine or hip BMD Measurement tool: DXA

(Continued)

TABLE 1 Continued

Author (Year)	Country and area	Subject type	Sample size (<i>n</i>)		Age		Bone status (diagnostic criteria, measurement sites, and measurement tools)
			EG	CG	EG	CG	
Pernambuco (27) (2013)	Brazil	Post-menopausal women	36	31	66.8 ± 4.2		Normal bone mass: T-score ≥ -1.0; osteoporosis: BMD T-score ≤ -2.5; osteopenia: -2.5 < T-score < -1.0 Measurement sites: lumbar spine (L ₂ –L ₄) and total hip BMD Measurement tool: DXA
Moreira (28) (2014)	Japan	Post-menopausal women	59	41	58.6 ± 6.71	59.3 ± 6.07	Normal bone mass: T-score ≥ -1.0; Osteopenia: -2.5 < T-score < -1.0; Osteoporosis: T-score ≤ -2.5 Measurement sites: lumbar spine (L ₁ –L ₄), femoral neck, trochanter, total hip, and whole-body BMD Measurement tool: DXA
Wen (6) (2017)	China, Taiwan	Post-menopausal women	24	24	57.5 ± 3.5	58.8 ± 3.2	Osteopenia: T-score ≤ -1.0; Osteoporosis: T-score ≤ -2.5 Measurement sites: lumbar spine, hip, and whole-body BMD Measurement tool: DXA
Baker (29) (2018)	Australia	Post-menopausal women	14	17	61.6 ± 9.2	61.6 ± 7.8	Only 4 participants (12.9%) met the criteria for osteoporosis (T-score ≤ -2.5)
Sen (30) (2020)	Turkey	Post-menopausal women	15	18	WG: 55.0 ± 4.6 HIG: 53.1 ± 4.4	54.5 ± 6.0	The BMD T-score at the lumbar spine (L ₁ –L ₄ or L ₂ –L ₄) and/or femoral neck and total hip ranges from -2.0 to -3.0, meeting the diagnostic criteria for osteopenia or osteoporosis (according to WHO standards: T-score ≤ -2.5 indicates osteoporosis, and -1.0 to -2.5 indicates low bone mass/osteopenia)
Linero (31) (2021)	South Korea	Post-menopausal women	7/6/6	5	MHIRT: 56.43 ± 0.72 LIBFR: 55.71 ± 0.52 LIRT: 56.50 ± 0.99	56.83 ± 0.70	Osteoporosis: T-score ≤ -2.5; Osteopenia: -2.5 < T-score < -1.0 Measurement sites: lumbar spine or femoral neck BMD Measurement tool: DXA
Pereira (32) (2021)	Portugal	Post-menopausal women	41	26	67.3 ± 6.5	69.9 ± 5.4	Healthy, no osteoporosis
Kim (33) (2022)	South Korea	Post-menopausal women	14	15	81.14 ± 3.98	80.80 ± 2.37	NR
Zaravar (34) (2024)	Iran	Post-menopausal women	7	6	65.100 ± 3.478	66.400 ± 3.238	The mean baseline BMD (0.517–0.585 g/cm ²) was significantly lower than that of healthy young adults. Based on the baseline BMD values, the participants were diagnosed with osteopenia or osteoporosis
Guzel (35) (2024)	Turkey	Post-menopausal women	12	12	55.67 ± 3.44	54.42 ± 4.01	Healthy, no osteoporosis
Pasa (36) (2024)	Indonesia	Post-menopausal women	14	14	45–69		According to the guidelines of the World Health Organization (WHO) and the International Society for Clinical Densitometry (ISCD, 2023), BMD T-scores are classified as follows: Normal bone mass: T-score ≥ -1; Osteopenia: -2.5 < T-score < -1; Osteoporosis: T-score ≤ -2.5 Measurement device: Sonost 3000 densitometer Measurement site: calcaneus

EG, exercise group; CG, control group; HG, high intensity group; MG, moderate intensity group; WG, whole-body vibration (WBV); SG, strength training group; HIG, high impact training group; QUS, quantitative ultrasound; BUA, broadband ultrasound attenuation; DXA, dual-energy X-ray absorptiometry; BMD, bone mineral density; MHIRT, moderate to high-intensity resistance training; LIBFR, low-intensity resistance training with blood flow restriction; LIRT, low-intensity resistance training.

TABLE 2 Characterization of research interventions.

Athor	Interventions	Frequency of intervention	Intervention cycle	Duration of one intervention	Exercise status of the control group during the trial	Outcome measures (units, baseline ranges, measurement methods)
Hatori (16)	Walking	3 times/week	7 months	30 minutes	Not undertaking a specific exercise program	Baseline ranges: Ca (mg/dL): 9.0 ± 0.2 (CG), 9.2 ± 0.4 (MG), 9.4 ± 0.5 (HG) P (ng/mL): 3.6 ± 0.3 (CG), 3.5 ± 0.3 (MG), 3.7 ± 0.5 (HG) OC (ng/mL): 11.8 ± 2.6 (CG), 12.0 ± 2.3 (MG), 11.6 ± 2.4 (HG) ALP (U/L): 167 ± 29 (CG), 177 ± 30 (MG), 196 ± 37 (HG) Measurement methods: OC was measured by RIA; Ca, P, and ALP were measured using automated methods
Nelson (17)	High-intensity strength training	2 times/week	1 year	45 minutes	No strength training program	Baseline ranges: OC (nmol/L): 1.163 ± 0.224 (CG), 1.094 ± 0.245 (EG) 25(OH)D (nmol/L): 79.8 ± 27.5 (CG), 68.3 ± 25.2 (EG) PTH (pmol/L): 2.853 ± 0.851 (CG), 2.855 ± 1.011 (EG) Measurement methods: OC and PTH were measured using IRMA, and 25(OH)D was measured using Competitive Protein-Binding Analysis
Iwamoto (18)	Brisk walking and gymnastic exercises	NR	2 years	NR	Daily activities only, no additional exercise interventions	Baseline ranges: Ca (mg/dl): 9.4 ± 0.4 (EG), 9.3 ± 0.4 (CG) P (mg/dl): 3.6 ± 0.4 (EG), 3.5 ± 0.4 (CG) ALP (IU/l): 214 ± 69 (EG), 216 ± 52 (CG) Measurement method: Ca, P, and ALP were measured using standard automated laboratory techniques
Ay (21)	Aquatic aerobics exercises	3 times/week	6 months	45 minutes	The control group was asked to maintain their sedentary lifestyle throughout the study period	Baseline ranges: PTH (pg/mL): 72.68 ± 47.01 (EG), 68.89 ± 25.34 (CG). Measurement method: Iodine-125 RIA
Wu (19)	Walking	3 times/week	24 weeks	45 minutes	No additional exercise intervention	Baseline ranges: OC (ng/mL): 9.50 ± 2.42 (EG), 9.23 ± 2.09 (CG) Measurement method: Sandwich enzyme immunoassay using polyclonal antibodies
Wu (20)	Walking	3 times/week	1 year	45 minutes	No additional exercise intervention	Baseline ranges: OC (ng/mL): 9.50 ± 2.42 (EG), 9.23 ± 2.09 (CG) Measurement method: Sandwich enzyme immunoassay using polyclonal antibodies
Shen (38)	Tai Chi	3 times/week	24 weeks	60 minutes	Placebo, no additional exercise intervention	Baseline ranges: P (mg/dl): 3.7 ± 0.5 (EG and CG), 3.7 ± 0.5 (CG) Ca (mg/dl): 9.4 ± 0.2 (EG), 9.4 ± 0.4 (CG) ALP (U/L): 81.6 ± 20.1 (EG), 75.3 ± 18.6 (CG) Detection method: NR

(Continued)

TABLE 2 Continued

Athor	Interventions	Frequency of intervention	Intervention cycle	Duration of one intervention	Exercise status of the control group during the trial	Outcome measures (units, baseline ranges, measurement methods)
Tartibian (22)	Walking and running exercises	3–4 times/week	12/24 weeks	25–30 minutes	Daily activities only, no additional exercise interventions	Baseline ranges: P (mg/dL): 3.8 ± 0.5 (EG), 3.6 ± 0.6 (CG) Ca (mg/dL): 9.5 ± 0.7 (EG), 9.3 ± 0.7 (CG) CTX (ng/mL): 0.5 ± 0.1 (EG and CG) 25(OH)D (pg/mL): 41.5 ± 21.9 (EG), 42.3 ± 20.6 (CG) PTH (pg/mL): 92.5 ± 46.6 (EG), 94.9 ± 46.6 (CG) OC (ng/mL): 25.8 ± 8.4 (EG), 24.4 ± 7.7 (CG) Measurement methods: CTX and OC were measured using ELISA, 25(OH)D by Radioreceptor Assay, PTH by Electrochemiluminescent Method P, Ca: NR
Wayne (37)	Tai Chi	4 times/week	9 mouths	90 minutes	No designated athletic training, only routine medical care	Baseline ranges: CTX (ng/mL): 0.554 ± 0.259 (Randomized to Tai Chi), 0.594 ± 0.30 (Per Protocol Tai Chi), 0.603 ± 0.231 (Randomized to Usual Care) OC (ng/mL): 16.29 ± 6.01 (Randomized to Tai Chi), 15.52 ± 4.94 (Per Protocol Tai Chi), 17.11 ± 7.02 (Randomized to Usual Care) Measurement methods: CTX was measured using ELISA, and OC was RIA
Bergström (23)	Aerobic exercise	3 times/week	1 year	30 minutes	Maintaining a sedentary lifestyle	Baseline ranges: CTX (ng/l): 421 ± 142 (EG), 419 ± 166 (CG) Measurement methods: ECLIA
Baset (24)	Strength Training/High Impact Training	3 times/week	6 mouths	45 minutes	No designated athletic training, just maintaining normal daily activities	Baseline ranges: OC (ng/ml): 13.6 ± 2.4 (SG), 13.6 ± 6.0 (HG), 14.2 ± 3.4 (CG) Measurement method: ELISA
Mosti (25)	Maximum Strength Squat Movement	3 times/week	12 weeks	30–40 minutes	Continue their daily activities and any existing exercise habits	Baseline ranges: CTX (ng/ml): 0.743 ± 0.200 (EG), 0.576 ± 0.051 (CG) P1NP (μg/l): 54.25 ± 15.36 (EG), 51.67 ± 12.36 (CG) Measurement methods: CTX by RIA; P1NP by Serum CrossLaps ELISA
Roghani (26)	Aerobics/Aerobic + Resistance	3 times/week	6 weeks	30 minutes	Daily activities only, no additional exercise interventions	Baseline ranges: P(mg/dl): 3.86 ± 0.40 (AG), 3.33 ± 0.43 (AG+RG), 3.79 ± 0.42 (CG) Ca (mg/dl): 9.10 ± 0.11 (AE), 8.91 ± 0.16 (AG+RG), 9.06 ± 0.38 (CG) ALP (ALP, U/L): 218.00 ± 68.32 (AG), 222.44 ± 60.96 (AG+RG), 181.50 ± 83.36 (CG) Measurement methods: P and Ca: standardized biochemical analysis ALP: ELISA

(Continued)

TABLE 2 Continued

Athor	Interventions	Frequency of intervention	Intervention cycle	Duration of one intervention	Exercise status of the control group during the trial	Outcome measures (units, baseline ranges, measurement methods)
Pernambuco (27)	Aquatic aerobics exercises	2 times/week	8 months	50 minutes	Daily activities only, no additional exercise interventions	Baseline ranges: OC (ng/ml): 16.4 ± 7.18 (EG), 19.9 ± 5.9 (CG) Measurement method: ELISA
Moreira (28)	High-intensity water exercise	3 times/week	24 weeks	50–60 minutes	Daily activities only, no additional exercise interventions	Baseline ranges: Ca (mg/dL): 9.61 ± 0.33 (EG), 9.50 ± 0.23 (CG) 25(OH)D (nmol/L): 51.8 ± 25.2 (EG), 48.1 ± 19.6 (CG) PTH (pg/mL): 46.62 ± 15.54 (EG), 43.61 ± 15.20 (CG) CTX (ng/mL): 0.330 ± 0.159 (EG), 0.352 ± 0.182 (CG) Measurement method: Ca and 25(OH)D: IRMA PTH: Chemiluminescence immunoassay CTX: ECLIA
Wen (6)	Aerobic exercise	3 times/week	10 weeks	90 minutes	Not participating in any other regular physical activity or sport	Baseline ranges: CTX (nmol/L): 0.69 ± 0.26 (EG), 0.89 ± 0.48 (CG) Measurement method: ELISA
Baker (29)	Whole Body Vibration Training	3 times/week	12 weeks	20 minutes	No designated athletic training, only routine medical care	Baseline ranges: P1NP (µg/L): 62.3 ± 27.0 (EG), 62.2 ± 25.3 (CG) Measurement method: NR
Sen (30)	Whole Body Vibration Training/ High Impact Training	3 times/week	24 weeks	20–60 minutes	No designated athletic training, just maintaining normal daily activities	Baseline Ranges: OC (ng/mL): 4.82 ± 1.69 (WG), 2.81 ± 1.84 (HG), 3.66 ± 2.29 (CG) CTX (ng/mL): 0.43 ± 0.23 (WG), 0.45 ± 0.20 (HG), 0.38 ± 0.20 (CG) Measurement methods: OC: Solid phase chemiluminescence CTX: ECLIA
Linero (31)	Resistance exercise	3 times/week	12 weeks	90 minutes	No specific exercise training	Baseline Ranges: CTX (ng/ml): 0.46 ± 0.10 (MHIRT), 0.52 ± 0.07 (MHIRT), 0.40 ± 0.05 (LIRT) Measurement method: ECLIA
Pereira (32)	Handball exercise	2–3 times/week	16 weeks	60 minutes	Daily activities only, no additional exercise interventions	Baseline ranges: OC (µg/L): 18.8 ± 7.1 (EG), 16.6 ± 13.1 (CG) P1NP (µg/L): 49.9 ± 18.9 (EG), 38.0 ± 27.5 (CG) Measurement method: Chemiluminescence method (for both OC and P1NP)

(Continued)

TABLE 2 Continued

Athor	Interventions	Frequency of intervention	Intervention cycle	Duration of one intervention	Exercise status of the control group during the trial	Outcome measures (units, baseline ranges, measurement methods)
Kim (33)	Aerobic + Resistance	2 times/week	6 months	60 minutes	Daily activities only, no additional exercise interventions	Baseline ranges: OC (ng/mL): 8.04 ± 3.93 (EG), 9.18 ± 3.09 (CG) ALP (µg/L): 7.75 ± 4.47 (EG), 10.15 ± 3.91 (CG) Measurement methods: OC: Immunoassay ALP: ELISA
Zaravar (34)	Aquatic aerobics exercises)	3 times/week	8 weeks	60 minutes	Did not train for a specific sport, but maintained their daily activities	Baseline ranges: 25(OH)D (ng/mL): 27.99 ± 6.540 (EG), 28.08 ± 5.995 (CG) PTH (pg/mL): 64.99 ± 14.516 (EG), 64.21 ± 16.097 (CG) Measurement methods: 25(OH)D: ECLIA PTH: Commercial reagent kits
Guzel (35)	Walking	3 times/week	10 weeks	25–40 minutes	Maintain daily activity level without any exercise training	Baseline ranges: 25(OH)D (ng/mL): 18.95 ± 10.08 (EG), 16.62 ± 9.2 (CG) Measurement method: NR
Pasa (36)	Walking and bone joint exercise	3 times/week	8 weeks	30 minutes	Maintain daily habits without any structured physical activity	Baseline ranges: PTH (pg/mL): 151.87 ± 39.84 (Walking), 175.91 ± 57.33 (Bone Joint Exercise), 142.61 ± 26.74 (Control Group, CG) Measurement method: ELISA

EG, exercise group; CG, control group; HG, high intensity group; MG, moderate intensity group; MG, moderate intensity group; WG, whole-body vibration (WBV); SG, strength training group; HIG, high impact training group; AG, aerobic exercise group; RG, resistance exercise group; RIA, radioimmunoassay; MHIRT, moderate to high-intensity resistance training; LIBFR, low-intensity resistance training with blood flow restriction; LIRT, low-intensity resistance training; IRMA, immunoradiometric Assay; ELISA, enzyme-linked immunosorbent Assay; ECLIA, electrochemiluminescence Assay; P, serum phosphorus; Ca, serum calcium; OC, osteocalcin; PTH, parathyroid hormone; ALP, alkaline phosphatase; 25(OH)D, 25-hydroxyvitamin D; CTX, type I collagen cross-linked C-terminal peptide; P1NP, N-terminal propeptide of type I procollagen; NR, not reported.

studies provided sufficient data, we did not conduct subgroup analyses by intensity.

2.8 Sensitivity analysis

We performed sensitivity analysis by eliminating studies one by one to verify the robustness of the results.

2.9 Publication bias

We used a funnel plot and Egger's test to detect publication bias when ≥ 10 studies with the same outcome were included in the analysis.

2.10 Certainty of evidence

We applied the Grading of recommendations assessment, development, and evaluation (GRADE) system to assess the certainty of evidence. Each outcome was evaluated from the following six aspects: study design, risk of bias, inconsistency, indirectness, imprecision and other considerations. Then the certainty of evidence was accordingly graded as "high", "moderate", "low", or "very low" (15). GRADE pro GDT online tool was used to present the summary of findings.

3 Results

3.1 Results of literature screening

The initial screening identified 1653 articles, including 331 articles in PubMed database, 365 articles in Embase database, 278 articles in Cochrane Library database, 225 articles in Web of Science database, 178 articles in Scopus database, and 276 articles in Google Scholar database. We obtained 835 articles by de-weighting with EndNote 20 software, excluded 751 articles after reading the titles and abstracts, excluded 7 articles with low relevance, and read through the full text of the remaining 84 articles to assess whether to include them. Among them, 13 interventions did not match the target group, 9 controls did not meet the criteria, 15 interventions did not meet the inclusion criteria, 12 outcome indicators did not match, 7 had no control, and 4 were unable to extract data, and finally, the remaining 24 papers (6, 16–38) were included in the Meta-analysis. (Figure 1).

3.2 Characteristics of the included studies

A total of 24 papers published between 1993–2024 were included in this study, and the total number of subjects was 1067 (575 in the experimental group and 492 in the control group), aged

45 years or older. Among the countries of publication, five articles were published in Japan (16, 18–20, 28), four in Turkey (21, 24, 30, 35), three in Iran (22, 26, 34), three in the United States (17, 37, 38), one in Brazil (27), one in Sweden (23), one in Norway (25), one in Indonesia (36), Taiwan, China 1 article (6), 1 article (29) in Australia, and 1 article in Portugal (32). The intervention group included 12 articles on aerobic exercise (6, 16, 18–23, 26, 27, 32, 34–36), 4 articles on resistance exercise (17, 24, 25, 31), 3 articles on aerobic combined with resistance exercise (26, 28, 33), 2 articles on whole-body vibration training (29, 30), 2 articles on percussive exercise (24, 30), 2 article on Tai Chi exercise (37, 38). The intervention period was 6 weeks–2 years, the frequency of exercise was 2–4 times/week, and the duration of exercise was 25–90 minutes/session (Table 2).

3.3 Risk of bias

Nine studies (6, 24, 25, 27–30, 32, 37) reported the method of random sequence generation (computer-generated random numbers, variable block randomization, stratified randomization, coin tossing, urn design). One study (29) provided information on allocation concealment, stating that sealed opaque envelopes were used. Twenty-two studies (6, 16–34, 37, 38) reported the number of dropouts and losses to follow-up. Four studies (17, 29, 37, 38) conducted an intention-to-treat (ITT) analysis, while seventeen (6, 16, 18–21, 23–28, 30–33, 37) performed a per-protocol (PP) analysis; four (22, 34–36) did not specify whether ITT or PP was applied. Four studies (29, 30, 37, 38) reported a trial registration number. In summary, since blinding is difficult to implement in exercise intervention studies, most studies were judged to be at "high risk" of bias. The results of the risk of bias assessment are shown in Figures 2 and 3.

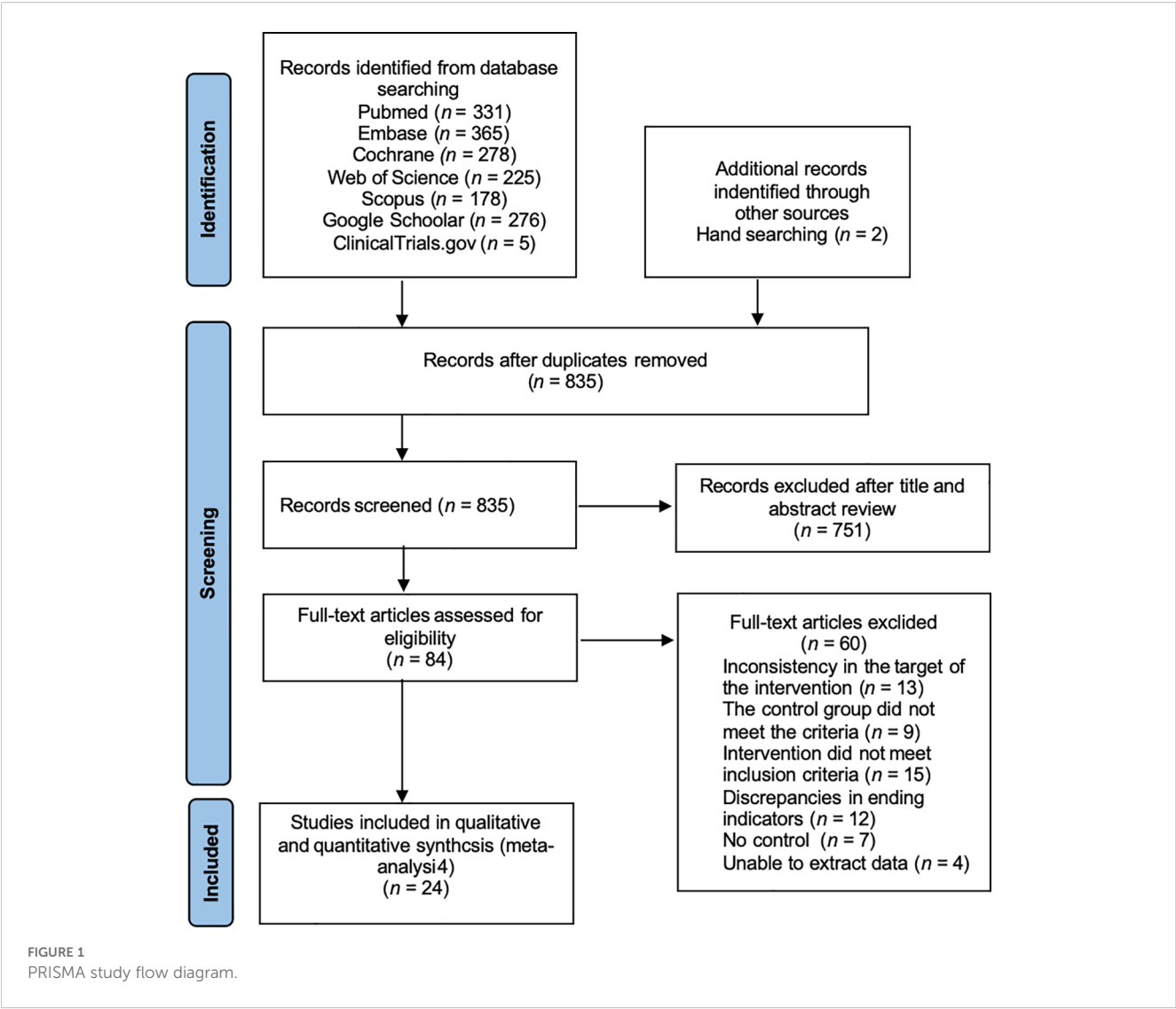
3.4 Meta-analysis results

3.4.1 Effect of exercise on serum phosphorus in postmenopausal women

There were 4 RCTs (16, 18, 22, 38) on the effect of exercise on serum phosphorus in postmenopausal women. Meta-analysis showed negligible heterogeneity of the included studies in the exercise group compared to the control group ($I^2 = 0\%$, $P = 0.71$), so a fixed-effects model was used (Figure 4). The results showed that serum phosphorus ($SMD = 0.10$, 95% CI : -0.18 to 0.39, $P = 0.48$) tended to increase in the exercise group compared to the control group but was not significant. (Figure 4).

3.4.2 Effect of exercise on serum calcium in postmenopausal women

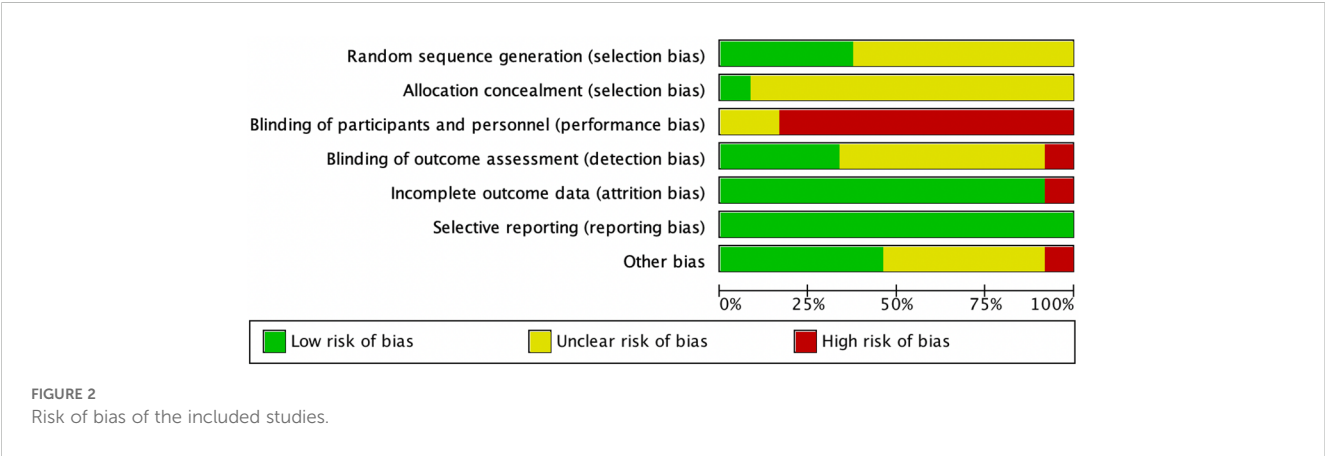
There were 5 RCTs (16, 18, 22, 26, 38) on the effect of exercise on serum calcium in postmenopausal women. Meta-analysis showed that the included studies could be mildly heterogeneous in the exercise group compared to the control group ($I^2 = 39\%$, $P =$

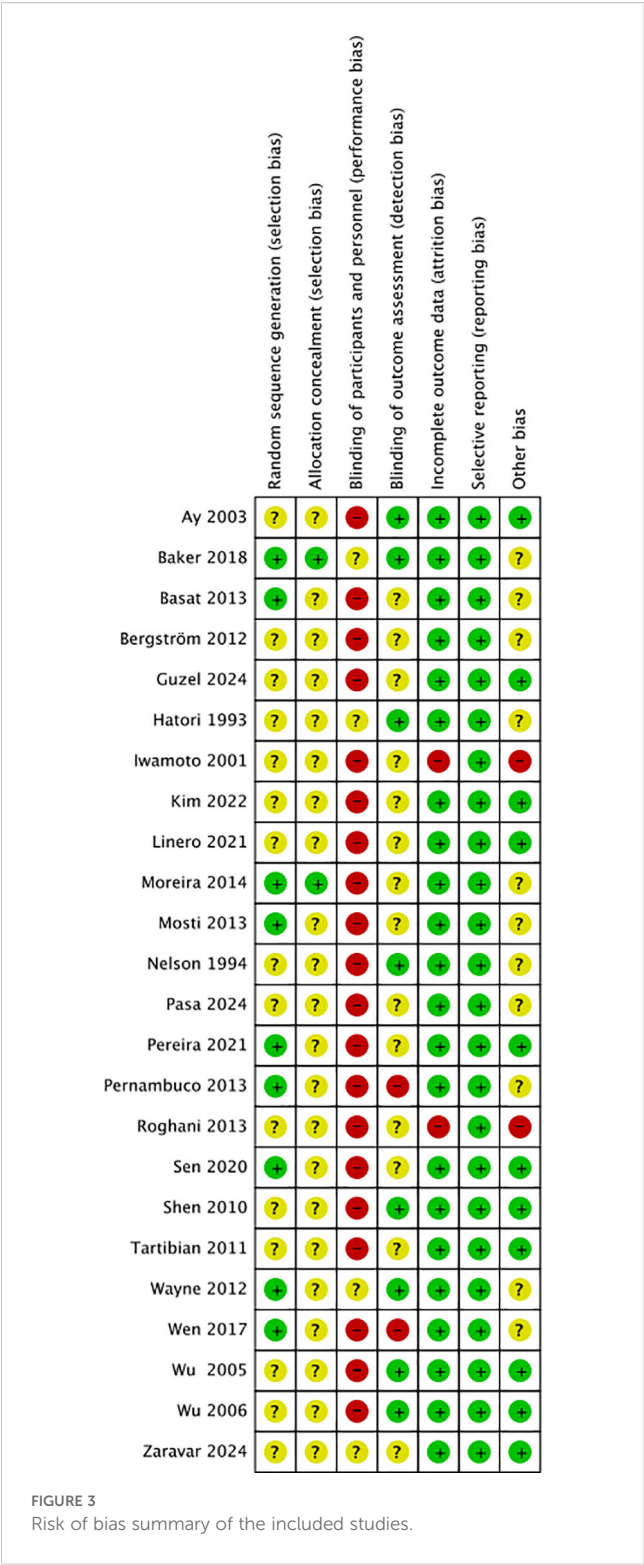


0.12), so a fixed-effects model was used (Figure 5). The results showed that serum calcium ($SMD = 0.10$, 95% CI : -0.13 to 0.34 , $P = 0.39$) tended to increase in the exercise group compared to the control group but was not significant (Figure 5).

3.4.3 Effect of exercise on 25(OH)D in postmenopausal women

There were 5 RCTs (17, 22, 28, 34, 35) on the effect of exercise on 25(OH)D in postmenopausal women. Meta-analysis showed





negligible heterogeneity in the included studies in the exercise group compared to the control group ($I^2 = 0\%$, $P = 0.76$), so a fixed-effects model was used (Figure 6). The results showed that serum calcium ($SMD = 0.18$, 95% CI : -0.04 to 0.41 , $P = 0.11$) tended to increase in the exercise group compared to the control group but was not significant (Figure 6).

3.4.4 Effect of exercise on PTH in postmenopausal women

There were 5 RCTs (17, 21, 22, 28, 34) on the effect of exercise on PTH in postmenopausal women. Meta-analysis showed that the included studies could be mildly heterogeneous in the exercise group compared to the control group ($I^2 = 32\%$, $P = 0.19$), so a fixed effects model was used (Figure 7). The results showed a significant decrease in PTH in the exercise group compared to the control group ($SMD = -0.51$, 95% CI : -0.77 to -0.25 , $P = 0.0001$) (Figure 7).

3.4.5 Effect of exercise on ALP in postmenopausal women

There were 5 RCTs (16, 18, 26, 33, 38) on the effect of exercise on ALP in postmenopausal women. Meta-analysis showed negligible heterogeneity in the included studies in the exercise group compared to the control group ($I^2 = 0\%$, $P = 0.93$), so a fixed-effects model was used (Figure 8). The results showed a significant increase in ALP in the exercise group compared to the control group ($SMD = 0.49$, 95% CI : 0.21 to 0.77 , $P = 0.0006$) (Figure 8).

3.4.6 Effect of exercise on P1NP in postmenopausal women

There were 3 RCTs (25, 29, 32) on the effect of exercise on P1NP in postmenopausal women. Meta-analysis showed negligible heterogeneity in the included studies in the exercise group compared to the control group ($I^2 = 13\%$, $P = 0.32$), so a fixed-effects model was used (Figure 9). The results showed a significant increase in P1NP in the exercise group compared to the control group ($SMD = 0.62$, 95% CI : 0.24 to 1.01 , $P = 0.002$) (Figure 9).

3.4.7 Effect of exercise on CTX in postmenopausal women

There were 7 RCTs (6, 22, 23, 25, 28, 31) on the effect of exercise on CTX in postmenopausal women. Meta-analysis showed moderate heterogeneity of the included studies in the exercise group compared to the control group ($I^2 = 35\%$, $P = 0.12$), so a fixed-effects model was used (Figures 10-12). The results showed that the CTX levels in the exercise group were significantly lower than those in the control group ($SMD = -0.32$, 95% CI : -0.51 to -0.12 , $P = 0.001$). The results of the subgroup analysis by exercise type showed that aerobic exercise ($SMD = -0.35$, 95% CI : -0.65 to -0.06 , $P = 0.02$) significantly reduced CTX levels; resistance exercise ($SMD = -0.32$, 95% CI : -1.10 to 0.47 , $P = 0.43$), combined aerobic plus resistance exercise ($SMD = -0.34$, 95% CI : -0.74 to 0.06 , $P = 0.10$) and Tai Chi ($SMD = -0.24$, 95% CI : -0.63 to 0.15 , $P = 0.23$) showed a trend toward reducing CTX, but without statistical significance (Figure 10). The further stratification of sample size may have resulted in smaller pooled effect sizes and an insufficient number of studies, leading to unstable statistical results and less convincing findings. The results of cycle subgroup analysis showed that exercise for ≤ 6 months ($SMD = -0.45$, 95% CI : -0.72 to -0.18 , $P = 0.001$) significantly reduced CTX levels; exercise for > 6 months ($SMD = -0.17$, 95% CI : 0.46 to 0.11 , $P = 0.22$) had a trend to reduce CTX levels and was not significant (Figure 11). Subgroup analysis of

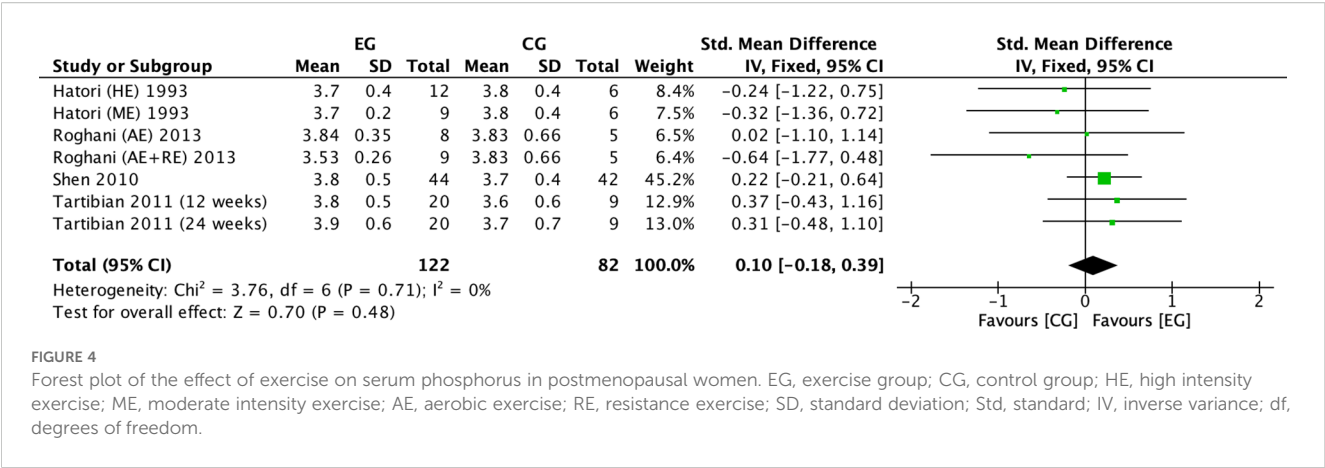


FIGURE 4 Forest plot of the effect of exercise on serum phosphorus in postmenopausal women. EG, exercise group; CG, control group; HE, high intensity exercise; ME, moderate intensity exercise; AE, aerobic exercise; RE, resistance exercise; SD, standard deviation; Std, standard; IV, inverse variance; df, degrees of freedom.

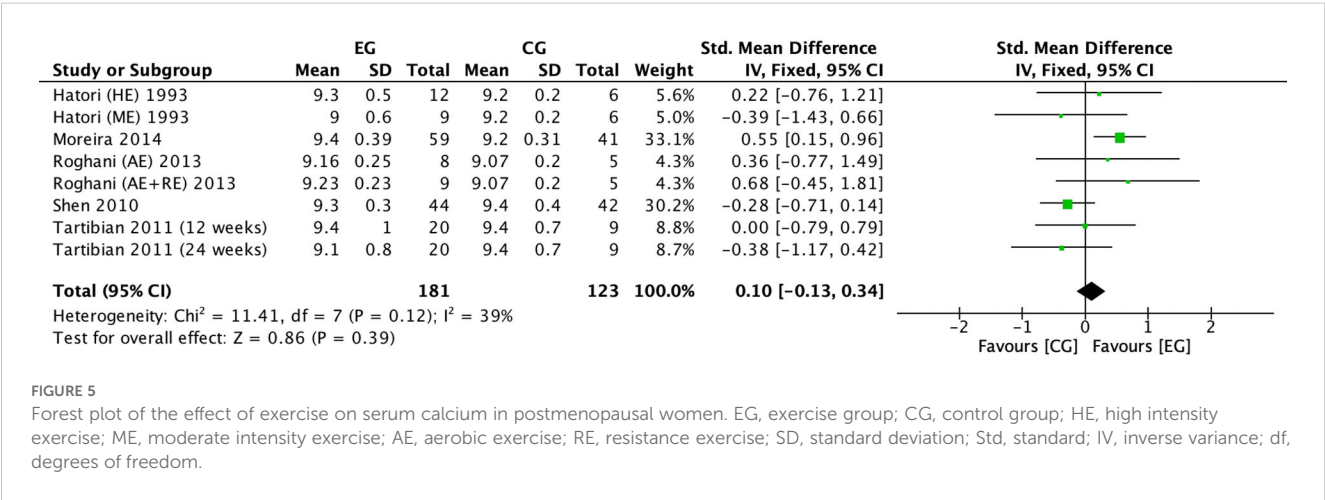


FIGURE 5 Forest plot of the effect of exercise on serum calcium in postmenopausal women. EG, exercise group; CG, control group; HE, high intensity exercise; ME, moderate intensity exercise; AE, aerobic exercise; RE, resistance exercise; SD, standard deviation; Std, standard; IV, inverse variance; df, degrees of freedom.

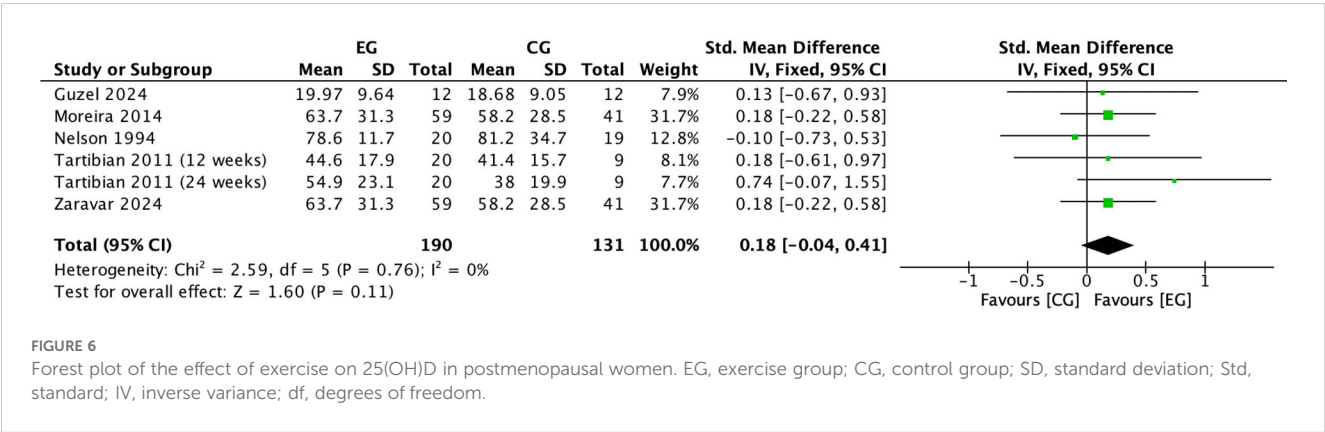
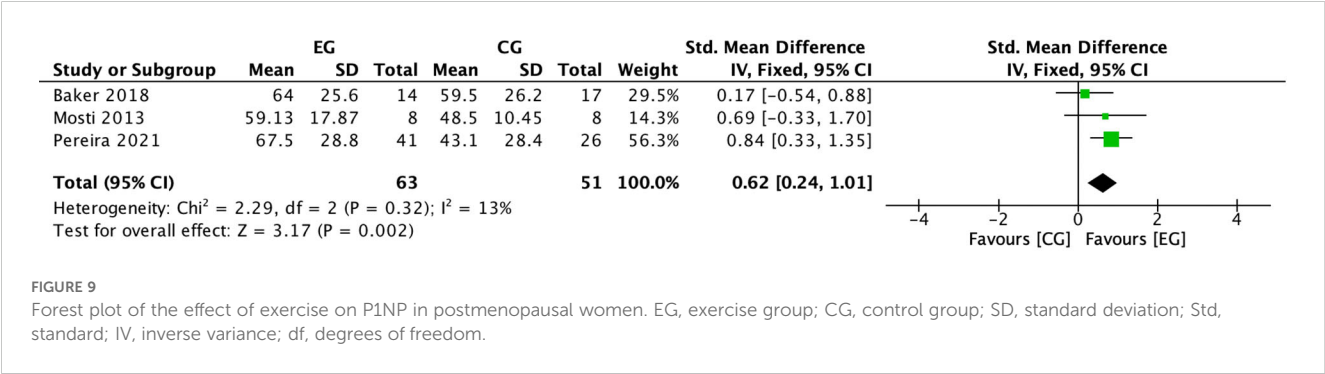
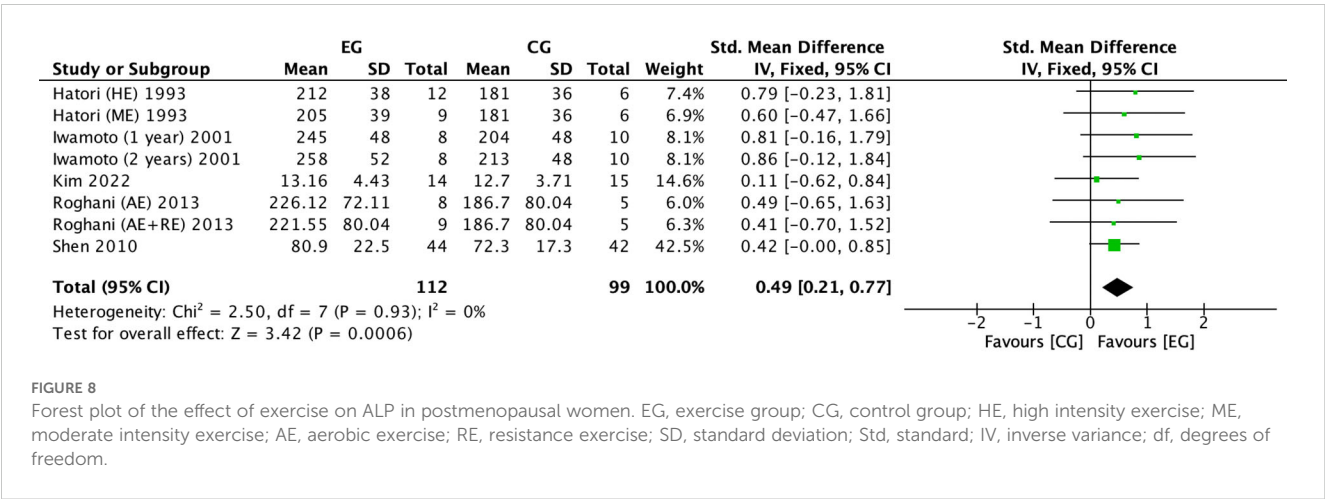
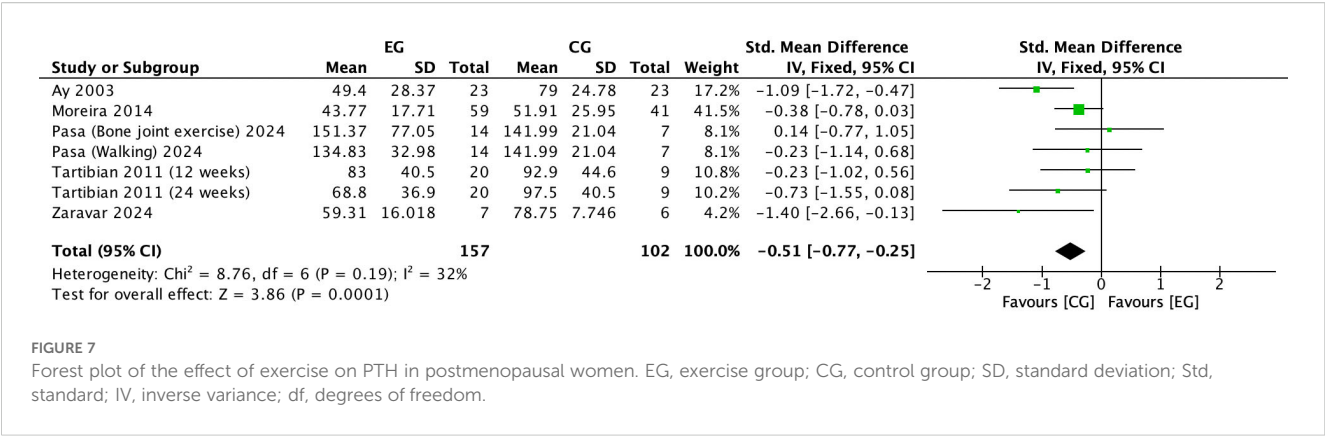


FIGURE 6 Forest plot of the effect of exercise on 25(OH)D in postmenopausal women. EG, exercise group; CG, control group; SD, standard deviation; Std, standard; IV, inverse variance; df, degrees of freedom.

the duration of a single exercise session showed that exercise of ≤ 60 min ($SMD = -0.48$, 95% CI : -0.80 to -0.17, $P = 0.003$) significantly reduced CTX levels, and exercise of > 60 min ($SMD = -0.22$, 95% CI : -0.47 to 0.03, $P = 0.09$) had a trend to reduce CTX levels and was not significant (Figure 12).

3.4.8 Effect of exercise on OC in postmenopausal women

There were 11 RCTs (16, 17, 19, 20, 22, 23, 25, 27, 32, 33, 37) on the effect of exercise on OC in postmenopausal women. Meta-analysis showed moderate heterogeneity of the included studies in



the exercise group compared to the control group ($I^2 = 14\%$, $P = 0.29$), so a fixed-effects model was used (Figures 13-15). The results showed a trend of increasing OC in the exercise group compared to the control group ($SMD = 0.21$, 95% CI: 0.05 to 0.37, $P = 0.01$) and were not significant. The subgroup analysis by exercise type showed that aerobic exercise ($SMD = 0.23$, 95% CI: 0.01 to 0.44, $P = 0.04$) and resistance exercise significantly ($SMD = 0.65$, 95% CI: 0.10 to 1.20, $P = 0.02$) increased OC levels; impact exercise ($SMD = 0.34$, 95% CI: -0.17 to 0.85, $P = 0.19$), combined aerobic plus resistance exercise ($SMD = 0.23$, 95% CI: -0.50 to 0.96, $P = 0.54$), Tai Chi ($SMD = -0.03$, 95% CI: -0.42 to 0.35, $P = 0.86$) and whole body vibration training ($SMD = -0.09$, 95% CI: -0.69 to 0.51, $P = 0.77$) showed a trend toward reducing OC, but without statistical significance (Figure 13). The refinement of sample size classification may have resulted in a smaller pooled effect size, and the insufficient number of studies led to unstable statistical results, making the findings less convincing. Cycle time subgroup analysis showed that exercise ≤ 6 months ($SMD = 0.35$, 95% CI: 0.13 to 0.57, $P = 0.002$) significantly elevated OC. exercise > 6 months ($SMD = 0.06$, 95% CI: -0.17 to 0.28, $P = 0.62$) showed a trend toward

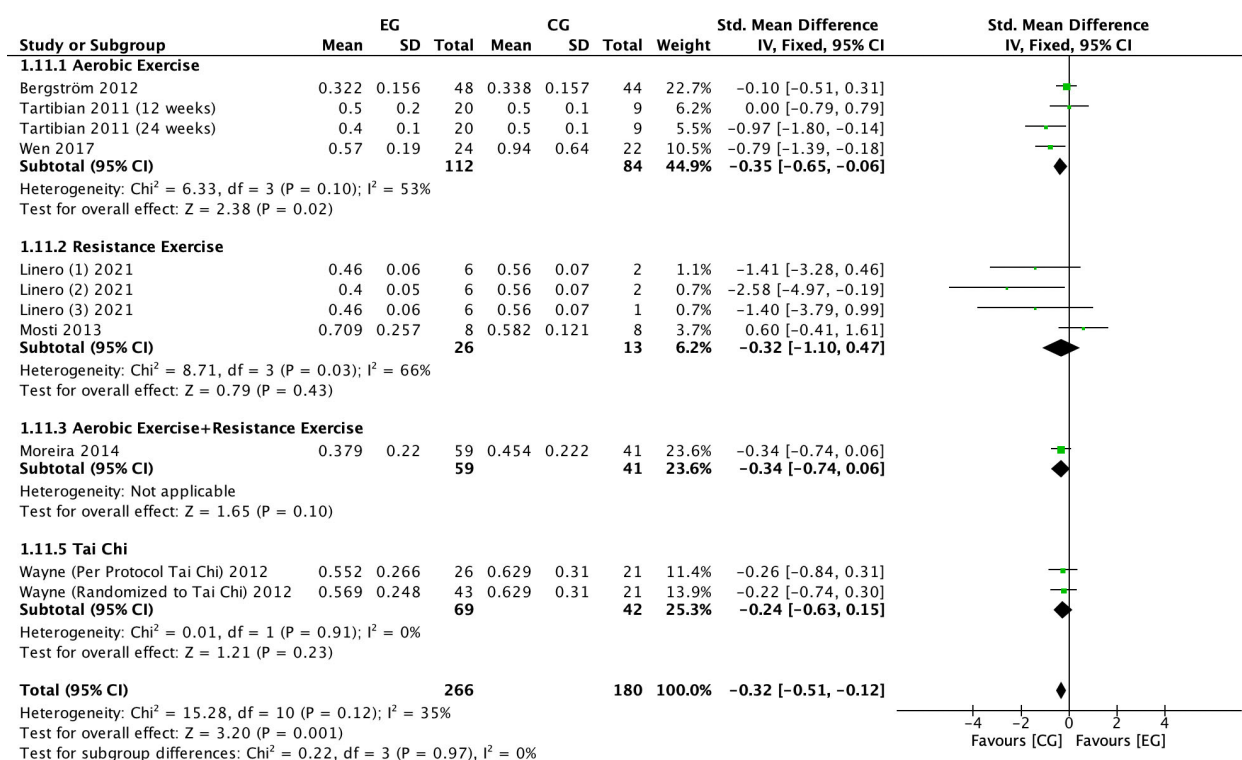


FIGURE 10

Forest plot of the effect of exercise on CTX in postmenopausal women (subgroup analysis of exercise type). EG, exercise group; CG, control group; SD, standard deviation; Std, standard; IV, inverse variance; df, degrees of freedom.

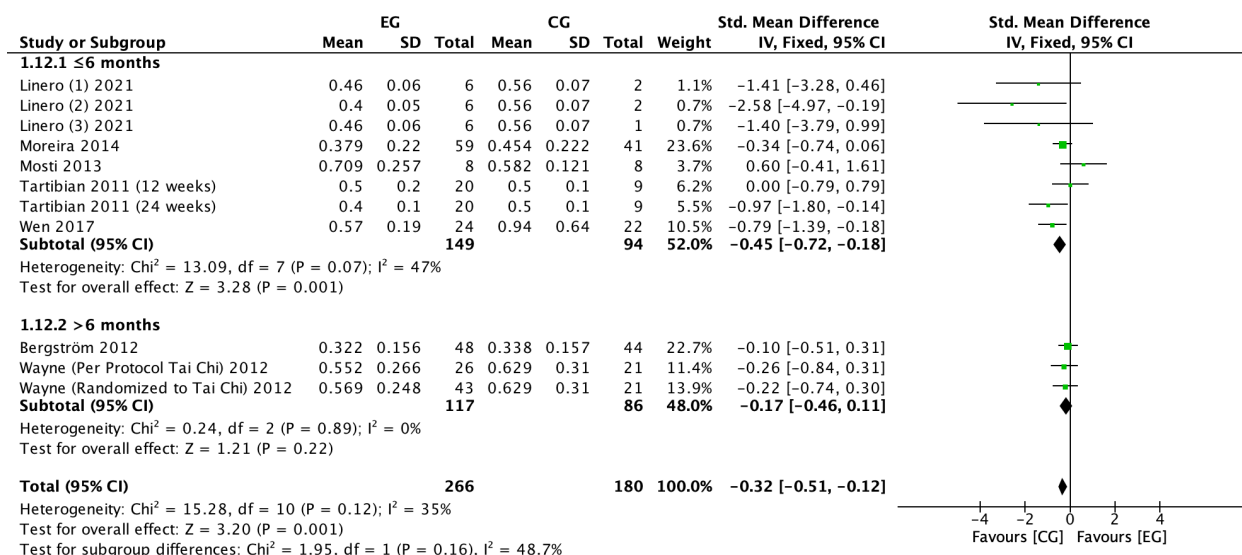
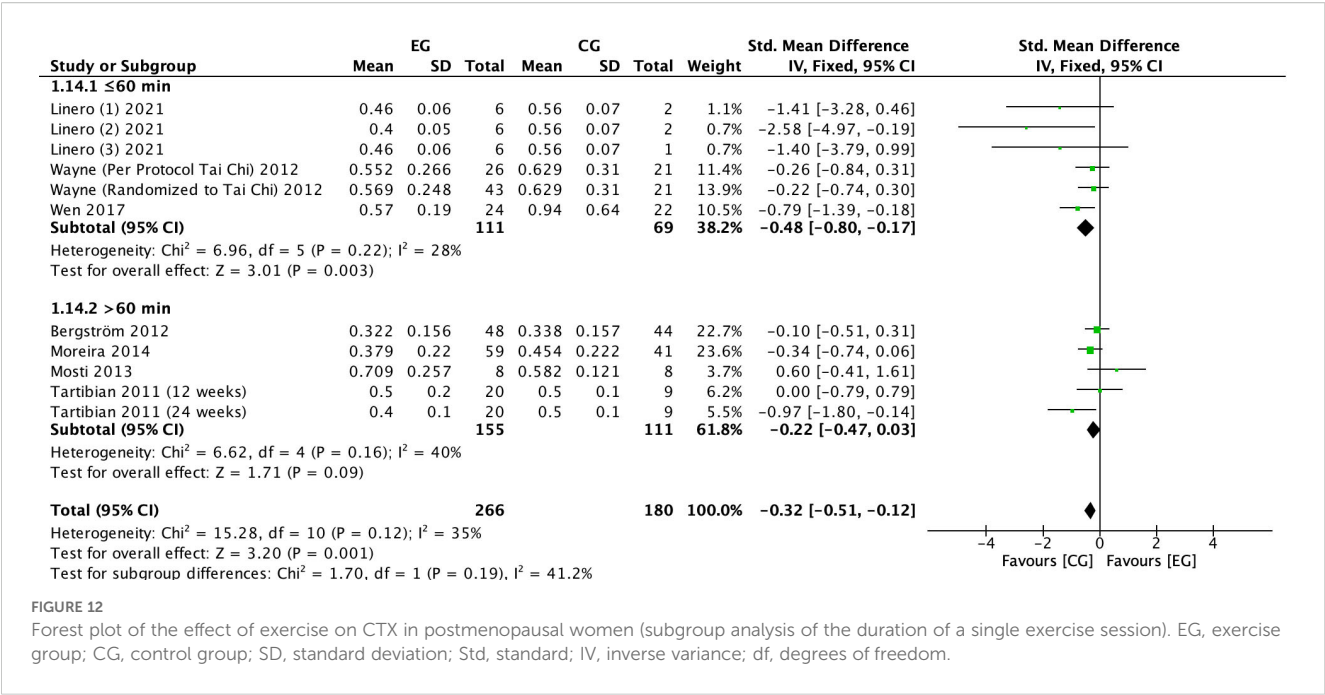


FIGURE 11

Forest plot of the effect of exercise on CTX in postmenopausal women (subgroup analysis of exercise cycles). EG, exercise group; CG, control group; SD, standard deviation; Std, standard; IV, inverse variance; df, degrees of freedom.



increasing OC levels and was not significant (Figure 14). Subgroup analysis of the duration of a single exercise session showed that exercise for ≤60 min (SMD = 0.20, 95% CI: 0.01 to 0.39, P = 0.04) elevated OC content; exercise for >60 min (SMD = -0.22, 95% CI: -0.07, 0.50, P = 0.13) tended to decrease OC content and was non-significant (Figure 15). 11 studies reported the effect of exercise on OC in postmenopausal women, so we assessed their publication bias. The funnel plot (Supplementary Figure S1) and Egger's test (P = 0.953) (Table 3) showed no evidence of publication bias.

3.5 Sensitivity analysis

The effect sizes after each indicator were removed from the study on a study-by-study basis were within the 95%CI of the total effect size, and therefore the effect on the total combined effect size was small and acceptable, strengthening the results of the original meta-analysis and making it more convincing (Supplementary Figures S2-S9).

3.6 Certainty of evidence

The certainty of evidence was rated as low for two outcomes (CTX and OC). The evidence of the remaining outcomes was rated as very low certainty. The reasons for downgrading were mainly attributed to the risk of bias of included studies and imprecision. The results of certainty of evidence are shown in Supplementary Table S3.

4 Discussion

Exercise, as an effective non-pharmacological intervention, may be the main reason for the improvement of bone health since bone

responds to mechanical loads and acts on the skeleton through muscular forces and ground reaction forces, which increase the density and strength of bone minerals (39). Exercise is widely recommended for the prevention of osteoporosis due to the osteogenic effects of these forces and the lack of side effects (39). To investigate the role of exercise on bone metabolism in postmenopausal women, the present study conducted a meta-analysis of relevant RCTs published to date, which is the gold standard for evaluating interventions and resides at the top of the evidence hierarchy for individual studies. The overall quality of the 24 RCTs included in the study was high, thus enhancing the reliability of the findings.

The results of the subgroup analysis in this study indicate that an exercise duration of ≤6 months and a session length of ≤60 minutes are more effective in reducing the bone resorption marker CTX, while significantly increasing the bone formation marker OC. Exercise exerts mechanical loading on bone tissue, which suppresses the secretion of sclerostin by osteocytes, thereby relieving the inhibition of the Wnt/β-catenin signaling pathway. This promotes the intracellular accumulation of β-catenin and its translocation into the nucleus, where it activates the expression of bone formation-related genes and enhances osteogenic activity (40–42). This pathway not only facilitates the differentiation and proliferation of osteoblasts but also upregulates osteoprotegerin expression, further inhibiting osteoclast activity and collectively shifting bone metabolism toward a state that favors bone formation (42, 43). In addition, Bone responds to mechanical loading with rapid saturation and recovery of sensitivity: during a single training bout, a limited number of loading cycles is sufficient to trigger osteogenic signaling, and prolonging the duration or increasing the number of cycles does not proportionally enhance the bone-forming effect (44). Short-duration (≤60 min) and regular mechanical loading, combined with adequate rest intervals, can

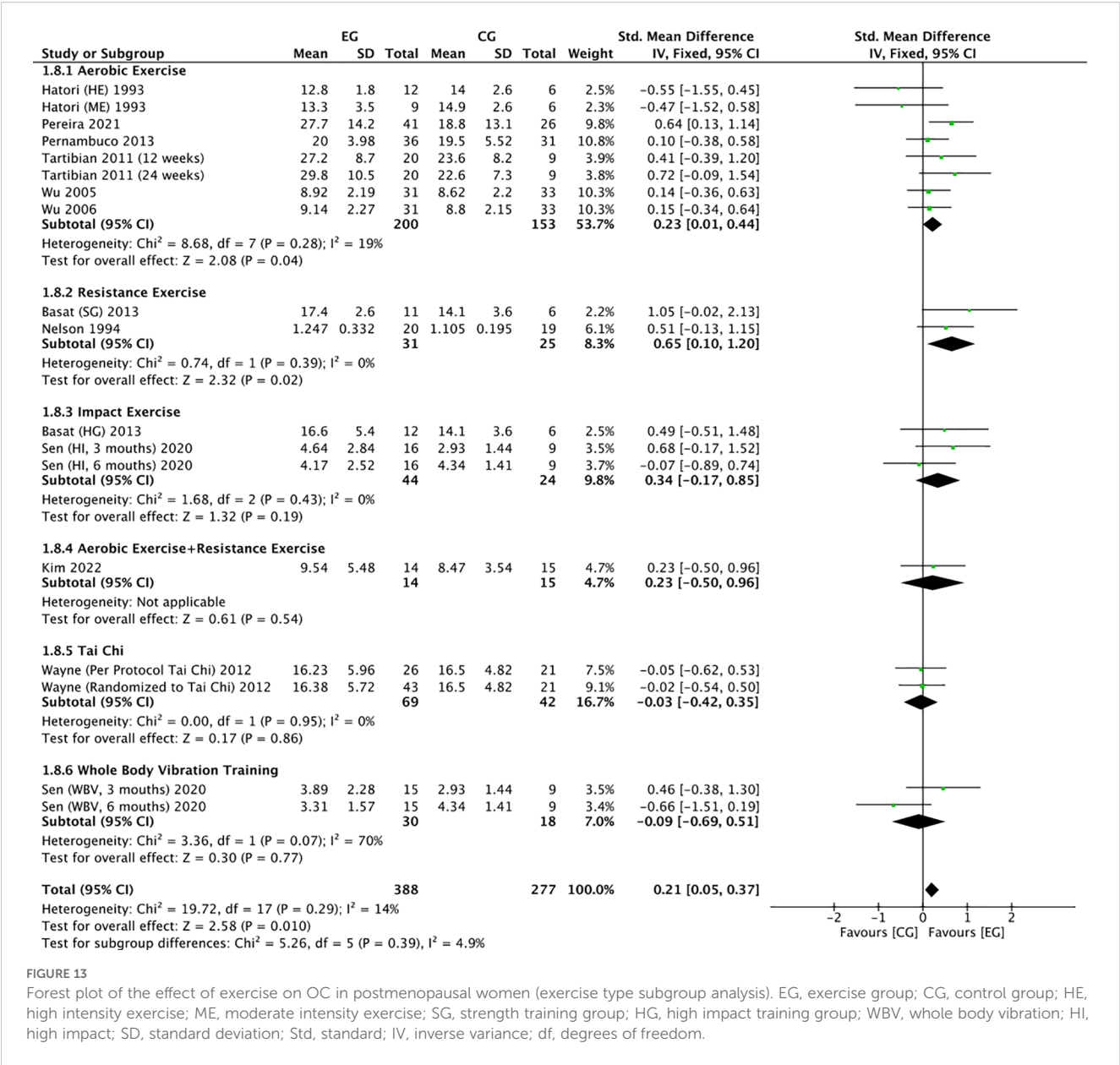


FIGURE 13 Forest plot of the effect of exercise on OC in postmenopausal women (exercise type subgroup analysis). EG, exercise group; CG, control group; HE, high intensity exercise; ME, moderate intensity exercise; SG, strength training group; HG, high impact training group; WBV, whole body vibration; HI, high impact; SD, standard deviation; Std, standard; IV, inverse variance; df, degrees of freedom.

effectively maintain the mechanosensitive of bone cells and thereby enhance bone metabolic responses (45). In addition, bone turnover markers such as P1NP and CTX have been shown to change significantly within several weeks to months of exercise intervention, suggesting that an intervention period of ≤ 6 months is sufficient to induce measurable improvements in bone metabolism (46). When mechanical loading is maintained in a fixed pattern over a long term, the mechanosensitive of bone cells gradually declines, leading to a “desensitization” phenomenon and reduced bone formation efficiency per training unit (47). Furthermore, long-term interventions are more likely to be affected by reduced adherence, soft tissue fatigue, hormonal fluctuations, and limited energy availability, all of which can attenuate positive adaptations in bone metabolism (48). Therefore, exercise prescriptions should emphasize moderate session duration, regular frequency, and periodic adjustments,

rather than simply extending the intervention time, to avoid plateaus and maximize the benefits of bone remodeling.

In their meta-analysis on the effects of Tai Chi on bone health in postmenopausal women, Liu et al. selected “6 months” as the cutoff point for intervention duration based on the physiological rationale of the bone remodeling cycle (49). The bone remodeling cycle typically takes 3–4 months to complete the sequential processes of bone resorption, formation, and mineralization, while achieving a new steady-state bone mass requires at least 6–8 months (50). Therefore, a 6-month intervention period ensures coverage of a full bone metabolic cycle, allowing for a more accurate assessment of the cumulative effects of exercise on bone mineral density.

Most meta-analyses related to the improvement of bone health by exercise have focused on bone mineral density (9, 51–54). In contrast, there are relatively few in-depth studies on the effects of exercise on bone metabolism. The health of bone metabolism is

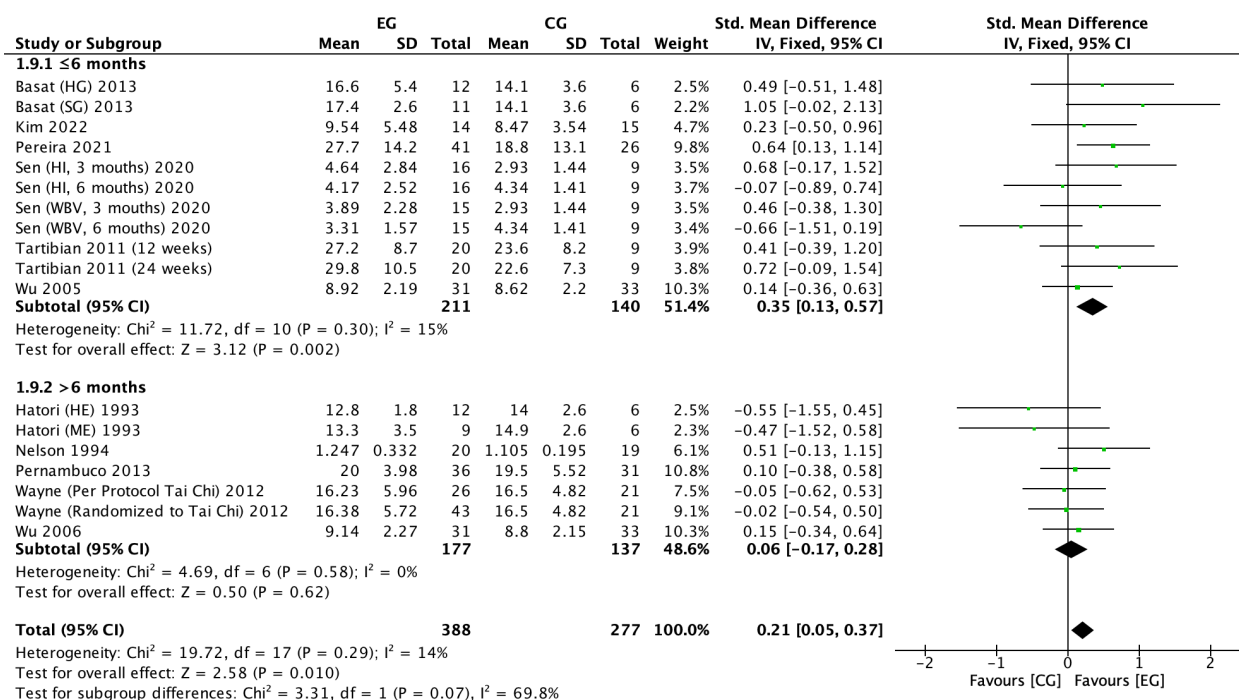


FIGURE 14

Forest plot of the effect of exercise on OC in postmenopausal women (exercise cycle subgroup analysis). EG, exercise group; CG, control group; HE, high intensity exercise; ME, moderate intensity exercise; SG, strength training group; HG, high impact training group; WBV, whole body vibration; HI, high impact; SD, standard deviation; Std, standard; IV, inverse variance; df, degrees of freedom.

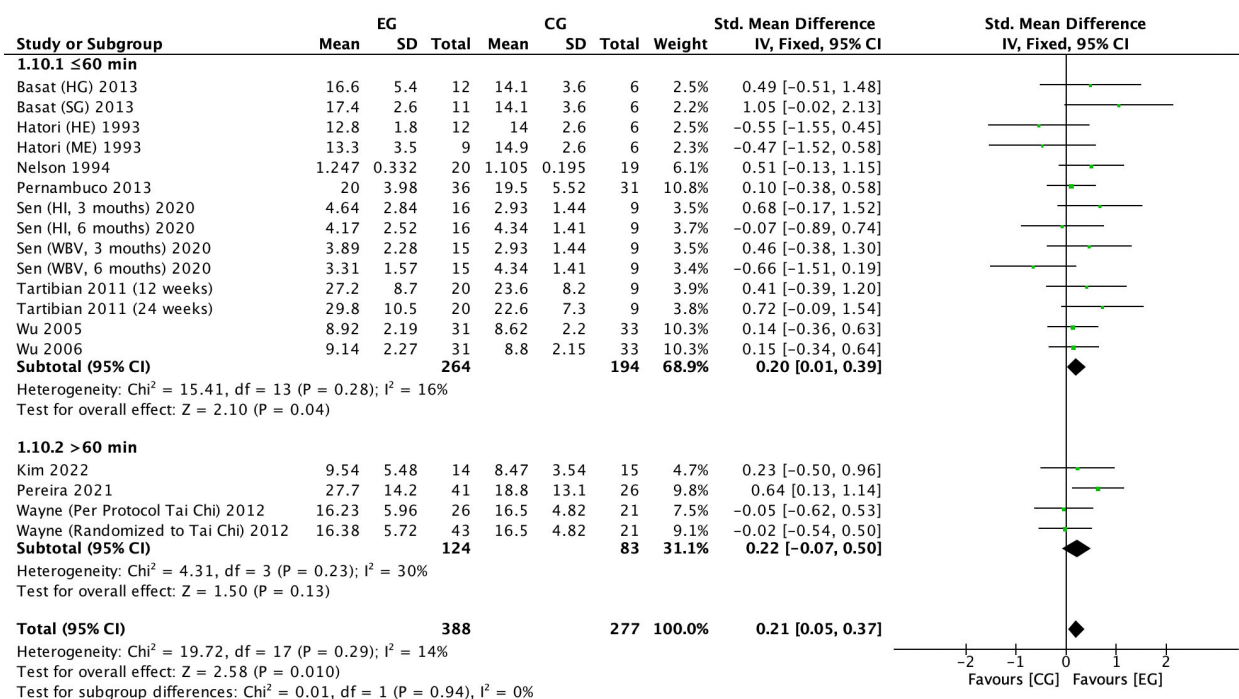


FIGURE 15

Forest plot of the effect of exercise on OC in postmenopausal women (subgroup analysis of the duration of a single exercise session). EG, exercise group; CG, control group; HE, high intensity exercise; ME, moderate intensity exercise; SG, strength training group; HG, high impact training group; WBV, whole body vibration; HI, high impact; SD, standard deviation; Std, standard; IV, inverse variance; df, degrees of freedom.

TABLE 3 Egger test results.

Std_Eff	Coefficient	Std. err	t	P> t	(95% conf. interval)
slope	.1926973	.3412466	0.56	0.580	-.5307131.9161077
bias	.0602132	.9994193	0.06	0.953	-2.058461 2.178887

crucial for maintaining bone strength and stability, which involves multiple aspects of bone growth, remodeling, and repair. By promoting bone metabolism, it not only enhances the stress resistance of bones and reduces the risk of fracture, but also improves the bone microstructure and enhances the overall quality of bones. Therefore, strengthening research on the relationship between exercise and bone metabolism is of great significance in preventing osteoporosis and promoting bone health. Under physiological conditions, bone resorption and bone formation maintain a dynamic balance in bone metabolism (55). Bone metabolism markers are metabolites produced in the process of bone transformation and play an important role in the diagnosis and treatment of osteoporosis because they can timely and accurately reflect the state of bone transformation in the human body (56). Bone metabolism includes two processes: bone resorption and bone formation. Bone resorption is a process in which osteoclasts break down part of the bone and form a cavity (bone resorption cavity), during which bone metabolites are formed that can enter the bloodstream or be excreted through urine, a process that lasts 4–6 weeks (57). Bone formation, on the other hand, takes place in the cavity formed by bone resorption, during which molecules secreted by osteoblasts can enter the bloodstream while completing cavity ossification (58). Bone formation markers reflect the activity of osteoblasts, and the bone formation markers included in this exploration are OC, ALP, BALP, and P1NP. Bone resorption markers reflect the activity of osteoclasts, and the bone resorption markers included in this study are CT. It has been suggested that bone resorption may have an impact on bone health in the context of reduced or unchanged bone resorption (59). In terms of predicting fracture risk, bone metabolism markers have been correlated with fracture risk, with higher concentrations of bone metabolism markers being associated with greater fracture risk (12). Other studies have shown that bone metabolism markers are more useful in understanding the state of bone mass by their ability to capture information about bone transition state, which is the 2nd most important factor in the development of osteoporosis and the occurrence of fragility fractures, as opposed to BMD by measuring bone mass (60). It has also been suggested that bone metabolic markers may influence fracture risk independently of BMD (by influencing bone strength) (61). Bone metabolism markers have a unique advantage in monitoring therapy in that they respond rapidly to changes in bone physiology and remain relatively stable, which can help physicians to have sufficient response time to determine adjustments to treatment regimens in the event of poor efficacy, which can be particularly useful in patients with demanding treatment regimens such as bisphosphonate therapy (62). In conclusion, through the unremitting efforts of researchers, bone metabolism markers are

becoming richer and richer, their application aspects are becoming broader and broader, and their role in the diagnosis and treatment of osteoporosis is becoming more and more prominent, but more research is needed to improve the diagnostic and therapeutic system of bone metabolism biochemical markers to be widely used in the clinic.

The results of the meta-analysis showed that, compared with the control group, exercise was effective in increasing the levels of bone formation markers, such as ALP, P1NP, and OC, in postmenopausal women. ALP on the other hand widely present in various tissues of the human body, serum ALP is mainly derived from liver, bone and kidney tissues, it is a marker of bone formation, and studies suggest that ALP has an important role in the pathogenesis of osteoporosis (63). Serum ALP levels are significantly elevated in pathological conditions, such as the occurrence of diseases of the hepatobiliary system, as well as bone diseases (64). The level of P1NP in the serum reflects the ability of osteoblasts to synthesize osteoclasts collagen and forms the basis of a laboratory index for monitoring osteoblast viability and bone formation (65). Its blood level mainly reflects the rate of type I collagen synthesis and bone conversion, and is a specific and sensitive indicator of new bone formation (66). The results of Kohrt et al. (67) showed that P1NP increased with exercise ($P<0.001$), suggesting that exercise promotes the synthesis of P1NP, which, in turn, enhances osteoclast viability and promotes bone formation. OC is a protein secreted by osteoblasts secreted protein that plays an important role in maintaining bone health (68). Numerous studies have shown that exercise can promote osteogenic differentiation of bone marrow mesenchymal stem cells and osteoblasts, promote bone formation, improve bone metabolism, and thus prevent and control osteoporosis (69). OC is a key osteogenic factor in the process of bone formation, and thus exercise can promote blood circulation and metabolism in the skeleton, which may stimulate osteoblasts to secrete more OC (70). Exercise activates the mechanotransduction pathways in osteocytes by applying mechanical load, thereby upregulating the expression of osteogenic markers such as OC and ALP, while simultaneously inhibiting bone resorption by regulating the balance of osteoprotegerin (OPG) and receptor activator of nuclear factor κ B ligand (RANKL). Specifically, exercise increases OPG expression and decreases RANKL expression, thereby suppressing osteoclast differentiation and activity (71). Animal studies have shown that treadmill and vibration training can reduce RANKL and increase OPG (72), and mechanical strain can directly inhibit RANKL expression (73).

The results of this study showed that exercise significantly reduced the levels of bone resorption markers such as PTH and CTX in postmenopausal women. PTH is a hormone that regulates

calcium and phosphorus metabolism, and 15.6% of postmenopausal osteoporosis patients had elevated PTH. The results of the study on the correlation between osteoporosis-related hormones and bone mineral density showed that the level of serum PTH was negatively correlated with bone mineral density, which allowed early detection of osteoporosis (74). Its reduction by exercise may imply improve bone health in middle-aged and older adults. CTX is the most widely used marker of collagen degradation, and the level of CTX reflects the bone resorption activity of osteoclasts. CTX is a valid marker for metabolic bone diseases characterized by significantly increased osteoclast activity (75). CTX correlates with the degree of bone resorption and responds rapidly and sensitively to antiresorptive therapy. Detection of serum CTX levels can predict the severity of bone conversion, and serve as a clinically important reference index for assessing bone conversion-related diseases (58). Exercise-induced changes in PTH and CTX concentration levels are consistent with a study on the effects of bath therapy and aquatic exercise on these two hormones (11).

The results also showed that exercise did not significantly affect serum phosphorus, serum calcium and 25(OH)D in postmenopausal women. Serum phosphorus and serum calcium play several important roles in bone metabolism with exercise intervention, which is involved in bone formation and repair, influences changes in bone metabolism markers, regulates acid-base balance and cellular osmotic pressure, and interacts with calcium and phosphorus (76–78). For serum phosphorus and serum calcium, exercise may indeed have some effect on them, but the exact effect varies from person to person. Exercise promotes an increase in metabolic rate, which in turn affects the phosphorus-calcium balance in the blood (79). 25(OH)D is the main form of vitamin D in the body and is essential for calcium absorption and bone health (80). 25(OH)D acts as a calcium-regulating hormone that inhibits the elevation of PTH, increases osteomineralization to prevent bone loss, strengthens muscles, improves balance, and prevents falls in the elderly (80). Groenendijk (81) and others showed that fortified milk supplementation and exercise intervention successfully improved 25(OH)D concentrations and the balance of bone turnover markers in Chinese middle-aged and elderly people. The effects of exercise on bone metabolism are complex, and although serum phosphorus, serum calcium, and 25(OH)D play important roles in bone health, the specific effects of exercise on serum phosphorus, serum calcium, and 25(OH)D may not be significant, possibly due to differences in exercise modalities and intensities, as well as individual differences.

Our subgroup analysis demonstrated that both aerobic and resistance exercise significantly increased OC levels in postmenopausal women, while aerobic exercise also reduced CTX levels. Previous studies suggest that aerobic exercise may increase osteoprotegerin levels, which helps suppress osteoclastogenesis and reduce bone loss, thereby leading to decreased serum CTX and elevated OC levels (23, 82). In contrast, resistance exercise promotes osteoblast activity through direct mechanical loading, resulting in increased OC levels (82, 83). High-load and explosive training methods enhance one-repetition maximum (1RM) strength and

rate of force development, thereby stimulating bone formation, increasing bone mineral content, and potentially triggering adaptive skeletal responses through mechanical stress (25). High-impact exercise, by increasing mechanical loading on the skeleton, significantly improves bone mineral density of the lumbar spine and femoral neck, while also promoting an increase in bone formation markers (e.g., OC) and reducing bone resorption markers (e.g., P1NP), thus improving bone metabolism in postmenopausal women with osteoporosis (30). Tai Chi, as a mind-body exercise, may indirectly reduce fall risk by improving balance and muscle strength, while also slowing bone loss and slightly increasing bone density (e.g., in the femoral neck region) through moderate mechanical loading (37). Whole-body vibration training promotes bone formation and reduces bone resorption through high-frequency, low-amplitude mechanical stimulation, thereby increasing bone density and mechanical strength, with particularly notable effects in the femoral neck and lumbar spine regions (29).

Limitations: (i) As the study was an analysis of different bone metabolism by different exercise types, the refinement of the sample size classification may have resulted in a smaller amount of combined effects, which may have had a certain impact on the results, so the analysis was not carried out on the exercise types; (ii) The included studies exhibited heterogeneity in the methods used to measure bone metabolism markers (e.g., IRMA, ELISA), which may affect the comparability and synthesis of the results; (iii) Most of the included studies involved short-term interventions and lacked long-term follow-up data (>2 years); therefore, the sustainability of the intervention effects and their long-term impact on bone health could not be clearly evaluated; (iv) Since all included studies were RCTs, the between-group differences at baseline should theoretically approach zero, which justified our use of post-intervention values for the meta-analysis. However, although randomization balances baseline differences, potential confounding factors may not be fully controlled, which could introduce some bias into the results. Future studies should prioritize reporting baseline data and change-from-baseline values to allow for more comprehensive analyses; (v) This study only searched English-language databases, potentially omitting relevant studies published in other languages (e.g., Chinese, Spanish), which may limit the comprehensiveness and representativeness of the results. Future research should include multilingual databases to reduce potential language bias; (vi) The applicability of our study results to populations from different regions or ethnic backgrounds may be limited, particularly in groups with substantial differences in baseline bone health, lifestyle, or genetic background, and thus should be generalized with caution; (vii) In the study, although the 6-month intervention duration was justified based on the physiological rationale of the bone remodeling cycle, the cut-off point of 60 minutes for single-session exercise duration lacks a clear physiological basis. The choice of this cut-off may be more related to the distribution of the data or operational convenience rather than physiological significance. Therefore, we acknowledge the potential bias that may be introduced by this arbitrary cut-off.

5 Conclusion

The systematic review and meta-analysis of this study demonstrated that regular exercise has significant effects on bone metabolism in postmenopausal women by reducing bone resorption and enhancing bone formation. Aerobic exercise effectively decreases CTX levels, while both aerobic and resistance exercise effectively increase OC levels. Short-term interventions (≤ 6 months) and moderate-duration sessions (≤ 60 minutes per session) show notable benefits in lowering CTX and elevating OC. However, more rigorously designed randomized controlled trials are needed to confirm the benefits of exercise on bone metabolism and to determine the optimal intervention strategies. Due to the small number of studies, it was not possible to determine the effects on other bone metabolism metrics. However, more rigorously designed randomized controlled trials are needed to validate the benefits of exercise on bone metabolism and to explore its optimal protocol.

Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**. Further inquiries can be directed to the corresponding author.

Author contributions

WZ: Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. XL: Data curation, Formal analysis, Investigation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. QH: Formal analysis, Methodology, Writing – original draft, Writing – review & editing. XW: Conceptualization, Funding acquisition, Supervision, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research and/or publication of this article. This study was supported

by the Social Science Planning Research Program of Shandong Province in 2021 (21DTYJ03).

Acknowledgments

Thanks to all authors for their contributions.

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.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

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/fendo.2025.1597046/full#supplementary-material>

References

- Mingjian N, Hongjuan L, Mei W. Effect of exercise on bone health in postmenopausal women with osteoporosis. *Med Sci Sports Exercise*. (2022) 54:532. doi: 10.1249/01.mss.0000881740.83096.11
- Levin VA, Jiang X, Kagan R. Estrogen therapy for osteoporosis in the modern era. *Osteoporos Int*. (2018) 29:1049–55. doi: 10.1007/s00198-018-4414-z
- Kelley GA, Kelley KS, Tran ZV. Exercise and lumbar spine bone mineral density in postmenopausal women: a meta-analysis of individual patient data. *J Gerontol A Biol Sci Med Sci*. (2002) 57:M599–604. doi: 10.1093/gerona/57.9.M599
- Li J, Gu Q, Li R, Wang R, Cai Y, Huang Y, et al. Effect of Yi Jin Jing exercise plus Elastic Band Resistance exercise on overall bone mineral density in postmenopausal women. *J Sci Med Sport*. (2023) 26:87–92. doi: 10.1016/j.jsams.2023.01.006
- Shen CL, Chyu MC, Yeh JK, Zhang Y, Pence BC, Felton CK, et al. Effect of green tea and Tai Chi on bone health in postmenopausal osteopenic women: a 6-month randomized placebo-controlled trial. *Osteoporos Int*. (2012) 23:1541–52. doi: 10.1007/s00198-011-1731-x
- Wen HJ, Huang TH, Li TL, Chong PN, Ang BS. Effects of short-term step aerobics exercise on bone metabolism and functional fitness in postmenopausal women with low bone mass. *Osteoporos Int*. (2017) 28:539–47. doi: 10.1007/s00198-016-3759-4
- Xiao CM, Kang Y, Zhuang YC. Effects of elastic resistance band exercise on postural balance, estrogen, bone metabolism index, and muscle strength of perimenopausal period women. *J Am Geriatr Soc*. (2016) 64:1368–70. doi: 10.1111/jgs.14172

8. Bonaïuti D, Shea B, Iovine R, Negrini S, Robinson V, Kemper HC, et al. Exercise for preventing and treating osteoporosis in postmenopausal women. *Cochrane Database Syst Rev*. (2002) 6:CD000333. doi: 10.1002/14651858
9. Zhang S, Huang X, Zhao X, Li B, Cai Y, Liang X, et al. Effect of exercise on bone mineral density among patients with osteoporosis and osteopenia: A systematic review and meta-analysis. *J Clin Nurs*. (2022) 31:2100–11. doi: 10.1111/jocn.16101
10. Shojaa M, von Stengel S, Kohl M, Schoene D, Kemmler W. Effects of dynamic resistance exercise on bone mineral density in postmenopausal women: a systematic review and meta-analysis with special emphasis on exercise parameters. *Osteoporos Int*. (2020) 31:1427–44. doi: 10.1007/s00198-020-05441-w
11. Lv X, Wang J, Bao Y, Tang Y, Xing W, Wu Q, et al. The effectiveness of balneotherapy and aquatic exercise on bone metabolism: A systematic review and meta-analysis. *Complement Ther Clin Pract*. (2021) 44:101429. doi: 10.1016/j.ctcp.2021.101429
12. Greenblatt MB, Tsai JN, Wein MN. Bone turnover markers in the diagnosis and monitoring of metabolic bone disease. *Clin Chem*. (2017) 63:464–74. doi: 10.1373/clinchem.2016.259085
13. 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
14. Higgins JP, Altman DG, Gotzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *Bmj*. (2011) 343:d5928. doi: 10.1136/bmj.d5928
15. Zhang Y, Akl EA, Schünemann HJ. Using systematic reviews in guideline development: the GRADE approach. *Res Synth Methods*. (2019) 10:312–29. doi: 10.1002/jrsm.1313
16. Hatori M, Hasegawa A, Adachi H, Shinokaki A, Hayashi R, Okano H, et al. The effects of walking at the anaerobic threshold level on vertebral bone loss in postmenopausal women. *Calcif Tissue Int*. (1993) 52:411–4. doi: 10.1007/BF00571327
17. Nelson ME, Fiatarone MA, Morganti CM, Trice I, Greenberg RA, Evans WJ. Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures. A randomized controlled trial. *Jama*. (1994) 272:1909–14. doi: 10.1001/jama.1994.03520240037038
18. Iwamoto J, Takeda T, Ichimura S. Effect of exercise training and detraining on bone mineral density in postmenopausal women with osteoporosis. *J Orthop Sci*. (2001) 6:128–32. doi: 10.1007/s007760100059
19. Wu J, Oka J, Higuchi M, Tabata I, Toda T, Fujioka M, et al. Cooperative effects of isoflavones and exercise on bone and lipid metabolism in postmenopausal Japanese women: a randomized placebo-controlled trial. *Metabolism*. (2006) 55:423–33. doi: 10.1016/j.metabol.2005.10.002
20. Wu J, Oka J, Tabata I, Higuchi M, Toda T, Fuku N, et al. Effects of isoflavone and exercise on BMD and fat mass in postmenopausal Japanese women: a 1-year randomized placebo-controlled trial. *J Bone Miner Res*. (2006) 21:780–9. doi: 10.1359/jbmr.060208
21. Ay A, Yurtkuran M. Evaluation of hormonal response and ultrasonic changes in the heel bone by aquatic exercise in sedentary postmenopausal women. *Am J Phys Med Rehabil*. (2003) 82:942–9. doi: 10.1097/01.PHM.0000098039.58584.59
22. Tartibian B, Hajizadeh Maleki B, Kanaley J, Sadeghi K. Long-term aerobic exercise and omega-3 supplementation modulate osteoporosis through inflammatory mechanisms in post-menopausal women: a randomized, repeated measures study. *Nutr Metab (Lond)*. (2011) 8:71. doi: 10.1186/1743-7075-8-71
23. Bergström I, Parini P, Gustafsson SA, Andersson G, Brinck J. Physical training increases osteoprotegerin in postmenopausal women. *J Bone Miner Metab*. (2012) 30:202–7. doi: 10.1007/s00774-011-0304-6
24. Basat H, Esmailzadeh S, Eskiurt N. The effects of strengthening and high-impact exercises on bone metabolism and quality of life in postmenopausal women: a randomized controlled trial. *J Back Musculoskeletal Rehabil*. (2013) 26:427–35. doi: 10.3233/BMR-130402
25. Mosti MP, Kaehler N, Stunes AK, Hoff J, Syversen U. Maximal strength training in postmenopausal women with osteoporosis or osteopenia. *J Strength Cond Res*. (2013) 27:2879–86. doi: 10.1519/JSC.0b013e318280d4e2
26. Roghani T, Torkaman G, Movasseghe S, Hedayati M, Goosheh B, Bayat N. Effects of short-term aerobic exercise with and without external loading on bone metabolism and balance in postmenopausal women with osteoporosis. *Rheumatol Int*. (2013) 33:291–8. doi: 10.1007/s00296-012-2388-2
27. Pernambuco CS, Borba-Pinheiro CJ, Vale RG, Di Masi F, Monteiro PK, Dantas EH. Functional autonomy, bone mineral density (BMD) and serum osteocalcin levels in older female participants of an aquatic exercise program (AAG). *Arch Gerontol Geriatr*. (2013) 56:466–71. doi: 10.1016/j.archger.2012.12.012
28. Moreira LD, Fronza FC, Dos Santos RN, Zach PL, Kunii IS, Hayashi LF, et al. The benefits of a high-intensity aquatic exercise program (HydROS) for bone metabolism and bone mass of postmenopausal women. *J Bone Miner Metab*. (2014) 32:411–9. doi: 10.1007/s00774-013-0509-y
29. Baker MK, Peddle-McIntyre CJ, Galvão DA, Hunt C, Spry N, Newton RU. Whole body vibration exposure on markers of bone turnover, body composition, and physical functioning in breast cancer patients receiving aromatase inhibitor therapy: A randomized controlled trial. *Integr Cancer Ther*. (2018) 17:968–78. doi: 10.1177/1534735418781489
30. Sen EI, Esmailzadeh S, Eskiurt N. Effects of whole-body vibration and high impact exercises on the bone metabolism and functional mobility in postmenopausal women. *J Bone Miner Metab*. (2020) 38:392–404. doi: 10.1007/s00774-019-01072-2
31. Linero C, Choi SJ. Effect of blood flow restriction during low-intensity resistance training on bone markers and physical functions in postmenopausal women. *J Exerc Sci Fit*. (2021) 19:57–65. doi: 10.1016/j.jesf.2020.09.001
32. Pereira R, Krstrup P, Castagna C, Coelho E, Santos R, Helge EW, et al. Effects of recreational team handball on bone health, postural balance and body composition in inactive postmenopausal women - A randomised controlled trial. *Bone*. (2021) 145:115847. doi: 10.1016/j.bone.2021.115847
33. Kim AR, Soeun L, Yoo-Jin S, Seung-Wook C. The effect of 6-month complex exercise on serum bone metabolism: focused on the elderly over 75 years old. *Appl Sci*. (2022) 12:11373. doi: 10.3390/app122211373
34. Zaravar F, Tamaddon G, Zaravar L, Koushkie Jahromi M. The effect of aquatic training and vitamin D3 supplementation on bone metabolism in postmenopausal obese women. *J Exerc Sci Fit*. (2024) 22:127–33. doi: 10.1016/j.jesf.2024.01.002
35. Guzel Y, Atakan MM, Areta JL, Turnagol HH, Kosar SN. Ten weeks of low-volume walking training improve cardiometabolic health and body composition in sedentary postmenopausal women with obesity without affecting markers of bone metabolism. *Res Sports Med*. (2024) 32:331–43. doi: 10.1080/15438627.2022.2113877
36. Pasa C, Pamungkasari EP, Doewes M, Purwanto B, Hartono H, Cilmiaty R, et al. Effect of walking and bone joint exercise on enhancing bone remodeling in menopausal women: A randomized controlled trial. *Narra J*. (2024) 4:e1321. doi: 10.52225/narra.v4i3.1321
37. Wayne PM, Kiel DP, Buring JE, Connors EM, Bonato P, Yeh GY, et al. Impact of Tai Chi exercise on multiple fracture-related risk factors in post-menopausal osteopenic women: a pilot pragmatic, randomized trial. *BMC Complement Altern Med*. (2012) 12:7. doi: 10.1186/1472-6882-12-7
38. Shen CL, Chyu MC, Pence BC, Yeh JK, Zhang Y, Felton CK, et al. Green tea polyphenols supplementation and Tai Chi exercise for postmenopausal osteopenic women: safety and quality of life report. *BMC Complement Altern Med*. (2010) 10:76. doi: 10.1186/1472-6882-10-76
39. Yan Y, Tan B, Fu F, Chen Q, Li W, Chen W, et al. Exercise vs conventional treatment for treatment of primary osteoporosis: A systematic review and meta-analysis of randomized controlled trials. *Orthop Surg*. (2021) 13:1474–87. doi: 10.1111/os.13036
40. Choi RB, Robling AG. The Wnt pathway: An important control mechanism in bone's response to mechanical loading. *Bone*. (2021) 153:116087. doi: 10.1016/j.bone.2021.116087
41. Kang KS, Robling AG. New insights into wnt-lrp5/6- β -catenin signaling in mechanotransduction. *Front Endocrinol (Lausanne)*. (2014) 5:246. doi: 10.3389/fendo.2014.00246
42. Wang X, Qu Z, Zhao S, Luo L, Yan L. Wnt/ β -catenin signaling pathway: proteins' roles in osteoporosis and cancer diseases and the regulatory effects of natural compounds on osteoporosis. *Mol Med*. (2024) 30:193. doi: 10.1186/s10020-024-00957-x
43. Maeda K, Kobayashi Y, Koide M, Uehara S, Okamoto M, Ishihara A, et al. The regulation of bone metabolism and disorders by wnt signaling. *Int J Mol Sci*. (2019) 20:5525. doi: 10.3390/ijms20225525
44. Turner CH, Robling AG. Designing exercise regimens to increase bone strength. *Exerc Sport Sci Rev*. (2003) 31:45–50. doi: 10.1097/00003677-200301000-00009
45. Robling AG, Turner CH. Mechanical signaling for bone modeling and remodeling. *Crit Rev Eukaryot Gene Expr*. (2009) 19:319–38. doi: 10.1615/CritRevEukaryotGeneExpr.v19.i4.50
46. Scott JP, Sale C, Greeves JP, Casey A, Dutton J, Fraser WD. The role of exercise intensity in the bone metabolic response to an acute bout of weight-bearing exercise. *J Appl Physiol*. (1985). (2011) 110:423–32. doi: 10.1152/jappphysiol.00764.2010
47. Robling AG, Hinant FM, Burr DB, Turner CH. Improved bone structure and strength after long-term mechanical loading is greatest if loading is separated into short bouts. *J Bone Miner Res*. (2002) 17:1545–54. doi: 10.1359/jbmr.2002.17.8.1545
48. Tenforde AS, Fredericson M. Influence of sports participation on bone health in the young athlete: a review of the literature. *Pm R*. (2011) 3:861–7. doi: 10.1016/j.pmrj.2011.05.019
49. Liu X, Jiang C, Fan R, Liu T, Li Y, Zhong D, et al. The effect and safety of Tai Chi on bone health in postmenopausal women: A meta-analysis and trial sequential analysis. *Front Aging Neurosci*. (2022) 14:935326. doi: 10.3389/fnagi.2022.935326
50. Kohrt WM, Bloomfield SA, Little KD, Nelson ME, Yingling VR. American College of Sports Medicine Position Stand: physical activity and bone health. *Med Sci Sports Exerc*. (2004) 36:1985–96. doi: 10.1249/01.MSS.0000142662.21767.58
51. Schinzel E, Kast S, Kohl M, von Stengel S, Jakob F, Kersch-Schindl K, et al. The effect of aquatic exercise on bone mineral density in older adults. A systematic review and meta-analysis. *Front Physiol*. (2023) 14:1135663. doi: 10.3389/fphys.2023.1135663
52. Kast S, Shojaa M, Kohl M, von Stengel S, Gosch M, Jakob F, et al. Effects of different exercise intensity on bone mineral density in adults: a comparative systematic review and meta-analysis. *Osteoporos Int*. (2022) 33:1643–57. doi: 10.1007/s00198-022-06329-7
53. Mages M, Shojaa M, Kohl M, von Stengel S, Becker C, Gosch M, et al. Exercise effects on bone mineral density in men. *Nutrients*. (2021) 13:4244. doi: 10.3390/nut13124244

54. Kemmler W, Shojaa M, Kohl M, von Stengel S. Effects of different types of exercise on bone mineral density in postmenopausal women: A systematic review and meta-analysis. *Calcif Tissue Int.* (2020) 107:409–39. doi: 10.1007/s00223-020-00744-w
55. Uenaka M, Yamashita E, Kikuta J, Morimoto A, Ao T, Mizuno H, et al. Osteoblast-derived vesicles induce a switch from bone-formation to bone-resorption *in vivo*. *Nat Commun.* (2022) 13:1066. doi: 10.1038/s41467-022-28673-2
56. Garnero P. New developments in biological markers of bone metabolism in osteoporosis. *Bone.* (2014) 66:46–55. doi: 10.1016/j.bone.2014.05.016
57. Qiu S, Rao DS, Palnitkar S, Parfitt AM. Dependence of bone yield (volume of bone formed per unit of cement surface area) on resorption cavity size during osteonal remodeling in human rib: implications for osteoblast function and the pathogenesis of age-related bone loss. *J Bone Miner Res.* (2010) 25:423–30. doi: 10.1359/jbmr.091003
58. Eastell R, Szulc P. Use of bone turnover markers in postmenopausal osteoporosis. *Lancet Diabetes Endocrinol.* (2017) 5:908–23. doi: 10.1016/S2213-8587(17)30184-5
59. Evans EM, Racette SB, Van Pelt RE, Peterson LR, Villareal DT. Effects of soy protein isolate and moderate exercise on bone turnover and bone mineral density in postmenopausal women. *Menopause.* (2007) 14:481–8. doi: 10.1097/01.gme.0000243570.78570.f7
60. Park SY, Ahn SH, Yoo JI, Chung YJ, Jeon YK, Yoon BH, et al. Position statement on the use of bone turnover markers for osteoporosis treatment. *J Bone Metab.* (2019) 26:213–24. doi: 10.11005/jbm.2019.26.4.213
61. Tian A, Ma J, Feng K, Liu Z, Chen L, Jia H, et al. Reference markers of bone turnover for prediction of fracture: a meta-analysis. *J Orthop Surg Res.* (2019) 14:68. doi: 10.1186/s13018-019-1100-6
62. Wu CH, Chang YF, Chen CH, Lewiecki EM, Wüster C, Reid I, et al. Consensus statement on the use of bone turnover markers for short-term monitoring of osteoporosis treatment in the Asia-Pacific region. *J Clin Densitom.* (2021) 24:3–13. doi: 10.1016/j.jocd.2019.03.004
63. Chen L, Jiang W, Huang J, He BC, Zuo GW, Zhang W, et al. Insulin-like growth factor 2 (IGF-2) potentiates BMP-9-induced osteogenic differentiation and bone formation. *J Bone Miner Res.* (2010) 25:2447–59. doi: 10.1002/jbmr.133
64. Anupam K, Dana E, Jennifer RG, Ian DH, Castro MR. Predicting outcomes in sporadic and hereditary medullary thyroid carcinoma over two decades. *Thyroid.* (2021) 31:616–26. doi: 10.1089/thy.2020.0167
65. Mentzel J, Kynast T, Kohlmann J, Kirsten H, Blüher M, Simon JC, et al. Reduced serum levels of bone formation marker P1NP in psoriasis. *Front Med (Lausanne).* (2021) 8:730164. doi: 10.3389/fmed.2021.730164
66. Samoszuk M, Leuther M, Hoyle N. Role of serum P1NP measurement for monitoring treatment response in osteoporosis. *biomark Med.* (2008) 2:495–508. doi: 10.2217/17520363.2.5.495
67. Kohrt WM, Wherry SJ, Wolfe P, Sherck VD, Wellington T, Swanson CM, et al. Maintenance of serum ionized calcium during exercise attenuates parathyroid hormone and bone resorption responses. *J Bone Miner Res.* (2018) 33:1326–34. doi: 10.1002/jbmr.3428
68. Dirckx N, Moorers MC, Clemens TL, Riddle RC. The role of osteoblasts in energy homeostasis. *Nat Rev Endocrinol.* (2019) 15:651–65. doi: 10.1038/s41574-019-0246-y
69. Huang X, Zhu Y, Sun S, Gao X, Yang Y, Xu H, et al. Exercise maintains bone homeostasis by promoting osteogenesis through STAT3. *Int J Biol Sci.* (2023) 19:2021–33. doi: 10.7150/ijbs.82744
70. Hiam D, Landen S, Jacques M, Voisin S, Alvarez-Romero J, Byrnes E, et al. Osteocalcin and its forms respond similarly to exercise in males and females. *Bone.* (2021) 144:115818. doi: 10.1016/j.bone.2020.115818
71. Tobeiha M, Moghadasian MH, Amin N, Jafarnejad S. RANKL/RANK/OPG pathway: A mechanism involved in exercise-induced bone remodeling. *BioMed Res Int.* (2020) 2020:6910312. doi: 10.1155/2020/6910312
72. Pichler K, Loreto C, Leonardi R, Reuber T, Weinberg AM, Musumeci G. RANKL is downregulated in bone cells by physical activity (treadmill and vibration stimulation training) in rat with glucocorticoid-induced osteoporosis. *Histol Histopathol.* (2013) 28:1185–96. doi: 10.14670/HH-28.1185
73. Rubin J, Murphy T, Nanes MS, Fan X. Mechanical strain inhibits expression of osteoclast differentiation factor by murine stromal cells. *Am J Physiol Cell Physiol.* (2000) 278:C1126–32. doi: 10.1152/ajpcell.2000.278.6.C1126
74. Kharroubi A, Saba E, Smoom R, Bader K, Darwish H. Serum 25-hydroxyvitamin D and bone turnover markers in Palestinian postmenopausal osteoporosis and normal women. *Arch Osteoporos.* (2017) 12:13. doi: 10.1007/s11657-017-0306-7
75. Wei X, Zhang Y, Xiang X, Sun M, Sun K, Han T, et al. Exploring the relationship of bone turnover markers and bone mineral density in community-dwelling postmenopausal women. *Dis Markers.* (2021) 2021:6690095. doi: 10.1155/2021/6690095
76. Azimi-Shomali S, Farshbaf-Khalili A, Eslamian F, Dolatkhan N, Ghassab-Abdollahi N. The relationship between usual daily physical activity with serum markers related to bone metabolism and demographic characteristics in postmenopausal women aged 50–65 years. *J Phys Act Health.* (2022) 19:417–24. doi: 10.1123/jpah.2021-0495
77. Kim JS, Kim MH, Shin JS. Effects of weight-bearing exercise on bone metabolism in college women. *Taehan Kanho Hakhoe Chi.* (2004) 34:760–70. doi: 10.4040/jkan.2004.34.5.760
78. Mu S, Xia Y, Wu Q, Ji C, Dai H, Zhang M, et al. Response of bone metabolism markers to ice swimming in regular practitioners. *Front Physiol.* (2021) 12:731523. doi: 10.3389/fphys.2021.731523
79. Min-Jae K, Do-Yeon K, Sol H, Jung-Sook K, Eadric B, Jong-Won K. Effect Of Combined Exercise On Lung Function, Blood Vitamin D, Calcium And Bone Metabolism Hormones In Elderly Women: 2365 Board #284 May 28 3:00 PM - 4:30 PM. *Med Sci Sports Exercise.* (2020) 52:638–9. doi: 10.1249/01.mss.0000681248.22186.ab
80. Xu SM, Lu K, Yang XF, Ye YW, Xu MZ, Shi Q, et al. Association of 25-hydroxyvitamin D levels with lipid profiles in osteoporosis patients: a retrospective cross-sectional study. *J Orthop Surg Res.* (2023) 18:597. doi: 10.1186/s13018-023-04079-8
81. Groenendijk I, Chan R, Woo J, Ong S, Parikh P, Bragt MCE, et al. A combined nutrition and exercise intervention influences serum vitamin B-12 and 25-hydroxyvitamin D and bone turnover of healthy Chinese middle-aged and older adults. *J Nutr.* (2020) 150:2112–9. doi: 10.1093/jn/nxaa149
82. Stunes AK, Brobakken CL, Suhan MAJ, Aagård N, Brevig MS, Wang E, et al. Acute effects of strength and endurance training on bone turnover markers in young adults and elderly men. *Front Endocrinol (Lausanne).* (2022) 13:915241. doi: 10.3389/fendo.2022.915241
83. Kistler-Fischbacher M, Weeks BK, Beck BR. The effect of exercise intensity on bone in postmenopausal women (part 2): A meta-analysis. *Bone.* (2021) 143:115697. doi: 10.1016/j.bone.2020.115697