



Effects of non-supervised exercise interventions on bone mineral density in adult women: a systematic review and meta-analysis

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Abstract

Mini abstract Osteoporosis is a major health issue worldwide. This study analyzes the effects of non-supervised osteoporosis prevention programs on bone mineral density. Non-supervised exercise increases femoral neck and lumbar spine bone mineral density in adult women. Thus, it might be effective for preventing or treating osteoporosis or osteopenia in this population.

Introduction Osteoporosis is a major health issue worldwide. Social distancing measures due to COVID-19 have hindered the chances to take part in supervised osteoporosis prevention exercise programs. The purpose of the present study is to systematically review and meta-analyze the effects of non-supervised osteoporosis prevention exercise programs on bone mineral density (BMD) in adult women.

Methods A comprehensive search of electronic databases ($n=7$) was conducted including (a) prospective randomized controlled trials (RCTs) comparing at least one exercise group vs. a control group with sedentary lifestyle or sham exercises; (b) baseline and follow-up BMD values, or BMD changes from baseline, at any skeletal site; (c) women over 30 years old; and (d) non-supervised exercise programs only. Subgroup analyses were performed for menopausal status, intervention duration, type of exercise, and osteopenia/osteoporosis status.

Results Ten studies were included ($n=668$). Random effect analyses showed that unsupervised exercise had beneficial effects on lumbar spine (LS) BMD with standardized mean difference (SMD)=0.40 (95% confidence interval (CI): 0.03–0.77), and femoral neck (FN) BMD with SMD=0.51 (95% CI: 0.16–0.85). Unsupervised exercise increased LS (SMD=0.73 (95% CI: 0.13–1.33)) and FN BMD (SMD=0.85 (95% CI: 0.33–1.37)) in women with osteopenia/osteoporosis, but not in healthy counterparts.

Conclusion Non-supervised exercise improves FN and LS BMD in adult women. Beneficial effects of exercise on FN and LS BMD might be more pronounced in those with poor bone health compared with healthy counterparts. More RCTs prescribing non-supervised, osteogenic exercise are required in this population. It is necessary to investigate the efficacy of remote/assistive technologies for delivering and monitoring non-supervised exercise interventions.

Keywords Exercise, Non-supervised, COVID-19, Osteoporosis, Bone

Introduction

Osteoporosis is a disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to increased bone fragility and fracture risk [1]. It is estimated that 25.5 million people in the European Union and 10.2 million people in the USA are affected by osteoporosis [2]. One in three women above 50 years old will suffer an osteoporotic fracture [3]. Fractures represent a large burden on health care systems. In Europe, costs associated with hospitalization and aftercare due to osteoporotic fractures amounted to 34 billion euro in 2010 [4]. These costs are expected to increase twofold by 2050 based on the expected

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population aging [5]. It is therefore of importance to develop interventions to prevent and treat osteoporosis that could reduce costs and mitigate the social impact of this highly prevalent disease. Such interventions should involve little risks and be sustainable over long periods.

Exercise is considered a safe, low-cost, non-pharmaceutical intervention for the prevention and treatment of osteoporosis [6, 7]. It has been shown that modalities such as resistance training or impact exercise prevent or reverse about 1% of bone loss per year at the lumbar spine (LS) and femoral neck (FN) in both pre- and postmenopausal women [8]. Bones adapt to mechanical loads with an osteogenic response, if these loads exceed those of habitual activities [9]. However, the optimum exercise program to improve bone health remains to be determined [10]. Exercises that involve weight-bearing loads and impacts, such as hopping and jumping, have shown improvements in bone mineral density (BMD) and microarchitecture [11]. As for the magnitude of these improvements, a previous meta-analysis reported a 0.37 standardized mean difference (SMD) at the LS (equivalent to mean changes in the BMD of +0.006 g/cm² in the intervention group and −0.010 g/cm² in the control group), and 0.33 SMD at the FN (equivalent to mean changes of +0.004 g/cm² in the intervention group and −0.012 g/cm² in the control group), with interventions lasting 11.7 ± 5.7 months [12].

While this evidence in favor of exercising for improving bone health is of importance, the question of adherence to such exercise-based osteoporosis prevention programs arises. A meta-analysis found a dropout rate of 21% and a compliance of 76% in supervised exercise interventions targeting bone mineral density in adults [13]. A recent review identified lack of time and transportation as the most common barriers to attending supervised exercise programs for osteoporosis prevention [14]. An obvious strategy to overcoming these barriers is the development of non-supervised home-based exercise programs to eliminate transportation needs, reduce costs, and allow for flexible scheduling [15].

In March 2020, when the World Health Organization declared COVID-19 a global pandemic, new challenges to engage in supervised exercise programs arose. COVID-19 is an infectious disease caused by a coronavirus discovered in 2019 known as SARS-CoV-2 [16]. Social distancing measures are negatively affecting people's physical activity behaviors and increasing sedentary time, deteriorating therefore physical health and well-being [17]. Inevitably, "lockdown" strategies have hindered the chances to participate in supervised osteoporosis prevention exercise programs [18], and it could well be that elements of social distancing persevere after the end of the COVID-19 pandemic.

Therefore, if the aim is to utilize exercise as a non-pharmacological strategy to improve bone health and prevent osteoporosis in adult women, and if participation is limited

for the abovementioned reasons, then one should look for alternative means of providing exercise interventions. Non-supervised interventions lend themselves as an ideal solution, because they can be carried out at home with complete time flexibility. Indeed, a recent study analyzed the consequences of COVID-19 lockdown on the adherence to exercise programs specifically designed for women with postmenopausal osteoporosis, and found that participation increased in non-supervised home training [19]. The question arises, however, whether such home-based exercise programs are effective enough to warrant formal, evidence-based recommendation. To our knowledge, no previous systematic review and meta-analysis has exclusively focused on the effects of non-supervised osteoporosis prevention exercise programs on BMD in pre- and postmenopausal women. The purpose of the present study is to systematically review and meta-analyze the effects of non-supervised exercise programs on BMD in this population.

Methods

Search strategy

The reporting of this systematic review was guided by the standards of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Statement [20] and was registered in advance in the International Prospective Register of Systematic Reviews (PROSPERO) with ID CRD42020189320.

The following bibliographic databases were searched: PubMed, PsycInfo, Web of Science, Scopus, SportDiscus, Cochrane, and Cinahl. Databases were systematically searched for articles published up to August 16, 2021, without language restrictions. The search strategy comprised of a combination of population (i.e., women), intervention (i.e., physical activity, exercise, training, walking), and outcome (i.e., BMD, bone, osteoporosis). Accordingly, the search term was ("physical activity" OR exercise OR training OR walking) AND (bone OR osteoporosis OR BMD) AND women. All citations were entered into a reference management software (Mendeley Desktop Software, version 1.19.4, Elsevier). Duplicates were excluded automatically, and the remaining studies were screened by title and abstracts according to the eligibility criteria.

Inclusion and exclusion criteria

Studies were included if they met the following criteria: (a) prospective randomized controlled trials (RCTs) comparing at least one exercise group vs. a control group with sedentary lifestyle or sham exercises; (b) baseline and follow-up BMD values, or BMD changes from baseline assessed by

dual-energy X-ray absorptiometry (DXA) or dual photon absorptiometry (DPA), at any skeletal site; (c) women over 30 years old; (d) non-supervised exercise programs only.

The following studies we excluded: (a) follow-up studies, review articles, case reports, editorials, conference abstracts, and letters; (b) mixed-gender cohorts without separate BMD analyses for each sex; (c) studies that included women with diseases that relevantly affect bone metabolism (e.g., hyperthyroidism, type I diabetes mellitus, renal or hepatic disease) [21], or undergoing chemo- and/or radiotherapy; (e) studies combining exercise with pharmacological therapy.

Data extraction

Titles and abstracts were screened by one reviewer (H. S.-T.) to exclude irrelevant studies. Two reviewers (H. S.-T. and B. S.) independently evaluated full-text articles and extracted data from the included studies. Disagreement was resolved by discussion between these two reviewers. Extracted data included subjects' characteristics, sample size for each group, length of intervention, compliance, exercise modality, BMD values with standard deviations (SD) at different skeletal sites (i.e., FN and LS) at baseline and study completion, attrition, and adverse event data. Corresponding authors were contacted for any missing data.

Outcome measures

While initially outcomes of interest were BMD at any skeletal site commonly assessed to diagnose osteoporosis, only LS and FN were included in the meta-analyses due to data availability in the selected studies. Besides, LS and FN are common osteoporotic fracture sites [22].

Exercise interventions

Non-supervised exercise interventions for treating or preventing osteoporosis were classified according to the following six categories [23]:

- Static weight-bearing (SWB), e.g., single-leg standing.
- Dynamic weight-bearing exercise low force (DWBLF), e.g., walking, and Tai chi.
- Dynamic weight-bearing exercise high force (DWBHF), e.g., jogging, jumping, running, dancing and vibration platform.
- Non-weight-bearing exercise low force (NWBLF), e.g., low load, high repetition strength training.
- Non-weight-bearing exercise high force (NWBHF), e.g., progressive resisted strength training.
- Combination (COMB); more than one of the above exercise interventions.

Quality assessment

All studies included were independently assessed for risk of bias by two independent raters (H. S.-T. and B. S.) using the Physiotherapy Evidence Database (PEDro) scale [24]. The methodological quality of the selected studies was classified as follows: ≥ 7 , high; 5–6, moderate; < 5 , low [25].

Statistical analysis

All statistical analyses were performed using the software Review Manager (RevMan, Version 5.4, The Cochrane Collaboration, 2020). Effect size (ES) values were considered the standardized mean differences (SMDs), computed as

$$\text{SMD} = \frac{\text{mean}(D_{\text{Int}}) - \text{mean}(D_{\text{Ctr}})}{\text{SD}(D_{\text{Int,Ctr}})}$$

where D_{Int} and D_{Ctr} are the post–pre differences in the intervention and control groups, respectively, and $D_{\text{Int,Ctr}}$ is the post–pre difference of the combined groups [26]. If the SDs of the post–pre differences in the intervention and control groups were not reported in the selected studies, then it was calculated from confidence intervals (CIs), standard error, or P -value of the absolute change of BMD using standardized formulae [27]. If none of these data were available, the following formula was employed:

$$\text{SD} = \sqrt{\text{SD}_{\text{pre}}^2 + \text{SD}_{\text{post}}^2 - (2 \cdot r \cdot \text{SD}_{\text{pre}} \cdot \text{SD}_{\text{post}})}$$

where r is the correlation coefficient that describes how similar the pre- and post-measurements were across participants [27]. Estimated values for this correlation coefficient for the intervention and control groups at LS and FN have been reported elsewhere [12]. Sensitivity analyses were performed by replacing correlation coefficients with 0.7 to explore whether weaker coefficients had any effect on overall findings.

The magnitude of the SMD in the social sciences can be interpreted as small, $\text{SMD} = 0.2$; medium, $\text{SMD} = 0.5$; and large, $\text{SMD} = 0.8$ [28]. CI for the SMDs were computed at the 95% confidence level. The variability in interventions employed in the different studies requires the use of a random effects model [26]. Heterogeneity between studies was examined using the Q statistic. Consistency of intervention effects across studies was assessed using the I^2 statistic. Generally, an I^2 below 40% is considered low heterogeneity, 30 to 60% represents moderate, and 50 to 90% substantial heterogeneity [27]. Z -score was computed to test for overall effect. The rank correlation between effect estimates and their standard errors was conducted using the t -test and Kendall's τ statistic [29]. The P -value < 0.05 was defined

as the significant level for all tests. Subgroup analyses were performed for menopausal status, intervention duration, type of exercise, and osteopenia/osteoporosis status. Sensitivity analyses were conducted omitting studies of low methodological quality to determine the robustness of the overall results. It is important to note that one of the included studies [30] reports results for premenopausal subjects and postmenopausal subjects separately; therefore, it was also included separately in the meta-analyses, and labeled as “SugiyamaPOSM” for postmenopausal data and “SugiyamaPREM” for premenopausal data in the forest plots.

Results

Study selection

Of 12,298 articles initially retrieved from all included databases, 3219 duplicate entries were automatically removed by the reference management software. Then, 7115 studies were excluded after title and abstract screening. The remaining 1964 studies were assessed according to the inclusion and exclusion criteria described above. As shown in the flow

diagram (Fig. 1), a total of 10 studies were finally selected [30–39]. Details of study design, subject characteristics, and BMD outcomes are presented in Table 1. Detailed information about the exercise interventions can be found in Table 2. The pooled number of participants was 668 (intervention group: $n = 334$; control group: $n = 334$) and sample size in individual studies ranged from 26 [30] to 97 participants [38]. The age of the participants ranged from 38 [36] to 77 years old [37], including therefore both premenopausal and postmenopausal women.

Exercise interventions

Three studies prescribed impact exercise such as jumping or skipping [30, 35, 36]. Four studies prescribed brisk walking [34, 37–39]. Tai Chi was employed in one study [33]. Unilateral standing on one leg was the chosen modality in one intervention [32]. Bodyweight exercises were utilized in one study [37] in combination with brisk walking. Another study used back extensions with external loading as exercise modality [31]. Intervention duration ranged from 6 months [30, 32] to 2 years [31, 37, 38]. The prescribed exercise frequency in the selected studies ranged from 3 sessions weekly

Fig. 1 Flow diagram of studies selection process according to the Preferred Reporting Items for Systematic Review and Meta-Analysis

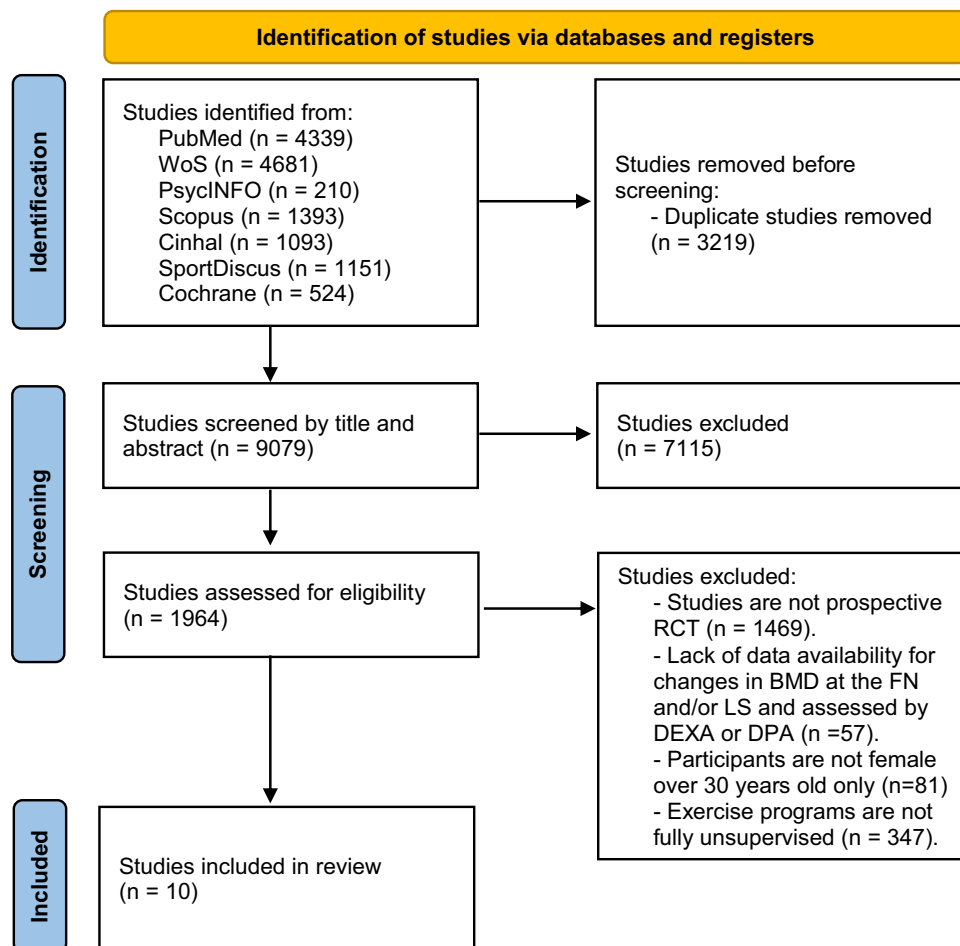


Table 1 Characteristics of selected studies

Study	Mean age	<i>N</i> exercise group	<i>N</i> control group	Subjects characteristics	Dietary supplements	Outcome
Greenway et al. (2015)	E: 41 ± 8 C: 41 ± 8	36	55	Premenopausal with osteopenia/ osteoporosis	Calcium (1 g/day)	BMD at LS, FN
Iwamoto et al. (2001)	E: 65 ± 5 C: 65 ± 6	8	20	Postmenopausal with osteoporosis	Calcium (2 g/day), vitamin D ₃ (1 µg/day)	BMD at LS
Niu et al. (2010)	E: 38 ± 1 C: 38 ± 1	34	33	Healthy premenopausal	Calcium (0.5 g/day)	BMD at LS, FN
Yamazaki et al. (2004)	E: 64 ± 3 C: 66 ± 3	27	15	Postmenopausal with osteopenia/osteoporosis	Calcium (0.8 g/day)	BMD at LS
Ebrahim et al. (1997)	E: 66 ± 8 C: 68 ± 8	49	48	Postmenopausal who had fractures in the previous 2 years		BMD at LS, FN
Brooke-Wavell et al. (1997)	E: 65 ± 3 C: 64 ± 3	38	40	Healthy postmenopausal	Calcium (0.85 g/day)	BMD at LS, FN
Liu et al. (2015)	E: 63 ± 7 C: 62 ± 8	48	42	Postmenopausal with osteoporosis	Calcium (1.5 g/day), vitamin D ₃ (15 µg/day)	BMD at LS, FN
Sakai et al. (2010)	E: 68 ± 1 C: 68 ± 1	47	37	Healthy postmenopausal		BMD at FN
Sugiyama et al. (2002)	E: 52 ± 1 C: 53 ± 1	13	13	Healthy premenopausal and postmenopausal		BMD at LS, FN
Sinaki et al. (1989)	E: 56 ± 4 C: 56 ± 4	34	31	Healthy postmenopausal		BMD at LS

E exercise group, *C* control group, *LS* lumbar spine, *FN* femoral neck

[30, 36, 38] to 3 sessions daily [32, 33]. Further details can be found in Table 2.

Methods of delivery and of adherence assessment

Different tools to administer and monitor these non-supervised programs were reported: filling exercise logs [35, 37, 39], following video-guided exercise sessions [36], heart-rate self-monitoring [34], or regular telephone calls [38]. The remaining studies included in this meta-analysis [30–33] do not describe the tools employed to deliver and monitor exercise programs.

Attrition, adherence, and adverse effects

Most of the selected studies reported data on attrition in their non-supervised exercise interventions: Brooke-Wavell et al. [39] report that 38 (out of 43) subjects in the intervention group and 40 (out of 41) in the control group completed the trial (12% and 2% dropout rate respectively), with dropouts due to reasons such as surgery, illness, or accident (not exercise-related). In the study by Ebrahim et al. [38], 49 (out of 81) subjects in the intervention group and 48 (out of 84) in the control group finished the intervention, registering therefore a substantial dropout rate (40% and 42% respectively) due to unwillingness to continue and illness among the main reasons. Liu et al. [33] reported that 48 (out of 50)

and 42 (out of 48) subjects in the intervention and control groups respectively completed the trial (4% and 12% dropout rate), with reasons for withdrawal being serious back pain, traumatic fracture, and sudden heart attack unrelated to the study. Niu et al. [36] informed a dropout rate of 24% in the intervention group and 28% in the control group, with 34 (out of 45) and 33 (out of 46) subjects completing the trial, respectively. In the study by Sakai et al. [32], the number of subjects who completed the study was 47 (out of 49) for the intervention group and 37 (out of 45) for the control group (4% and 12% dropout rate respectively). Sixty-five (out of 68) subjects completed the study by Sinaki et al. [31] (4% dropout rate), with all three withdrawals happening in the control group for reasons such as moving to a different state or illness. Finally, Yamazaki et al. [34] reported that 42 (out of 50) subjects completed the trial (16% dropout rate). Therefore, the dropout rate ranged from 0 to 40% in the exercise groups (mean ± SD = 14.2% ± 13.9%) and 2.4 to 42% in the control groups (mean ± SD = 18.4% ± 13.4%).

Adherence to the exercise programs was reported by most of the studies included in this meta-analysis. Thus, Greenway et al. [35] reported a mean compliance of 53% of prescribed sessions (range 20–90%). Niu et al. [36] describes that the median number of exercise sessions attended was 2.4 times per week. The study by Ebrahim et al. [38] informs that all the women who remained in the intervention reported carrying out the prescribed exercise sessions. Brooke-Wavell

Table 2 Exercise interventions

Study	Exercise category	Intervention duration	Frequency (sessions per week)	Intervention description
Greenway et al. (2015)	DWBHF	15 months	4	Unilateral landings after walking off a raised step. Step height progressed from 18.5 to 63.5 cm (increments of 7.5 or 5 cm every 8 weeks). Landings were divided into 2 to 5 sets per foot, ranging from 3 to 10 repetitions per set. Total number of landings per session started at 12 and progressed to 80, where it remained constant from week 16. Landing foot alternated after every set
Iwamoto et al. (2001)	COMB	24 months	7	Walking: Subjects were encouraged to increase their baseline daily step count by 30% thorough brisk walking Gymnastic training: 2 sets × 15 repetitions of straight leg raising, squatting, and abdominal and back muscle exercises
Niu et al. (2010)	DWBHF	12 months	≥ 3	Each session included a 3-min warm-up (stretching), 5 sets × 10 countermovement jumps, and a 3-min cooldown (stretching)
Yamazaki et al. (2004)	DWBLF	12 months	4	Outdoor walking at a speed corresponding to 50% of the maximal oxygen consumption, a minimum of 8000 steps per session
Ebrahim et al. (1997)	DWBLF	24 months	3	Self-paced brisk walking for 40 min per session. Subjects were instructed to walk at a faster pace than usual but avoiding discomfort or shortness of breath
Brooke-Wavell et al. (1997)	DWBLF	12 months	7	Self-paced brisk walking, 280 min per week
Liu et al. (2015)	DWBLF	12 months	21 (3 × daily)	Tai-Chi sessions consisting of 7 repetitions of the “modified eighth section of Eight-Section Brocade.”
Sakai et al. (2010)	SWB	6 months	21 (3 × daily)	Unilateral standing exercise: each session consisted of standing on each leg for 1 min
Sugiyama et al. (2002)	DWBHF	6 months	3	Rope skipping, 100 jumps/session
Sinaki et al. (1989)	NWBLF	24 months	5	Back extensions in prone position with backpack containing weights equivalent to 30% of each subject’s maximal isometric back muscle strength, 10 repetitions per session

E exercise group, *C* control group, *SWB* static weight-bearing, *DWBLF* dynamic weight-bearing exercise low force, *DWBHF* Dynamic weight-bearing exercise high force, *NWBLF* non-weight-bearing exercise low force, *COMB* combination.

et al. [39] report that participants completed, on average, 20.4 min/day, during an average of 4.8 walks per week, out of the 7 weekly sessions prescribed. Liu et al. [33] inform that average compliance was 96%, while Sakai et al. [32] describe a 71.4% compliance to prescribed sessions. Finally, in the study by Sugiyama et al. [30], an average compliance of 75% is reported among premenopausal women, and 71.4% among postmenopausal women. In summary, adherence to the non-supervised exercise programs ranged from 53 to 100% (mean ± SD = 78.3% ± 16.1%).

Regarding the safety of non-supervised exercise interventions, the selected studies reported the following injuries and adverse effects: Brooke-Wavell et al. [39] report that two women had minor foot problems. Ebrahim et al. [38] reported 71 falls in the intervention group and 54 falls in the control group, as well as 6 fractures in the

intervention group and 4 fractures in the control group during the 2-year period. Finally, Greenway et al. [35] specified that no injuries occur during their intervention, while Liu et al. [33] reported no serious injuries or adverse events associated with exercises, and four minor injuries related to knee, back, or hip pain.

Methodology quality

PEDro scores are shown in Table 3. The methodological quality of one study is classified as high [38], seven studies demonstrated moderate [31–33, 35–37, 39], and the remaining two studies are classified as being of low methodological quality [30, 34].

Table 3 Assessment of risk of bias for included studies

Study	Eligibility criteria	Random allocation	Allocation concealment	Inter group homogeneity	Blinding subjects	Blinding personnel	Blinding assessors	Participation ≥ 85% allocation	Intention to treat analysis	Between group comparison	Measure of variability	Total score
Greenway et al. (2015)	Y	1	0	1	0	0	0	0	1	1	1	5
Iwamoto et al. (2001)	Y	1	0	1	0	0	0	0	1	1	1	5
Niu et al. (2010)	Y	1	1	1	0	0	0	0	1	1	1	6
Yamazaki et al. (2004)	Y	0	0	1	0	0	0	0	1	1	1	4
Ebrahim et al. (1997)	Y	1	1	1	0	0	1	0	1	1	1	7
Brooke-Wavell et al. (1997)	Y	1	0	1	0	0	0	1	0	1	1	5
Liu et al. (2015)	Y	1	0	1	0	0	0	1	1	1	1	6
Sakai et al. (2010)	Y	1	1	1	0	0	0	1	0	1	1	6
Sugiyama et al. (2002)	Y	0	0	1	0	0	0	0	0	1	1	3
Sinaki et al. (1989)	Y	1	0	1	0	0	0	1	1	1	1	6

Meta-analysis results

The following meta-analyses were performed to investigate the effect of non-supervised exercise on BMD. BMD was measured by DXA in 9 of the selected studies [30, 32–39], and by DPA in one of the selected studies [31]. Nine of the studies reported BMD at LS [30, 31, 33–39], and seven studies reported BMD at FN [30, 32, 33, 35, 36, 38, 39].

Effect of non-supervised exercise on BMD at the LS

Nine studies assessed the effect of non-supervised exercise interventions on BMD at the LS. Random effect analysis showed that non-supervised exercise significantly increased LS BMD relative to control (SMD: 0.40, 95% CI: 0.03–0.77, $P < 0.05$). Heterogeneity between studies was substantial ($I^2 = 79%$, $Q = 41.93$, degrees of freedom = 9, $P < 0.00001$; Fig. 2). A sensitivity analysis omitting the two studies with lowest methodological quality [30, 34] revealed likewise significant positive effects of non-supervised exercise on BMD at the LS (SMD: 0.55, 95% CI: 0.09–1.00, $P < 0.05$).

Effect of non-supervised exercise on BMD at the FN

Seven studies assessed the effect of non-supervised exercise on BMD at the FN. Random effect analysis showed that non-supervised exercise significantly increased FN BMD relative to control (SMD: 0.51, 95% CI: 0.16–0.85, $P < 0.05$). Heterogeneity between studies was substantial ($I^2 = 74%$, $Q = 27.26$, degrees of freedom = 7, $P = 0.0003$; Fig. 3). A sensitivity analysis omitting the study with lowest methodological quality [30] revealed likewise significant positive effects of non-supervised exercise on BMD at the FN (SMD: 0.48, 95% CI: 0.08–0.88, $P < 0.05$).

Replacing correlation coefficients with 0.7 in sensitivity analyses did not affect the findings of this study.

Subgroup analyses

Subgroup analyses were performed to determine the effect of menopause and osteoporosis/osteopenia status, trial duration, and exercise mode on exercise-related BMD changes. Results are summarized in Table 4.

Menopausal status

Similar non-significant effects on LS BMD were found in premenopausal (SMD = 0.48; 95% CI: – 0.44, 1.41) and postmenopausal women (SMD = 0.36, 95% CI: – 0.04, 0.75), with no significant differences between subgroups according to random effects analysis ($P = 0.81$; Supplementary Fig. 1). Non-supervised exercise improved FN BMD in premenopausal women (SMD = 0.76; 95%

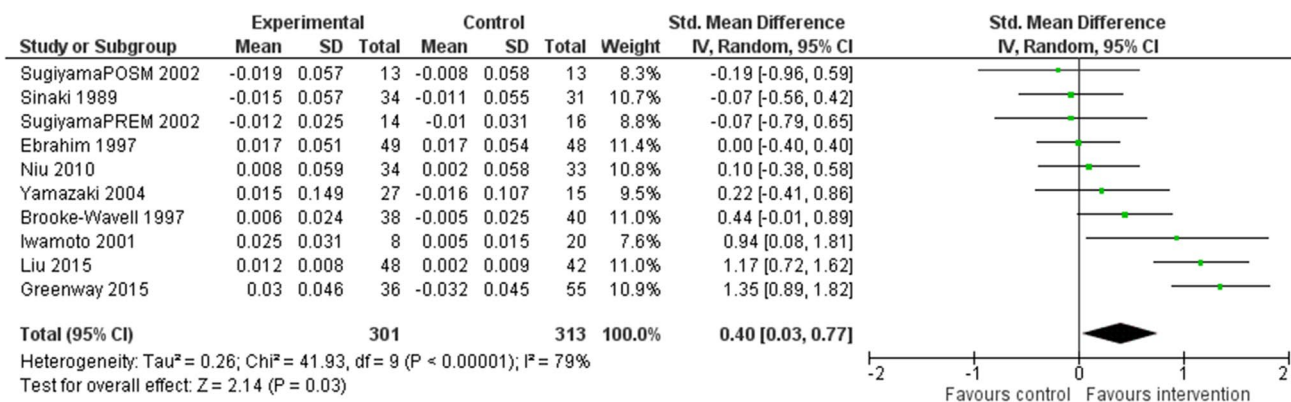


Fig. 2 Forest plot of meta-analysis results on BMD at the LS

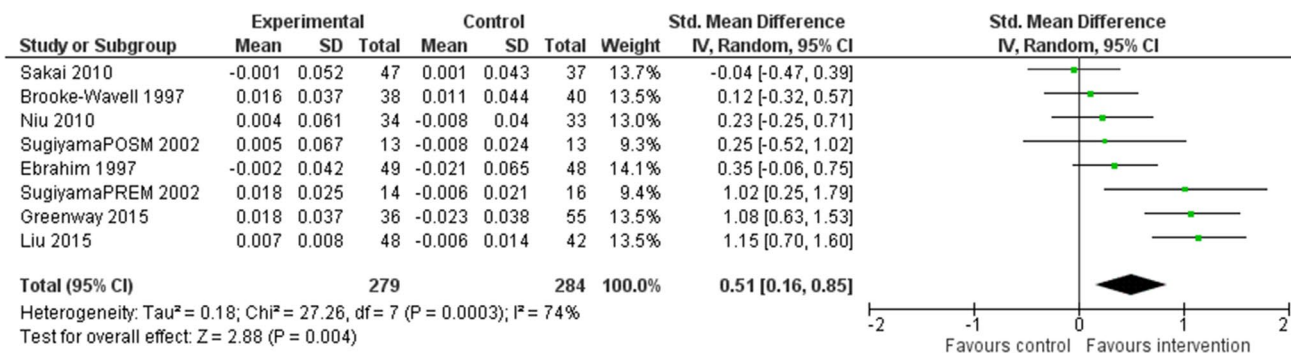


Fig. 3 Forest plot of meta-analysis results on BMD at the FN

CI: 0.16, 1.35), but not in postmenopausal women (SMD = 0.37; 95% CI: -0.06, 0.80). However, there were no differences between subgroups according to random effects analysis (P = 0.30; Supplementary Fig. 2).

Trial duration

Similar non-significant effects on LS BMD were found in trials with duration ≤ 1 year (SMD = 0.33; 95% CI: -0.09, 0.75) and trials with duration > 1 year (SMD = 0.53; 95% CI: -0.21, 1.28), with no significant differences between subgroups according to random effects analysis (P = 0.63; Supplementary Fig. 3). Non-supervised exercise improved FN BMD in trials that went for a duration of 1 year or less (SMD = 0.44; 95% CI: 0.01, 0.86), but not in trials that exceeded 1 year in duration (SMD = 0.71; 95% CI: -0.02, 1.43). However, there were no differences between subgroups according to random effects analysis (P = 0.53; Supplementary Fig. 4).

Exercise modality

Non-significant effects on LS BMD were found for DWBLF (SMD = 0.46; 95% CI: -0.07, 1.00) and DWBHF (SMD = 0.33; 95% CI: -0.45, 1.11). There were no differences between subgroups according to random effects analysis (P = 0.78; Supplementary Fig. 5). Non-significant effects on FN BMD were found for DWBLF (SMD = 0.54; 95% CI: -0.06, 1.13). DWBHF had a significant positive effect on FN BMD (SMD = 0.65; 95% CI: 0.16, 1.15). There were no differences between subgroups according to random effects analysis (P = 0.77; Supplementary Fig. 6).

Osteopenia/osteoporosis status

A subgroup analysis was performed to assess whether the effect of exercise on BMD is dependent on bone health status. Thus, in this subgroup analysis, BMD adaptations between women with osteopenia or osteoporosis [33–35, 37, 38] and healthy women (i.e., women with no diagnosed bone disease)

Table 4 Summary of subgroup analyses

Subgroup	<i>N</i> (<i>K</i>)	SMD (95% CI)	<i>P</i> (Z-test)	τ^2	<i>Q</i> statistic	<i>I</i> ²	<i>P</i> (χ^2 test)	<i>P</i> (subgroup differences)
LS BMD								
<i>Menopausal status</i>								
-Premenopausal	188(3)	0.48 (−0.44, 1.41)	0.31	0.59	17.56	89%	0.0002	0.81
-Postmenopausal	426(7)	0.36 (−0.04, 0.75)	0.08	0.20	22.59	73%	0.0009	
<i>Trial duration</i>								
- ≤ 1 year	333(6)	0.33 (−0.09, 0.75)	0.13	0.19	16.90	70%	0.005	0.63
- > 1 year	281(4)	0.53 (−0.21, 1.28)	0.16	0.49	25.02	88%	<0.0001	
<i>Exercise modality</i>								
-DWBLF	307(4)	0.46 (−0.07, 1.00)	0.09	0.23	15.23	80%	0.002	0.78
-DWBHF	214(4)	0.33 (−0.45, 1.11)	0.40	0.53	21.02	86%	0.0001	
<i>Osteopenia/osteoporosis status</i>								
-Healthy women	266(5)	0.11 (−0.13, 0.35)	0.37	0.00	3.45	0%	0.49	0.06
-Women with osteopenia/ osteoporosis	348(5)	0.73 (0.13, 1.33)	0.02	0.38	26.12	85%	<0.0001	
FN BMD								
<i>Menopausal status</i>								
-Premenopausal	188(3)	0.76 (0.16, 1.35)	0.01	0.19	7.05	72%	0.03	0.30
-Postmenopausal	375(5)	0.37 (−0.06, 0.80)	0.09	0.18	16.45	76%	0.002	
<i>Trial duration</i>								
- ≤ 1 year	375(6)	0.44 (0.01, 0.86)	0.04	0.20	19.41	74%	0.002	0.53
- > 1 year	188(2)	0.71 (−0.02, 1.43)	0.05	0.22	5.72	82%	0.02	
<i>Exercise modality</i>								
-DWBLF	265(3)	0.54 (−0.06, 1.13)	0.08	0.23	11.41	82%	0.003	0.77
-DWBHF	214(4)	0.65 (0.16, 1.15)	0.01	0.16	8.36	64%	0.04	
<i>Osteopenia/osteoporosis status</i>								
-Healthy women	285(5)	0.22 (−0.77, 0.51)	0.13	0.03	5.70	30%	0.22	0.04
-Women with osteopenia/ osteoporosis	278(3)	0.85 (0.33, 1.37)	0.001	0.16	8.76	77%	0.01	

Data in boldface type indicate significance. *N* number of subjects, *K* number of studies, *SMD* standardized mean difference, *CI* confidence interval, *BMD* bone mineral density, *DWBLF* dynamic weight-bearing exercise low force, *DWBHF* dynamic weight-bearing exercise high force. —: Not enough studies to compute heterogeneity.

[30, 31, 36, 39] were compared. A significant positive effect on LS BMD was found for women with osteopenia or osteoporosis (SMD=0.73; 95% CI: 0.13, 1.33), while effects were non-significant in healthy women (SMD=0.11; 95% CI: −0.13, 0.35). However, there were no differences between subgroups according to random effects analysis ($P=0.06$; Supplementary Fig. 7). A significant positive effect on FN BMD was found for women with osteopenia or osteoporosis (SMD=0.85; 95% CI: 0.33, 1.37), while effects were non-significant in healthy women (SMD=0.22; 95% CI: −0.07, 0.51). Differences between subgroups were significant according to random effects analysis ($P=0.04$; Supplementary Fig. 8).

Discussion

The main aim of this study was to assess the effectiveness of non-supervised exercise programs for bone health via a systematic review and meta-analysis of RCTs. Non-supervised

exercise programs improved BMD at the FN and LS in adult women. An intervention based on DWBHF (e.g., jumping, plyometrics) could be most beneficial on FN BMD. The positive effects of non-supervised exercise on BMD might be observable in less than 1 year and more pronounced in women with osteopenia or osteoporosis.

Our study reveals that non-supervised, home-based exercise programs can be an effective alternative to supervised exercise. More specifically, our findings show that non-supervised exercise programs can be effective at significantly improving BMD at the LS and FN in adult women. Moreover, the effect size found in the current study (SMD-LS=0.40, SMD-FN=0.51) was comparable to a recent meta-analysis that included both supervised and non-supervised exercise interventions [12] (SMD-LS=0.37, SMD-FN=0.33). In order to make our results more clinically relevant, standardized mean differences between intervention and control groups were converted to areal BMD units, finding a value of 0.015 g/cm² (95% CI: 0.004–0.026) at

FN and 0.013 g/cm^2 (95% CI: 0.002–0.024) at LS. Looking specifically at women with osteopenia/osteoporosis, mean differences are greater: 0.024 g/cm^2 (95% CI: 0.005–0.042) at FN and 0.023 g/cm^2 (95% CI: 0.001–0.046) at LS. This mean difference in BMD between groups equates to 3.14% at the FN and 2.88% at the LS. According to recent studies, these BMD improvements reduce fracture risk by an estimated 35%, 25%, and 15% in vertebral, hip, and non-vertebral fractures respectively [40–42]. Indeed, epidemiological evidence suggests that exercise significantly reduces the risk of osteoporotic fractures, probably through a combined effect of improved BMD, muscle strength, flexibility, and balance [43].

Non-supervised exercise improved BMD at the FN in studies with intervention durations of < 1 year, but it had no effect on BMD in studies with intervention durations of > 1 year at both the FN and LS. This result is inconsistent with other studies showing that longer exposure to exercise generally results in better bone health [44]. Longer exercise interventions are required to observe bone adaptations and physiological changes in BMD, at least when there is an adequate progression of the exercise load [6]. This required progression might have been insufficient in the four selected studies that had trial durations over 1 year: two of them maintained the exercise load constant throughout the intervention [31, 37], another study just instructed the participants to progressively increase the amount and speed of walking “in a manner that suited them” [38], and only one of the selected studies with a trial duration of over 1 year designed a protocol to progressively increase the exercise load [35], obtaining the highest size effect within the subgroup (see Supplementary Figs. 3 and 4). Therefore, it could be argued that longer interventions can only elicit better effects if they are paired with an adequate progression in exercise loads. If consistent progression is missing, further BMD changes after initial adaptations may be hindered, due to non-compliance with the overload principle [45]. Bone tissue must be stimulated with loads exceeding a certain threshold to elicit positive bone adaptations [46]. Therefore, it has been suggested that bone-loading forces should be objectively quantified and monitored to ensure the efficacy of interventions for osteoporosis prevention or treatment [47]. New technologies such as accelerometers could assist in the implementation of effective non-supervised interventions to improve bone health [10].

Exercise modality is a key factor to achieve sufficient mechanical forces. The type of exercise and the forces it generates might be the most critical determinants of the effect of exercise on bone [48]. In this respect, the current official guidelines on exercise prescription for the prevention and management of osteoporosis underscore the efficacy of impact activities and high-intensity progressive resistance training [6]. The subgroup analysis performed in the current

study to analyze differences in BMD changes between exercise modalities found significant effects for DWBHF (e.g., jumping) at the FN, as well as a trend towards significance at both skeletal sites for DWBHL (e.g., brisk walking) (see Supplementary Figs. 5 and 6). Combining resistance and impact training to improve BMD at the FN and LS has produced very positive results in the LIFTMOR trial, which prescribed a high-intensity resistance and impact exercise intervention in postmenopausal women with low bone mass [49]. These results are consistent with the outcomes of recent meta-analyses, where a combination of resistance training with impact training appears to elicit the highest osteogenic response at the spine and hip [6, 50]. Moreover, these results echo findings from two recent studies from two independent cohorts of masters athletes. Masters athletes are people who continue to train for and compete in athletic events beyond their 4th, and often into their 8th and 9th decade of life [51]. A 10-year follow-up of 69 male sprinters revealed maintained or improved tibia bone strength for athletes who continued to train, but maintenance or loss in those who reduced or abandoned regular sprint training [52]. An independent cohort of 71 track-and-field masters athletes with mean followed-up period of 4.2 years confirms improvements in tibial bone strength over time in male power athletes, with maintenance of bone strength at best in female power athletes, and with age-related bone losses in endurance athletes of either sex [53]. These findings are remarkable in two ways. Firstly, they highlight the efficacy of certain track-and-field-related training modes (strength, plyometric and high-intensity interval training) for maintaining or improving BMD. Secondly, these two studies suggest that intrinsic motivation and positive affect, which are intrinsically high in masters athletes [54], may be instrumental allies when trying to enhance acceptance of and adherence to exercise programs. Other studies also support the benefits of multi-modal programs that incorporate not only osteoanabolic exercises, but also activities aimed to develop balance and proprioception to prevent falls [55, 56].

The effect of non-supervised exercise on BMD at different skeletal sites did not differ in premenopausal and postmenopausal women (see Supplementary Figs. 1 and 2). As bone loss increases rapidly after menopause [57], osteoporosis prevention programs to attain and maintain healthy bones in young premenopausal women are critical to reduce the risk or at least delay the development of the disease in later life [58, 59]. Despite these findings, BMD responses to exercise appear to be greater in women with osteopenia/osteoporosis compared to healthy counterparts. Our subgroup analysis showed a greater positive effect on BMD at both the LS and FN for women with osteopenia or osteoporosis (SMD-LS = 0.73, SMD-FN = 0.85) than for healthy women (SMD-LS = 0.11, SMD-FN = 0.22). This suggests that exercise interventions will be most beneficial

for women who already start with an impaired bone health status. Different factors could mediate this increased adaptation of exercise in women with poorer bone health, such as enhanced physiological response in weaker bones [60], or a higher commitment and adherence to exercise among women who have been diagnosed with such a condition [61].

A low dropout rate was generally reported in the selected studies. Specifically, the percentages of participants in the intervention groups completing the whole study ranged from 53 [38] to 96% [32, 33]. Three of the included studies [30, 35, 37] did not report any information regarding attrition. No major differences were observed between intervention and control groups, since average attrition rate was 14.2% and 18.4% respectively. A meta-analysis assessing dropouts in exercise interventions targeting BMD in adults reported similar attrition rates in supervised exercise interventions (21% for the intervention groups and 16% for the control groups), and found no statistically significant differences between non-supervised versus supervised exercise, or a combination of supervised and non-supervised exercise [13].

Average compliance to the prescribed exercise sessions was 78.3% in the included studies. These results are similar to previous studies. In a recent meta-analysis, average attendance rate was 82% for supervised interventions, and 75% for non-supervised interventions [12]. As mentioned above, it is possible that home-based non-supervised training increases adherence by overcoming barriers such as lack of time and difficulties with transportation [14, 15]. On the other hand, fear of falling and safety concerns might decrease adherence to non-supervised intervention for older adults [62]; in fact, one of the studies included in this meta-analysis, Ebrahim et al. [38], reported a higher number of falls and fractures in the intervention group compared with the control. Some factors suggested in the literature to improve adherence in home-based interventions include social or familiar support, and a reduced number of exercises in the program [63]. The use of new technologies to monitor and guide non-supervised training may also have a positive effect on exercise adherence in older adults [64, 65]. It would be of interest to develop intervention programs in which technologies are used to monitor intensity, provide tailored guidelines, and implement an adequate progression while allowing subjects to carry out the training sessions at home without direct supervision.

There are limitations that could reduce the validity of this systematic review and meta-analysis. First, there were notable variations between effect sizes across the selected studies, raising questions about the importance of confounding variables in the included studies (e.g., diet), or dissimilar methodologies (e.g., precision of outcome measurements) when attempting to aggregate data for meta-analysis [66]. This study has focused on LS and FN BMD; it would be of interest to extend this analysis to other sites, such as the

radius or total hip. Another limitation in our approach is that, due to the reduced number of studies meeting the inclusion criteria, sub-analyses were likely under powered to detect significance differences in BMD changes between groups. Our analyses were also performed on aggregate data, not individual patient data. Despite such limitations, the findings in this study demonstrate that non-supervised exercise is an effective intervention for improving BMD in adult women. Further research is required to evaluate the contribution of single exercise variables (e.g., intensity, volume, density) on bone health that may illuminate even more efficient recommendations.

Conclusion

Non-supervised exercise programs improve BMD at FN and LS in adult women. Interventions based on DWBHF (e.g., jumping, plyometrics) might be most effective for improving FN BMD in adult women. Positive effects of non-supervised exercise on BMD might be observed in periods shorter than a year and especially effective in women already diagnosed with osteopenia or osteoporosis. Due to the low number of trials conducted to date, more RCTs prescribing non-supervised, osteogenic exercise are required in adult women. More trials investigating the efficacy of remote/assistive technologies for delivering and monitoring non-supervised exercise interventions are also necessary.

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Declarations

Conflicts of interest None.

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