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REVIEW

Exercise training and bone mineral density in postmenopausal women: an updated systematic review and meta-analysis of intervention studies with emphasis on potential moderators

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Abstract

The aim of this systematic review and meta-analysis was (1) to determine exercise effects on bone mineral density (BMD) in postmenopausal women and (2) to address the corresponding implication of bone and menopausal status or supervision in postmenopausal women. A comprehensive search of eight electronic databases according to the PRISMA statement up to August 9, 2022, included controlled exercise trials ≥ 6 months. BMD changes (standardized mean differences: SMD) at the lumbar spine (LS), femoral neck (FN), and total hip (TH) were considered as outcomes. Study group comparisons were conducted for osteopenia/osteoporosis versus normal BMD, early versus late postmenopausal women, and predominantly supervised versus predominantly non-supervised study arms. We applied an inverse heterogeneity (IVhet) model. In summary, 80 studies involving 94 training and 80 control groups with a pooled number of 5581 participants were eligible. The IVhet model determined SMDs of 0.29 (95% CI: 0.16–0.42), 0.27 (95% CI: 0.16–0.39), and 0.41 (95% CI: 0.30–0.52) for LS, FN, and THBMD, respectively. Heterogeneity between the trial results varied from low (I^2 = 20%, TH BMD) to substantial (I^2 = 68%, LS-BMD). Evidence for publication bias/small study effects was negligibly low (FN-, TH-BMD) to high (LSBMD). We observed no significant differences ($p > .09$) for exercise effects on LS-, FN-, or TH-BMD-LS between studies/study arms with or without osteopenia/osteoporosis, early versus late postmenopausal women, or predominantly supervised versus non-supervised exercise programs. Using robust statistical methods, the present work provides further evidence for a positive effect of exercise on BMD in postmenopausal women. Differences in bone status (osteopenia/osteoporosis versus normal bone), menopausal status (early versus late postmenopausal), and supervision (yes versus no) did not significantly affect the exercise effects on BMD at LS or proximal femur.

Keywords Bone strength · Exercise trials · Menopause · Older women · Osteoporosis · Supervision

Introduction

Exercise is a promising agent for preventing osteoporosis in postmenopausal women. In their recent comprehensive systematic review and meta-analysis with 75 eligible studies, Shojaa et al. [1] provided definite evidence for the favorable effect of exercise on bone mineral density (BMD). Nevertheless, effect sizes in the predominantly healthy cohorts for lumbar spine (LS) and femoral neck (FN)-BMD were moderate at best. However, the substantial heterogeneity between the trials indicates that some studies were much more effective in improving BMD at LS or FN than others. Several factors might contribute to this aspect. Two factors, bone and menopausal status, might particularly contribute to the high degree of heterogeneity between the trials. While the early-postmenopausal stage is related to increased bone turnover with negative net effects on BMD in many women [2, 3], a factor that might dilute the exercise-induced effect on BMD, there is some evidence for more favorable exercise effects in people with osteopenia/osteoporosis compared to people with normal BMD [4]. However, the most striking effect on heterogeneity of exercise trial findings

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within comprehensive meta-analysis is differences in the exercise protocols. In this context, supervision of the exercise protocol has far-reaching consequences on setting, exercise composition, feasibility, safety, motivation, and adherence [5, 6]. In a recent systematic review and meta-analysis, we clearly demonstrated the favorable effect of supervised exercise protocols on fracture incidence [7]. Considering the higher complexity of exercise protocols for improving BMD compared to decreasing the number of falls [8], the role of supervision might be even more important in the area of bone strengthening.

In the present comprehensive systematic review and meta-analysis, we thus aimed to (a) provide a 2022 update regarding the effect of exercise on BMD at the LS, FN, and total hip (TH) regions of interest (ROI) using the inverse heterogeneity model (IVhet, [9]) that is less susceptible to underestimation of statistical error in heterogeneous studies and (b) to determine the relevance of the potentially confounding effect of bone status, menopausal status, and supervision of the session on exercise effects on BMD at LS, FN, and TH.

Methods

Data sources and search strategy

Electronic literature searches were conducted using PubMed, Web of Science, Cochrane, Science Direct, Eric, and ProQuest databases up to August 09, 2022, without any language restriction. The keywords and MeSH terms used in the search strategy included (“Bone” or “Bone mass” or “Bone status” or “Bone structure” or “Bone turnover” or “Bone metabolism” or “Bone mineral content” or “Skeleton” or “Bone Mineral Density” or “BMD” or “Bone Density” or “Osteoporosis” or “Osteopenia”) AND (“Postmenopause” or “Post-Menopause” or “Postmenopausal”) AND (“Exercise” or “Training” or “physical exercise” or” “physical activity” or “exercise training” or “weight bearing” or “strength training” or “resistance training” or “aerobic exercise” or “isometric exercise”) AND (“Clinical trial” or “Randomized controlled trial”). Furthermore, reference lists of the included articles were searched manually to extract additional eligible articles.

The present study was conducted following the Preferred Repointing Items for Systematic Reviews and Meta-Analyses (PRISMA) approach [10]. The study was registered in the international prospective register of systematic reviews (PROSPERO ID: CRD42021241407).

Inclusion and exclusion criteria

Articles were included in this meta-analysis if they met the following inclusion criteria: (a) clinical trials with at least one exercise group as an intervention versus one control group with sedentary/habitual active lifestyle without designed exercise, (b) women with postmenopausal status at study onset, (c) intervention of at least 6 months, (d) areal BMD of the LS or/and the proximal femur regions “TH” and/or “FN” were listed as outcome measures at baseline and follow-up assessment, (e) BMD determined by dual-energy X-ray absorptiometry (DXA) or dual-photon absorptiometry (DPA), (f) $\leq 10\%$ of participants on hormone (replacement) therapy (HT or HRT), osteoanabolic/antiresorptive (e.g., bisphosphonate, Denosumab), or osteocatabolic (glucocorticoids) and pharmaceutic agents, albeit only if the number of users was comparable between exercise and control.

The exclusion criteria were as follows: (a) mixed gender or mixed pre- and postmenopausal cohorts without separate BMD analysis for postmenopausal women; (b) women undergoing chemo- and/or radio-therapy; (c) women with diseases that relevantly affect bone metabolism; (d) interventions applying novel exercise technologies (e.g., whole-body vibration), or cycling, and swimming/aqua fitness as the only type of exercise training; (e) the synergistic/additive effect of exercise and pharmaceutic therapy; (f) double/multiple publications from one study and preliminary data from subsequently published trials; and (g) review articles, case reports, editorials, conference abstracts, letters, and unpublished reports or articles for which only abstracts were available were not considered.

Data extraction and quality assessment

Two reviewers (RM and WK) independently evaluated the full-text articles and extracted data from all the eligible publications independently. If they could not reach a consensus, a third reviewer was consulted (SvS). Information including author’s name, year of publication, country, population, number of participants, age, years since menopause, BMI, study duration, type of exercise, interventions, frequency, intensity, duration, sets and repetition, compliance, BMD values at baseline and study completion was extracted.

Two authors (RM and WK) independently assessed the risk of bias using the PEDro (Physiotherapy Evidence Database) scale [11, 12], and any discrepancy was resolved by consulting with a third reviewer (SvS). The categories assessed were randomization, allocation concealment, similarity at baseline, blinding of participants and staff, assessor blinding, incomplete outcome data, intention-to-treat analysis, between-groups comparison, and measure of variability. If a criterion was met, a point was awarded for the study; otherwise, a point was not awarded. For each trial included, a total score ranging from 0 to 10 could be obtained. The methodological quality of the included studies was classified as follows: ≥ 7 = high quality, 5–6 = moderate quality, and < 5 = low quality [13].

Outcome measures and data synthesis

The primary endpoint was the change in BMD at the LS, the femoral neck (FN), and the total hop (TH) region of interest (ROI) from baseline to follow-up. For subanalyses, the intervention was classified for (a) bone status (i.e., cohorts with versus without osteopenia/osteoporosis), (b) menopausal status of the women (i.e. early (≤ 5 years) versus late postmenopausal > 8 years (or cohort 60 years and older)) [14], and (c) supervision considering the net exercise frequency reported for the study arm. For the latter aspect, we differentiated between predominantly supervised and predominantly non-supervised exercise programs.

If the studies presented a confidence interval (CI) or standard errors (SE), these were converted to standard deviation (SD) with standardized formulas [15, 16].

Statistical analysis

We applied a random-effects meta-analysis using the metafor package [17] that is included in the statistical software R [18]. Effect size (ES) values were presented as standardized mean differences (SMDs) in combination with the 95% confidence interval (95% CI). We applied the inverse heterogeneity (IVhet) model proposed by Doi et al. [9] Heterogeneity between the studies was checked using I^2 statistics. I^2 of 0–40% was considered as "low," 30–60% as "moderate," 50–90% as "substantial," and 75–100% as "considerable" heterogeneity [16]. Along with regression test and the rank correlation effect estimates and their standard errors using the *t*-test and Kendall's τ statistic for potential publication bias, we also conducted trim and fill analyses using the L0 estimator proposed by Duval et al. [19] Additionally, we used Doi plots and the Luis Furuya-Kanamori index (LFK index) [20] to check for asymmetry. LFK values within ± 1 were considered negligible, while values ≥ ± 1 to ± 2 were considered as showing minor asymmetry. Values higher than ± 2 indicate major asymmetry. Sensitivity analyses were applied to determine whether the overall result of the analysis is robust to the use of the imputed correlation coefficient (minimum, mean or maximum). *P*-value < 0.05 was considered as the significance level for all the tests. SMD values of 0.2, 0.5, and 0.8 were interpreted as small, medium, and large effects.

Results

Study selection

Figure 1 illustrates the search process of the study. After removing 267 duplicates, 2251 articles were screened based on title and abstract. The full texts of 101 potentially relevant articles were screened, and finally, a total of 80 articles were included in this systematic review and meta-analysis [21–100]. Studies were published from 1989 to 2022 (Fig. 1). Three studies included contained English abstracts but with Italian [77, 94], Portuguese [82], and German [58] full texts.

Study and participant characteristics

The 80 studies included in this systematic review and meta-analysis comprise 94 training groups and 80 control groups (Table 1). The pooled number of participants was 5581 (intervention group: 3036, control group: 2545) and sample size in individual studies ranged from 5 [77, 94] to 125 [21] participants per group. Participants in the individual studies were on average between 50 [26] and 79 [68, 102] years old. Accordingly, the average menopausal age ranges from 0.5 [91, 97] to 24 years [56]; however, many studies do not provide this important information (Table 1). The mean body mass indexes (BMI, kg/m^2) of individual studies indicate that cohorts were underweight on average (e.g., [103] while others were obese [90]) (Table 1).

Difficult to rate but highly relevant for the intervention effect, 28 studies included participants with sedentary life styles, while 36 trials involved participants with some kinds of pre-study exercises activities (up to < 7 h/week [83]; Table 2). Unfortunately, many studies did not provide any information on the health and exercise status of their cohorts (Table 1).

Exercise characteristic description

Program duration varied considerably in the trials from 6 to 30 months (Table 2). Most studies ($n = 42$) applied an intervention period of between 9 and 18 months, while 27 trials scheduled a shorter — and 11 studies a longer — intervention period. A similarly large number of the 92 intervention groups employed either aerobic exercise (predominantly walking and/or jogging) or combined aerobic and resistance exercise as the primary exercise component. Twenty-eight interventions prescribed resistance exercise as the major component. Tai Chi was applied in five training groups [35, 69, 97, 98], hopping and jumping as the primary intervention was evaluated in six intervention groups [24, 51, 72, 77,

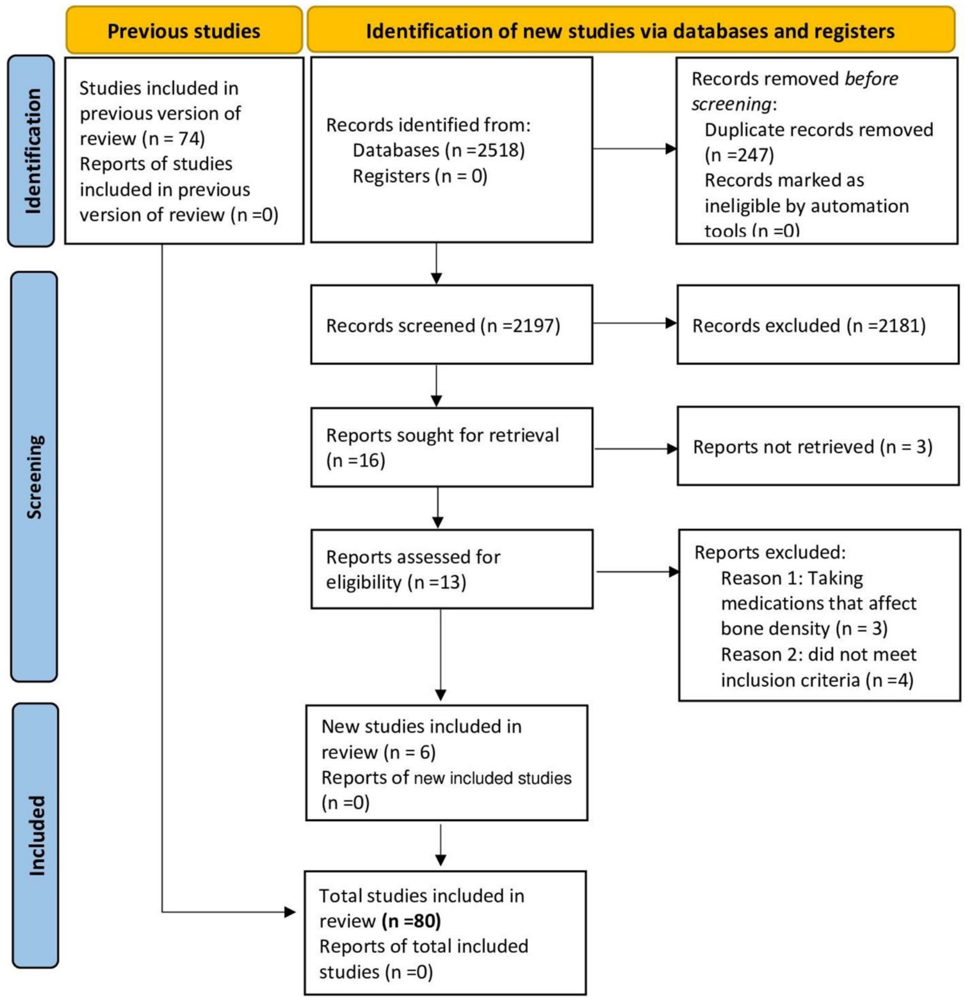

Fig. 1 PRISMA 2020 flow diagram for updated systematic reviews for the present project [101]

92]. Exercise frequency prescribed by the trials ranged from 2 sessions ([21, 34, 45, 50, 54, 70, 71, 79] to nine sessions/week [55]. The exercise session of eight studies [23, 24, 49, 77, 89, 91, 92] averaged about 10 min or less. Prescription of exercise intensity for aerobic exercise predominantly ranged between 60 and 80% of maximum heart rate (HRmax). Ground reaction forces during dynamic weight bearing exercise averaged from about ≈1.5 [48] to ≈4 × body mass [24] or potentially higher [72]. Resistance training protocols scheduled an exercise intensity of between 70 and 80% of the one repetition maximum (1-RM). In detail, four studies [26, 71, 81, 86] prescribed exercise intensities of 50% 1RM or lower. During resistance training, 1–21 exercises [42, 81, 91], with up to 108 repetitions [81], structured in 1–5 sets [22, 41, 42, 85, 91], were applied per session. Time under tension (i.e. movement velocity) was reported in only 10 studies [40, 50, 53, 59–61, 71, 74, 79, 87] and ranged between 3 and 9 s per repetition, with 3 studies using fast or explosive movements in the concentric part of the exercise [53, 61, 71]. In 57 exercise groups, the exercise intensity was progressively increased during the intervention period [26, 28–31, 36–43, 45–47, 49–56, 58–67, 71–76, 79–82, 85–88, 91, 93, 95].

Apart from one study with a very low attendance rate of 39% [84], all the other studies reported attendance rates of > 60%. Four [32, 44, 100] studies listed 100% attendance (Table 2). Unfortunately, 15 studies did not provide information on participant attendance.

Methodological quality

Methodological quality according to PEDro is shown in Table 3. Fifteen trials demonstrated high and 49 studies moderate methodological quality, while the remaining studies were classified as being of low quality (Table 3). Higher scores were frequently hindered by the lack of allocation concealment, participant, caregiver or assessor blinding, and < 85% of subjects assessed for at least one primary outcome. However, given that successful blinding of participants and caregivers (i.e., instructors) is hardly possible in exercise trials, 8 out of 10 score points can be considered an excellent result.

Table 1 Study and participant characteristics of the studies

First author Year	Sample size (*n*)	Age (years)	Bone status	Menopausal age (years)	BMI (kg/m^2)
Adami 1999	E: 125 C: 125	E: 65 ± 6 C: 63 ± 7	Healthy	E: 16 ± 7 C: 14 ± 8	E: 25 ± 3 C: 24 ± 3
Basat 2013	RE: 14 HI: 14 C: 14	RE: 56 ± 5 HI: 56 ± 3 C: 56 ± 4	Osteopenia	RE: 6 ± 4 HI: 7 ± 2 C: 6 ± 3	RE: 25 ± 5 HI: 26 ± 4 C: 28 ± 4
Bassey 1998	E: 45 C: 32	E: 56 ± 3 C: 55 ± 4	Healthy	E: 7 ± 4 C: 5 ± 4	E: 25 ± 3 C: 25 ± 3
Bassey 1995	E: 31[1] C: 32	E: 54 ± 4 C: 55 ± 3	Healthy	E: 7 ± 4 C: 7 ± 5	E: 25 ± 3 C: 25 ± 4
Bello 2014	E: 10 C: 10	E: 61 ± 6 C: 61 ± 6	Healthy	n.g n.g	n.g n.g
Bemben 2010	E: 22[2] C: 12	E: 64 ± 1 C: 63 ± 1	Healthy	E: > 5 C: > 5	E: 30 ± 1 C: 29 ± 1
Bemben 2000	HR: 11 HL: 13 C: 11	HR: 52 ± 2 HL: 50 ± 2 C: 52 ± 1	Healthy	HL: ≤ 7 HR: ≤ 7 C: ≤ 7	HL: 29 ± 2 HR: 23 ± 1 C: 24 ± 2
Bergström 2008	E: 60 C: 52	E: 59 ± 4 C: 60 ± 3	forearm fractures	n.g. n.g	E: 24 ± 3 C: 25 ± 2
Bloomfield 1993	E: 7 C: 7	E: 62 ± 1 C: 59 ± 4	Healthy	E: 11 ± 3 C: 15 ± 2	E: 28 ± 1 C: 25 ± 1
Bocalini 2009	E: 23 C: 12	E: 69 ± 9 C: 67 ± 8	Healthy	n.g n.g	E: 28 ± 4 C: 27 ± 6
Bolton 2012	E: 19 C: 20	E: 60 ± 6 C: 56 ± 5	Osteopenia	E: 13 ± 7 C: 12 ± 7	E: 25 ± 4 C: 25 ± 4
Brooke-Wavell 2001	E: 18 C: 21	E: 65 ± 3 C: 65 ± 3	Healthy	E: > 5 C: > 5	#E: 26 #C: 27
Brooke-Wavell 1997	E: 43 C: 41	E: 65 ± 3 C: 64 ± 3	Healthy	E: 15 ± 5 C: 15 ± 7	E: 26 ± 4 C: 26 ± 4
Caplan 1993[*]	E: 19 C: 11	E: 66 ± 1 C: 65 ± 1	Healthy	E: 18 ± 2 C: 21 ± 3	E: 25 ± 1 C: 24 ± 1
Chan 2004	E: 67 C: 65	E: 54 ± 3 C: 54 ± 3	Healthy	E: ≤ 10 C: ≤ 10	E: 24 ± 5 C: 24 ± 5
Chilibeck 2013	E + Pl: 86 Pl: 88	E + Pl: 55 ± 6 Pl: 56 ± 7	Healthy	E + PL: > 1 Pl: > 1	#E + PI: 28 #PI: 28
Chilibeck 2002[*]	E: 14 C: 14	E: 57 ± 2 C: 59 ± 2	Healthy	E: 9 ± 2 C: 8 ± 2	E: 27 ± 2 C: 27 ± 1
Choquette 2011	E + Pl: 25 Pl: 26	E + Pl: 58 ± 6 Pl: 59 ± 6	Healthy	E + Pl: 8 ± 8 Pl: 10 ± 8	E + Pl: 29 ± 4 Pl: 31 ± 3
Chuin 2009	E + Pl: 11 Pl: 7	E + Pl: 65 ± 3 Pl: 67 ± 4	Healthy	n.g n.g	E + Pl: 27 ± 3 Pl: 26 ± 3
de Matos 2009	E: 30 C: 29	E: 57 ± 5 C: 57 ± 5	≥ Osteopenia	E: 10 C: 7	E: 24 ± 3 C: 26 ± 3
Deng 2009	E: 45 C: 36	E: 54 ± 4 C: 51 ± 5	Healthy	E: ≤ 10 C: ≤ 10	n.g n.g
de Oliveira 2018	E: 17 C: 17	E: 56 ± 7 C: 54 ± 5	Healthy	E: 8 ± 7 C: 9 ± 7	E: 27 ± 3 C: 27 ± 3
Duff 2016	E: 22 C: 22	E: 65 ± 5 C: 65 ± 5	Healthy	n.g n.g	n.g n.g
Ebrahim 1997	E: 81 C: 84	E: 66 ± 8 C: 68 ± 8	Previous upper limb fractures	n.g n.g	E: 27 ± 4 C: 26 ± 5
Englund 2005	E: 24 C: 24	E: 73 ± 4 C: 73 ± 5	Healthy	E: 25 C: 23	E: 25 ± 3 C: 26 ± 3
Evans 2007	E + SP: 11[3] SP: 10	E + SP: 62 ± 5 SP: 63 ± 5	Healthy	E + SP: 8 ± 6 SP: 8 ± 5	#E + SP: 25 #SP: 26

Table 1 (continued)

First author Year	Sample size (n)	Age (years)	Bone status	Menopausal age (years)	BMI (kg/m^2)
Going 2003	E: 91 C: 70	E: 56 ± 5 C: 57 ± 5	Healthy	E: > 3 C: > 3	E: 26 ± 3 C: 26 ± 4
Grove 1992	LI: 5 HI: 5 C: 5	LI: 57 ± 4 HI: 54 ± 2 C: 56 ± 4	Healthy	LI: ≤ 8 HI: ≤ 8 C: ≤ 8	n.g n.g n.g
Hans 2002	E: 110 C: 35	E: 68 ± 5 C: 66 ± 5	≥ Osteopenia	E: > 5 C: > 5	E: 24 C: 23
Hartard 1996	E: 18 C: 16	E: 64 ± 6 C: 67 ± 10	Osteopenia	E: > 2 C: > 2	#E: 25 #: 25
Hartley 2020	E: 32 C: 32	E: 62 ± 4 C: 62 ± 4	Healthy	E: 11 ± 6 C: 11 ± 6	E: 24 ± 3 C: 24 ± 3
Hatori 1993	E: 23[4] C: 12	H: 56 ± 4 M: 58 ± 5 C: 58 ± 8	Healthy	H: 7 ± 5 M: 6 ± 4 C: 9 ± 8	H: 23 ± 2 M: 24 ± 2 C: 25 ± 3
Hettchen 2021	E: 21 C: 20	E: 54 ± 2 C: 54 ± 2	Osteopenia	E: ≤ 5 C: ≤ 5	E: 24 ± 3 C: 25 ± 5
Holubiac 2022	E: 15 C: 14	E: 56 ± 3 C: 57 ± 2	≥ Osteopenia	n.g	E: 25 ± 2 C: 25 ± 2
Iwamoto 2001	E: 8 C: 20	E: 65 ± 5 C: 65 ± 6	Osteoporosis	E: 16 ± 6 C: 15 ± 6	E: 20 ± 1 C: 20 ± 2
Jessup 2003	E: 10 C: 10	E: 69 ± 3 C: 69 ± 4	Healthy	E: 24 ± 11 C: 22 ± 11	n.g n.g
Karakiriou 2011*	E: 10 C: 9	E: 53 ± 1 C: 53 ± 1	Osteopenia	E: 5 ± 3 C: 3 ± 3	E: 28 ± 1 C: 30 ± 1
Kemmler 2013	E: 43 C: 42	E: 52 ± 2 C: 52 ± 3	Healthy	E: ≤ 3 C: ≤ 3	#E: 26 #C: 26
Kemmler 2010	E: 123 C: 123	E: 69 ± 4 C: 69 ± 4	Healthy	n.g n.g	#E: 26 #C: 27
Kemmler 2004	E: 86 C: 51	E: 55 ± 3 C: 56 ± 3	Osteopenia	E: > 1 C: > 1	E: 25 ± 3 C: 25 ± 4
Kemmler 1999	E-PM: 15 L-PM: 17 C: 18	E-PM: 54 ± 5 L-PM: 65 ± 6 C: 56 ± 8	Healthy	E-PM ≤ 8 L-PM > 8 C > 1	E-PM: 26 ± 4 L-PM: 26 ± 4 C: 27 ± 5
Kerr 2001	RE: 42 Fit: 42 C: 42	RE: 60 ± 5 Fit: 59 ± 5 C: 62 ± 6	Healthy	RE: > 4 Fit: > 4 C: > 4	#RE: 27 #Fit: 25 #C: 26
Kerr 1996	En: 28[5] RE: 28	En: 56 ± 5 RE: 58 ± 4	Healthy	En: 1–15 RE: 1–15	En: 26 RE: 25
Kohrt 1997*	JRF: 15 GRF: 18 C: 15	JRF: 65 ± 1 GRF: 66 ± 1 C: 68 ± 1	Healthy	JRF: 16 GRF: 16 C: 21	#JRF: 27 #GRF: 27 #C: 27
Kohrt 1995	E: 8[6] C: 8	E: 65 ± 3 C: 66 ± 3	Healthy	E: > 10 C: > 10	#E: 25 #C: 25
Korpelainen 2006	E: 84 C: 76	E: 73 ± 1 C: 73 ± 1	Osteopenia	n.g n.g	E: 26 ± 3 C: 26 ± 4
Kwon 2008	E: 20 C: 20	E: 77 ± 2 C: 77 ± 3	Healthy	n.g n.g	E: 26 ± 2 C: 25 ± 3
Lau 1992	E + Pl: 15 Pl: 15	E + Pl: 79 Pl: 75	Healthy	n.g n.g	n.g n.g
Liu 2015	E: 50 C: 48	E: 63 ± 7 C: 62 ± 8	Osteoporosis	E: 14 ± 6 C: 13 ± 7	n.g n.g
Lord 1996	E: 90 C: 89	E: 72 ± 5 C: 71 ± 5	Healthy	n.g n.g	#E: 27 #C: 26
Maddalozzo 2007	E: 35 C: 34	E: 52 ± 3 C: 52 ± 3	Healthy	E: ≤ 3 C: ≤ 3	n.g n.g

Table 1 (continued)

First author Year	Sample size (n)	Age (years)	Bone status	Menopausal age (years)	BMI (kg/m^2)
Marin-Cascales 2019	E: 13 C: 10	E: 58 ± 7 C: 62 ± 5	Healthy (?)	E: ≥ 3 C: ≥ 3	E: 30 ± 4 C: 29 ± 5
Marques 2011	E: 30 C: 30	E: 70 ± 5 C: 68 ± 5	Healthy	n.g n.g	E: 28 ± 4 C: 28 ± 4
Marques 2011	RE: 23 AE: 24 C: 24	RE: 67 ± 5 AE: 70 ± 5 C: 68 ± 6	Healthy	n.g n.g n.g	RE: 29 ± 5 AE: 28 ± 4 C: 28 ± 4
Martin 1993	45 ^{mE}: 25 30 ^{mE}: 27 C: 24	45 ^{mE}: 58 ± 7 30 ^{mE}: 60 ± 8 C: 57 ± 7	Healthy	45 ^{mE}: 9 ± 9 30 ^{mE}: 13 ± 9 C: 8 ± 7	#45 m E: 26 #30 mE: 26 #C: 28
Milliken 2003	E: 26 C: 30	E: 57 ± 5 C: 57 ± 5	Healthy	E: 6 ± 3 C: 6 ± 3	#E: 26 #C: 26
Montgomery 2020	E1: 5 E2: 5 C: 7	Co: 56 ± 3 In: 53 ± 3 C: 54 ± 4	Healthy	E1: ≤ 5 E2: ≤ 5 C: ≤ 5	Co: 25 ± 2 In: 25 ± 5 C: 25 ± 3
Nelson 1994	E: 21 C: 19	E: 61 ± 4 C: 57 ± 6	Healthy (6 women with spine fracture)	E: 12 ± 5 C: 10 ± 5	E: 24 ± 3 C: 23 ± 2
Nelson 1991*	E: 21[7] C: 20	E: 60 ± 1 C: 60 ± 1	Healthy	E: 11 ± 1 C: 11 ± 1	E: 24 ± 1 E: 24 ± 1
Nichols 1995*	E: 17 C: 17	E: 68 ± 2 C: 65 ± 1	Healthy	E: 18 ± 1 C: 18 ± 1	#E: 26 #C: 27
Nicholson 2015	E: 28 C: 29	E: 66 ± 4 C: 66 ± 5	Healthy	E: > 5 C: > 5	E: 26 ± 3 C: 25 ± 3
Orsatti 2013	E + Pl: 20 Pl: 20	E + Pl: 56 ± 9 Pl: 55 ± 8	Healthy	E + Pl: 9 ± 6 Pl: 8 ± 6	E + Pl: 26 ± 3 Pl: 30 ± 5
Park 2008	E: 25 C: 25	E: 68 ± 4 C: 68 ± 3	Healthy	E: 18 ± 2 C: 19 ± 3	n.g n.g
Prince 1995	E + Ca: 42 Ca: 42	E + Ca: 63 ± 5 Ca: 62 ± 5	Healthy	E + Ca: ≥ 10 Ca: ≥ 10	n.g n.g
Pruitt 1995	HI: 15 LI: 13 C: 12	HI: 67 LI: 68 ± 1 C: 70 ± 4	Healthy	n.g n.g n.g	HI: 25 ± 3 LI: 24 ± 2 C: 25 ± 3
Pruitt 1992*	E: 17 C: 10	E: 54 ± 1 C: 56 ± 1	Healthy	E: ≤ 7 C: ≤ 7	#E: 25 #C: 25
Rhodes 2000	E: 22 C: 22	E: 69 ± 3 C: 68 ± 3	Healthy	n.g n.g	#E: 26 #C: 24
Ryan 1998	E: 18 C: 18	E: 62 ± 6 C: 63 ± 6	Healthy	E: > 2 C: > 2	E: 31 ± 3 C: 31 ± 3
Sakai 2010*	E: 49 C: 45	E: 68 ± 1 C: 68	Healthy	n.g n.g	E: 22 ± 0 C: 23 ± 0
Silverman 2009	E: 46 C: 40	E: 60 ± 5 C: 58 ± 5	Healthy	E: 12 ± 8 C: 11 ± 7	E: 32 ± 4 C: 33 ± 5
Sinaki 1989	E: 34 C: 34	E: 56 ± 4 C: 56 ± 4	Healthy	E: > 0.5 C: > 0.5	E: 25 C: 26
Sugiyama 2002*	E: 13[8] C: 13	E: 52 ± 1 C: 53 ± 1	Healthy	E: ≤ 5 C: ≤ 5	E: 23 ± 1 C: 22 ± 1
Tartibian 2011	E: 20 C: 18	E: 61 ± 7 C: 59 ± 8	Healthy	E: ≥ 8 C: ≥ 8	E: 25 ± 7 C: 29 ± 4
Tolomio 2009	E: 81 C: 79	E: 62 ± 5 C: 64 ± 5	≥ Osteopenia	n.g n.g	#E: 26 #C: 25
Verschueren 2004	E: 22 C: 24	E: 64 ± 4 C: 64 ± 3	Healthy	E: 15 ± 6 C: 15 ± 7	E: 27 ± 4 C: 27 ± 6
Waltman 2022	E: 92 C: 93	E: 54 ± 3 C: 54 ± 3	Osteopenia	E: ≤ 6 C: ≤ 6	E: 26 ± 4 C: 26 ± 5

Table 1 (continued)

First author Year	Sample size (*n*)	Age (years)	Bone status	Menopausal age (years)	BMI (kg/m^2)
Wang 2015	TC: 40 TCRT: 40 C: 39	TC: 58 ± 3 TCRT: 58 ± 3 C: 58 ± 3	Healthy	TC: > 0.5 TCRT: > 0.5 C: > 0.5	#TC: 24 #TCRT: 23 #C: 24
Woo 2007	TC: 30 RE: 30 C: 30	TC: 70 ± 3 RE: 70 ± 3 C: 69 ± 3	Healthy	n.g n.g n.g	TC: 24 ± 4 RE: 25 ± 4 C: 25 ± 3
Wu 2006	E + Pl: 34 Pl: 34	E + Pl: 55 ± 3 Pl: 55 ± 3	Healthy	E + Pl: ≤ 5 Pl: ≤ 5	E + Pl: 22 ± 3 Pl: 21 ± 2
Yamazaki 2004*	E: 32 C: 18	E: 64 ± 3 C: 66 ± 3	≥ Osteopenia	E: 17 ± 9 C: 15 ± 9	E: 21 ± 8 C: 21 ± 6

All values are presented as mean value ± SD, unless stated otherwise

AE aerobic exercise, *C* control, *Ca* calcium, *E* exercise, *En* endurance, *Fit* fitness, *GRF* ground-reaction forces, *H* high, *HI* high impact, *HL* high load, *HR* high repetition, *JRF* joint-reaction forces, *LI* low impact, *M* moderate, *n.g.* not given, *Pl* placebo, *RE* resistance exercise, *SP* soy protein, *TC* Tai Chi, *TCRT* Tai Chi resistance training

*Numbers are presented as mean ± SE

#Calculated (body mass (kg)/body height (m^2)). "Bone status": We focus on osteoporosis/osteopenia and fractures — otherwise, subjects were considered "healthy"

[1] According to the text, 63 women were randomized equally

[2] It is not stated to which groups the seven drop outs belong

[3] It is not stated to which group the nine drop outs belong

[4] It is not clear to which exercise groups two persons who failed to complete the program belong

[5] One side of body is considered as control and the other side as intervention

[6] No data concerning participants/group; we assumed an equal allocation

[7] Exercise with or without 831 mg/day Ca versus sedentary control with or without 831 mg/day Ca

[8] According to the baseline table, there are 13 women in the exercise group; six persons in exercise groups were excluded due to low compliance, but it is not clear whether these participants are in the pre- or postmenopausal group

Outcome measures

Most of the trials determined BMD at the LS and femoral neck and/or total hip ROI. Ten studies measured BMD exclusively at the LS [46, 48, 52, 54, 55, 57, 75, 91, 95, 100], and seven studies determined BMD only at the proximal femur [25, 49, 62, 66, 74, 89, 94].

Meta-analysis results

Effects of exercise on BMD at the lumbar spine

Eighty-five comparisons addressed exercise effects at BMD-LS (Fig. 2). In summary, the inverse heterogeneity model (IVhet) (Fig. 2) with imputation of the mean correlation demonstrated a significant effect ($p < 0.001$) of exercise on BMD at the LS (SMD: 0.29; 95% CI: 0.16 to 0.42). Heterogeneity between the trial results ($I^2 = 68\%$) can be classified as substantial (Fig. 2). Applying sensitivity analysis with imputation with minimum correlation (i.e., maximum SD, SMD: 0.21; 95% CI: 0.12 to 0.29) or maximum correlation (i.e., minimum SD, SMD: 0.45; 95% CI: 0.21 to 0.69) led to diverging, but consistently significant ($p < 0.001$) results.

The IVhet model–based funnel plot analysis with trim and fill suggests significant evidence for a publication/small study bias (Fig. 3). The analysis imputes nine missing studies on the left-hand side (i.e., favors control group). However, even the corrected, i.e., imputation-adjusted, intervention effect remains significant ($p = 0.008$). The significant asymmetry was confirmed by the LFK Index (1.50), the regression ($p = 0.011$), and the rank correlation test ($p = 0.016$).

Effects of exercise on BMD at the femoral neck

Thirty-one group comparisons determined exercise effects at BMD-FN (Fig. 4). In summary, the IVhet model with imputation of the mean correlation demonstrated a significant effect ($p < 0.001$) of exercise on BMD at the FN (SMD: 0.27; 95% CI: 0.16 to 0.39) (Fig. 4). Heterogeneity between the trial results ($I^2 = 58\%$) was moderate (Fig. 4). Applying imputation with minimum correlation (SMD: 0.20; 95% CI: 0.13 to 0.27) or maximum correlation (SMD: 0.55; 95% CI: 0.24 to 0.86) led to diverging, but consistently significant ($p < 0.001$), results.

The funnel plot analysis with trim and fill suggests no relevant evidence for a publication/small study bias (Fig. 5).

Table 2 Exercise characteristics of the studies

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Adami 1999	6	Sedentary	DRT (focus on forearm sites), volleyball in a sitting/standing position	SJE: 2×95–110 min: 15–30 min warm up (walking), 70 min press-up, volleyball, 10 min DRT for the forearm with a 500-g weight. Number of reps (10–25)/min increased progressively. HE: 7×30 min: "repeat all exercise"	S-JE: 83% HE: ng
Basat 2013	6	No BSE	DRT (lower body with few trunk exercises)	3×60 min: 15 min warm up (walking, cycling), 30–40 min RT (≥9 exercises, 1 set, 10 reps (more details ng))	> 60%
	6		Rope skipping	7×35 min: 15 min warm up (walking, cycling), maximum 50 jumps/session (more details ng)	> 60%
Bassey 1995	12	No BSE	Heel drops, jumping, skipping	HE: 7×?min/w, 50 heel-drops barefoot on a thinly covered floor with knee and hip extended. S-JE: 1×? jumping and skipping (more details ng)	84%
Bassey 1998	12	No vigorous Ex > 1 h/week	Jumping: counter-movement jumps (CMJ)	6×10 min: 50 CMJ barefoot with both legs, 5 sets×10 reps with ground reaction forces (GRF): 4×body mass	91%
Bello 2014	8	No BSE	Walking, DRT (all main muscle groups), aquatic exercise (DRT)	3×40–? min/w: 40 min walking 1×w, WB-circuit training 1×w with easy loads: 6 exercises, 3 sets, 15–20 reps. Aquatic exercise 1×w: 4 exercise, 3 sets, 15–20 reps, all at RPE 12–15 of Borg CR 20. 1×week each type of exercise	85%
Bemben 2000	6	No RT	DRT (all main muscle groups) with machines	High intensity: 3×60 min: DRT: 45 min, 8 exercises, 3 sets, 8 reps, 80% 1RM	87%
				Low intensity: 3×60 min: DRT: 45 min, 8 exercises, 3 sets, 16 reps, 40% 1RM	93%
Bemben 2010	8	No RT	DRT (all main muscle groups) with machines	3×≈60 min: 5 min warm up (walking, cycling), 8 exercises, 3 sets, 10 reps, 80% 1RM and dumbbell wrist curls, abdominal flexion low-moderate intensity	90%
Bergström 2008	12	No BSE	DRT (all main muscle groups), AET, walking	4–5×week: S-JE: 1–2×60 min, 25 min DRT, 25 min WB-AET (more details ng), HE: 3×30 min fast walking (more details ng)	95%
Bloomfield 1993	8	Sedentary	Cycle ergometer	3×50 min: 15 min warm up (flexibility and calisthenics (more details ng)), 30 min cycling at 60–80% HR_{max}, 5 min walking (cool down) (more details ng)),	82%

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Bocalini 2009	6	Sedentary	DRT (all main muscle groups)	3 × 60 min: 10 min warm up (low impact running), 12 exercises, 3 sets, 10 reps, 85% 1RM with focus on eccentric exercises, 1 min rest (alternate upper and lower body exercises) between exercises	> 90%
Bolton 2012	12	No BSE	DRT (muscle groups ng: "loading the proximal femur"), jumping	S-JE: 3 × 60 min: 40 min (?) exercises, 2 sets, 8 reps, 80% 1RM with slow velocity, 1 set with reduced load & high velocity (12 rep). HT: daily 3 sets, 10 reps of jumps (more details ng)	88%
Brooke-Wavell 1997	12	Sedentary	Brisk walking	In total, 140 min/w, 20–50 min long for each walk, ≈ 70% HR_{max}	100%
Brooke-Wavell 2001	12	Sedentary	Brisk walking	4–5 × 25–35 min at ≈ 70% HR_{max}	> 90%
Caplan 1993	24	n.g	Aerobic dance, ball games, DRT: floor exercises (more details ng)	2 × 60 min: 20–25 min AET, 10 min ball games (more details ng) ≥ 1 × 20–30 min DRT (more details ng)	ng
Chan 2004	12	Sedentary	Tai Chi: Yang style (all main muscle groups)	5 × 50 min: slow, smooth movements with constant velocity (more details ng)	≈84%
Chilibeck 2002	12	No vigorous exercise	DRT (all main muscle groups) on machines	3 × ? min/w: 12 exercises, 2 sets, 8–10 reps, ≈70% 1RM	78%
Chilibeck 2013	24	No BSE	Walking, DRT (all main muscle groups) on machines	6 × week: S-JE: 2 × ng: 15 exercises, 2 sets, 8 reps, 80% 1RM HT and S-JE: 4 × 20–30 min: walking at 70% HR_{max}	77%
Choquette 2011	6	Sedentary	AET (treadmill and cycling), DRT (all main muscle groups) on machines and with free weights	3 × 60, AET: 30 min at 40–85% HR_{max}, after 3 months H-intensity intervals of 4 × 4 min ≥ 90% HR_{max}, 3 min rest at 50–65% HR_{max}. RT: 30 min, ? exercise, 1 set, 12–15 reps increased to 4 sets 4–6 reps, at 60–85% 1RM	≥ 85%
Chuin 2009	6	n.g	DRT (most main muscle groups) on machines	3 × 60 min: 15 min warm up (treadmill/cycle ergometer), DRT: 45 min, 8 exercises, 3 sets, 8 reps at 80% 1RM, rest between sets 90–120 s, 1RM test each 4 weeks	> 90%

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
De Matos 2009	12	n.g	DRT (all main muscle groups) on machines or free weights, AET (bike, treadmill)	3 × 45–65 min, WB-/ non-WB-AET (bike, treadmill, stepper): 5–20 min (RPE 4–6 on Borg CR 10). DRT: 30–40 min, 9 exercises, ? sets, 10–15 reps, ? 1RM, TUT: 3 s conc-3 s eccentric, 1 min rest between sets/exercise (more details ng)	ng
Deng 2009	12	No BSE	Brisk walking, stepping, jumping, DRT (all main muscle groups) on machines with free weights	5–7 × w: S-EJ: 2 × 60 min: 45 min DRT, 9 exercises, 2–5 sets, 12–40 reps, at 50–60% 1RM, self-selected rest (more details ng), HE: 3–5 × 60 min: 30 min walking, at 50–80% HR_{max}, 15 min step routine, 50–300 jumps from a 4-inch bench	82%
De Oliveira 2018	6	Sedentary	Pilates (all main muscle groups) on machines	3 × 60 min: 21 exercises (strengthening and flexibility), 1 set, 10 reps, 1 min rest between exercises, 5–6 at Borg CR10	93%
Duff 2016	9	No RT	DRT (all main muscle groups) on machines and with free weights	3 × ? min/w: 12 exercises, 2 sets, 8–12 reps to muscular fatigue, ? 1RM (more details ng)	84%
Ebrahim 1997	24	No limit	Brisk walking	3 × 40 min: 40 min walking, "faster than usual, but not so fast as to be uncomfortable"	100%
Englund 2005	12	n.g	Walking/jogging, DRT (all main muscle groups)	2 × 50 min, WB-AET: 10 min warm up, 15 min walking/jogging. DRT: 12 min, 2 sets, 8–12 reps, ? 1RM (more details ng)	67%
Evans 2007	9	n.g	Walking/running, rowing, stair-climbing (machines)	3 × 45 min: WB and non-WB AET (machines) at 55–80% $VO_{2, peak}$. Rest by changing exercise mode	ng
Going 2003	12	No RT, < 120 min/w. exercise	WB with weighted vests, DRT (all main muscle groups) on machines with free weights	3 × ≈60 min: 10 min warm up (walking), 20–25 min WB-AET (walking, jogging, skipping, hopping, stepping) at 60% HR_{max}, 120–300 stair/steps with 5–13 kg weighted vest DRT: 7 exercises, 2 sets, 6–8 reps 70–80% 1RM	72%

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Grove 1992	12	Sedentary	Jumping variations, heel drops (GRF ≥ 2 × body mass)	3 × 60 min: 20 min of high impact exercises. 15 min cool down (RT with abdominal and leg adduction/abduction exercises) (more details ng)	83%
	12		Walking, Charleston, heel jacks (GRF < 1.5 × body mass)	3 × 60 min: 20 min of low impact exercises. 15 min cool down (RT with abdominal and leg adduction/abduction exercises) (more details ng)	80%
Hans 2002	24	n.g	Heel drops: barefoot on a force measuring platform (osteocare protocol)	5 × 3–5 min: impact loading: strength or height 25–50% above the estimated resting force, daily 120 correct force impacts	65%
Hartard 1996	6	No BSE	DRT (all main muscle groups) on machines	2 × ? min/w: 14 exercises, 1–2 sets, 8–12 reps, 70% 1RM, TUT: concentric: 3–4 s–eccentric: 3–4 s. ≥ 2 min rest between sets	> 83%
Hartley 2020	6	Sedentary	Unilateral multidirectional hopping	7 × 10 min, warm up (n.g.), 5 sets × 10 reps of unilateral multidirectional hops, 15 s rest between set, GRF: ≈2.2 × body weight	77%
Hatori 1993	7	Sedentary	Walking below the anaerobic threshold at "flat grass covered ground"	3 × 30 min: 30 min walking at 90% anaerobic threshold HR (6.2 km/h)	ng
			Walking above the anaerobic threshold on "flat grass covered ground"	3 × 30 min: 30 min walking at 110% anaerobic threshold HR (7.2 km/h)	ng
Hettchen 2021	13	No BSE	Block periodized AET, jumping, isometric and DRT (all main muscle groups) exercise on machines with free weight, body mass	3 × 45–60 min, 2 × 45 min aerobic dance (GRF: 2–3 × body mass), 8 sets × 7 reps of high and drop jumps with 20 s rest/sets (GRF: 4–4.5 × body mass), circuit training with free weights: 1–2 sets × 6–20 reps at 55–80% 1RM, 30 s rest/exercise. 1 × 60 min DRT on machines: 12 exercises, 1 set, 8–16 reps, 30 s rest up, with varying movement velocities, 60–85% 1RM (12 weeks) intermitted by 8–10 weeks of 25 min of non-supervised floor/functional exercise at home (more details ng)	79%
Holubiac 2022	6	No BSE	DRT (all main muscle groups) with machines	2 × 60 min: 11 exercises, 2 sets, 12 reps, at 50–70% 1RM	ng
Iwamoto 2001	24	Sedentary	Walking, DRT ("Gymnastics": lower limbs and trunk exercises)	Daily (walking) min?: additionally (to basic activity walking) ≈3000 steps/d, 2 × daily DRT: ≥ 4 exercises, 2 sets, 15 reps, ?% 1RM (more details ng)	ng

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Jessup 2003	8	Sedentary	Walking, stairclimbing, DRT (most main muscle groups) on machines	3×60–90 min, DRT: 20–35 min, 8 exercises, ? sets, 8–10 reps, 50–75% 1RM. WB-AET: 30–45 min with weighted vest (increased up to 10% body mass)	ng
Karakiriou 2011	6	Sedentary	Step aerobic exercise, DRT (all main muscle groups)	3×w: 1×15 min warm up (walking on treadmill/cycling ergometer and jumping). Abdominal and back extension exercises (one exercise for all main muscle groups, 2–4 sets of 16 repetitions (more details ng)). DRT: 2×: 11 exercises, 2–3 sets, 10–12 reps at 70% 1RM, 30 s rest between exercises, 3 min between sets. AET: 1×45 min AET: 20 min, 9 exercise, 2 circuits of 40 s, rest: 20 between exercises, 2 min between circuits, 70–85% HR_{max}	80%
Kemmler 1999	9	No BSE	Running, gaming, jumping, DRT (all main muscle groups)	4×week: 2×90 min: AET: 25 min at 70–80% HR_{max}. RT: 65 min, 12–15 exercises, 2–4 sets of 8 s maximum isometric contractions, 6 trunk, upper back, lower extremity exercises, 20–25 reps at 60–65% 1RM 2×35 min, HT: resistance exercises	S-JE: 82% HE: 59%
Kemmler 2004	26	No BSE	Aerobic dance, jumping, DRT (all main muscle groups) on machines with free weight, and own body mass	4×week: 2×60–70 min, AET: 20 min at 65–85% HR_{max}. Jumping started after 5–6 months with 4×15 multi-lateral jumps. DRT: 30–40 min, 1/w. The first 6 month: 13 ex, 2 sets, 20–12 reps, TUT: 2 s concentric, 2 s eccentric at 50–65% 1RM, 90 s rest between sets and exercises. Then, 12 w blocks of H-intensity at 70–90% 1RM interleaved by 4 w at 55–79% 1RM. Isometric RT: 30–40 min, 1/w, 12–15 exercises (trunk and femur), 2–4 sets, 15–20 reps, 15–20 s rest 2×25 min, HT: rope skipping (3 sets, 20 reps), RT (more details ng)	S-JE: 79% HE: 61%

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Kemmler 2010	18	No BSE	Aerobic dance, DRT (all main muscle groups)	4 × w: 2 × 60, AET: 20 min at 70–85% HR_{max}. RT: 10–15 exercises, 1–3 sets of 6–10 s maximum isometric contractions, 20–30 s rest, 3 upper body exercises, 2–3 sets 10–15 reps, TUT: 2 s concentric, 2 s eccentric at 65–70% 1RM, 3 lower extremity exercises, 2 sets 8 reps, 1 min rest at 80% 1RM 2 × 20, HE: RT 1–2 sets, 6–8 exercise, 10–15 reps. 2–3 belt exercises, 2 sets, 10–15 reps (more details ng)	S-JE: 76% HE: 42%
Kemmler 2013	12	No BSE	Block periodized AET, jumping, isometric and DRT (all main muscle groups) exercise on machines with free weight, body mass	3 × 45–60 min: Block I: 1 × 45 min/w H-impact aerobic 75–85% HR_{max}, 2 × 20 min/w aerobic 75–85% HR_{max}, 4 × 15–20 jumps, 90 s rest. RT: 15 min, 8–12 floor exercises (trunk, hip, legs), 1–2 sets, rep?, 30 s rest. RT: 20 min, 8 exercises, 2 sets, 8–9 reps, 45 s rest up, TUT: 2 s concentric, 2 s eccentric, to 80% 1RM	67%
Kerr 1996	12	No RT, no racquet sports, ≤ 3 h/w exercise	Unilateral DRT (all main muscle groups, randomized allocation of the left side or right side to exercise or control group) on machines or free weights	3 × 45–60 min: 13 exercises, 3 sets at 20 RM, 3–5 reps (≈60–65% 1RM), 2–3 min rest between sets	89%
	12			3 × 20–30: 13 exercises, 3 sets at 8 RM, 3–5 reps (≈75–80% 1RM), 2–3 min rest between sets	87%
Kerr 2001	24	≤ 2 h/w Exercise	DRT (all main muscle groups)	3 × 60 min: ≈30 min brisk walking and stretching, RT: 30 min, 9 exercises, 3 sets at 8 RM (≈75–80% 1RM)	74%
	24		DRT (all main muscle groups), Stationary cycling	3 × 60 min: ≈30 min brisk walking and stretching. RT: 30 min, 9 exercises, 3 sets, 8 reps, 40 s/exercise with "minimal load", 10 s rest between the exercises (more details ng). Stationary cycling 40 s, HR < 150 beats/min	77%
Kohrt 1995	11	Sedentary	Walking, jogging, stair climbing	3–5 × 45 min: first 2 months flexibility, 9 months WB: 5–10 min warm up (treadmill 60–70% HR_{max}), 30 min WB at 65–85% HR_{max}	≈70%

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Kohrt 1997	11	Lower intensity compared to intervention	Walking, jogging, stair climbing	3–5 × 30–45 min: first 2 months flexibility, 9 months WB at 60–85% HR_{max}	≈70%
	11		DRT (all main muscle groups) with free weights and on machines, rowing	3–5 × 40–60 min: first 2 months flexibility, DRT: 2/w, ≈20–30 min, 8 exercises, 2–3 sets, 8–12 reps "to fatigue" (≈70–80% 1RM). Rowing: 3/w, 15–30 min, 2–3 sets × 10 min at 60–85% HR_{max}	≈70%
Korpelainen 2006	30	n.g	Jumping, walking/jogging, dancing, stamping, chair climbing	8 × w: S-JE: 45 min WB-AET. The first 6 months: 1 × 60 min S-JE and daily × 20 min HE. The second 6 months: HE: daily × 20 min HE applying the same exercise to S-JE (more details ng)	≈75%
Kwon 2008	6	< 2 h/w exercise	Aerobic dance, DRT (6 upper & lower body exercises) with free weights	3 × 80 min: 30 min AET at 40–75% HR_{max}, 30 min DRT of 6 exercises, ? sets, 3–10 reps to voluntary fatigue (i.e., 75% 1RM)	ng
Lau 1992	10	n.g	Stepping up and down, Upper trunk movements	4 × ≈20–25 min: 100 steps on a 23-cm block, 15 min upper trunk movements (?) in a standing position with submaximum effort (more details ng)	ng
Liu 2015	12	n.g	Tai Chi	3 × daily ≈3–5 min: 8 exercise brocade, 7 reps (raising slowly the arms coming on the toes stretching the back and go back on the heel with arms hanging down) (more details ng)	96%
Lord 1996	12	lower intensity compared to intervention	Conditioning period: Brisk walking, multilateral stepping, lunges, heel rises, DRT (all main muscle groups) using owns body mass	2 × 60 min: 5 min warm up (paced walking), conditioning period 35–40 min: AET and guided functional gymnastics for all main muscle groups (sets?, reps?, intensity?) (more details ng)	73%
Maddalozzo 2007	12	n.g	DRT (back squat, deadlifts) with free weights	2 × 50 min: 15–20 min warm up (exercise focusing on posture, muscle engagement, abdominal strength, flexibility) 2 sets, 10–12 reps, 50% 1RM. Main part: 20–25 min, 2 exercises, 3 sets, 8–12 reps, 60 s rest between sets at 60–75% 1RM, TUT: 1–2 s concentric, 2–3 s eccentric	85%

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Marin-Cascales 2019	6	Sedentary	Multi-component E, drop-jumps, AE	3 × w, 4–6 sets × 10 drop jumps from 5 to 25 cm height and 30–60 min walking at 50–75% HRR (progressively increased during the intervention)	96%
Marques 2011	8	sedentary	Marching, bench stepping, heel-drops, DRT (most main muscle groups) with weighted vests, elastic bands, free weights	2 × 60 min: 15 min WB-AET with peak-GRF up to 2.7 × body mass and high strain frequency (120–125 beats/min), 10 min for ≥ 7 muscle endurance exercises, 1–3 sets, 8–15 reps, ?1RM (more details ng), 10 min balance and dynamic exercise (walking, playing with ball, rope, sticks, etc.), 10 min agility training (coordination, balance, ball games, dance) (more details ng)	72%
Marques 2011	8	Sedentary	Walking, stepping, skipping, jogging, dancing	3 × 60 min: Only the first 6 w 10 min DRT (lower body). 35–40 min of WB-AET (50–85% HRR) with peak-GRF up to 2.7 × body mass with up to 120 beats/min	78%
	8		DRT (all main muscle groups) on machines	3 × 60 min: 8–10 min warm up (cycling/rowing ergometer) at low intensity. 30–40 min DRT, 8 exercises, 2 sets, 6-15 reps, 50–80% 1RM with variable TUT (3–6 s/rep), 120 s rest between sets, 5–10 min cool down (walking and stretching)	78%
Martin 1993	12	No BSE	Brisk walking on treadmill	3 × 36–40 min: 30 min brisk walking (4–6.2 km/h at 3–7% incline) at 70–85% HR_{max}	79%
	12		Brisk walking on treadmill	3 × 51–55 min: 45 min brisk walking (4–6.2 km/h at 3–7% incline) at 70–85% HR_{max}	82%
Milliken 2003	12	< 2 h/w exercise	Walking, skipping, multilateral stepping, jumping with weighted vests, DRT (all main muscle groups) with free weights, on machines, functional gymnastics	3 × 75–min: 20 min WB-AET at 50–70% HR_{max}. 35 min DRT: 8 exercises, 2 sets, 6–8 reps, 70–80% 1RM. Functional gymnastics for shoulder and abdominals using elastic bands and physio-balls	ng

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Montgomery 2020	12	No BSE	Continuous jumping	3 × 30 reps/session of high impact jumps (frequency 15 jumps per min) "jump as high as possible and land on feet-balls," barefoot on hard surface	60%
	12		Intermittent jumping	3 × 30 reps/session of high impact jumps (frequency 4 jumps per min) "jump as high as possible and land on feet-balls," barefoot on hard surface	68%
Nelson 1991	12	Sedentary	Walking with weighted vest	4 × 50 min: walking with a 3.1-kg weighted vest at 75–80% HR_{max}	90%
Nelson 1994	12	Sedentary	DRT (most main muscle groups) on machines	2 × 55 min: 45 min, 5 exercises, 3 sets, 8 reps, 50–80% 1RM, TUT 6–9 s/rep, 3 s rest between reps, 90–120 s rest between sets	88%
Nichols 1995	12	≥ 3 × 30 min/w exercise	DRT (all main muscle groups) on machines	3 × ≈45–60 min: 5 min warm up (walking), 8 exercises, 1–3 sets, 10–12 reps, 50–80% 1RM, 30–60 s rest between exercises, 60 s rest between sets	82%
Nicholsen 2015	6	No RT	DRT (all main muscle groups): "Body Pump Release 83" (i.e., barbell exercises)	2 × 50 min: 10 × up to 6 min blocks of exercises for all main muscle groups (21 exercises in total), up to 108 reps (squats), ≤ 30% 1RM	89%
Orsatti 2013	9	Sedentary	DRT (all main muscle groups) with free weights and on machines	3 × 50–60 min: 8 exercises 3 sets, 8–15 reps at 40–80% 1RM, 3 sets —20–30 reps for trunk flexion and calf raises (more details ng), 1–2 min rest between sets	ng
Park 2008	12	≤ 7 h/w exercise	WB-AET, RT (more details ng)	3 × 60 min: 10 min RT, 23 min of WB exercise at 65–70% HR_{max} (more details ng)	ng
Prince 1995	24	≤ 2 h/w exercise	WB-AET (more details ng)	4 × 60 min: 4 × WB exercise (including 2 × walking) at 60% HR_{max} (more details ng)	39%
Pruitt 1992	9	No BSE	DRT (all main muscle groups) with free weights and on machines	3 × 60 min: 40 min, 11 exercises, 1 set, at 10–12 RM for upper body and 10–15 RM for lower body (more details ng)	83%
Pruitt 1995	12	No RT	DRT (all main muscle groups) on machines	3 × 55–65 min: 50–55 min, 10 exercises, 1 warm up set, 14 reps, at 40% 1RM, 2 sets, 7 reps, 80% 1RM	81%
	12		DRT (all main muscle groups) on machines	3 × 55–65 min: 50–55 min, 10 exercises, 3 sets, 14 reps, at 40% 1RM	77%

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Rhodes 2000	12	Sedentary	DRT (all main muscle groups) on machines	3 × 60 min: 10 min warm up (cycle ergometer), DRT: 40 min, ≥ 6 exercises, 3 sets, 8 reps, 75% 1RM, TUT: 2–3 s concentric–3–4 s eccentric movement/rep applied in a circuit mode	85%
Ryan 1998	6	Sedentary	Walking, jogging on treadmill	3 × 55 min: up to (4th month) 35 min walking/jogging at 50–70% $VO_{2,max}$, 10 min cool down (cycle ergometer), energy-intake restriction of 250–350 kcal/d (weight loss study)	> 90%
Sakai 2010	6	n.g	Unilateral standing on one leg	7 × 2 min: 3 sets (early, at noon, in the evening) of unilateral standing for 1 min on each leg with eyes open (more details ng)	≥ 70%
Silverman 2009	6	Sedentary	Walking	3 × 45–60 min: walking at 50–75% HR_{max} Energy-intake restriction of 250–350 kcal/d (weight loss study)	78%
Sinaki 1989	24	n.g	DRT (back strengthening exercise in a prone position using a back pack, ≈hyperextensions) with free weights	5 × ?: one back strengthening exercise, 1 set, 10 reps, with a weight equivalent to 30% of the maximum isometric back muscle strength in pounds (maximum 23 kg)	ng
Sugiyama 2002	6	n.g	Rope skipping (more details ng)	2–3 × ?min/w.: 100 jump/session (more details ng)	82%
Tartibian 2011	6	Sedentary	Walking/jogging on treadmill	3–6 × 25–45 min: first 12 w: 3–4 × 25–30 min at 45–55% HR_{max}, second 12 weeks: 4–6 × 40–45 min at 55–65% HR_{max}	95%
Tolomio 2009	11	n.g	DRT (joint mobility, elastic bands, balls), aquatic exercise (more details ng)	3 × 60 min: the first 11 w only in gym, then 2 times in gym and once in water. 15 min warm up (brisk walking, stretching), 2 × 30 min/w RT, 1 × 30 min/w water gymnastics (more details ng). 2 periods (6, 10 w) training at home (more details ng)	ng
Verschueren 2004	6	n.g	DRT (leg press, leg extension)	3 × 60 min: 20 min warm up (running, stepping, or cycling) at 60–80% HR_{max}, DRT: 2 exercises, 1–3 sets, 20–8 reps	ng
Wang 2015	12	No Tai Chi	Tai Chi (Yang style)	4 × 60 min: 40 min: 5 reps × 6 min set, 42 type compositions each, 2 min rest (more details ng)	ng
	12		Tai Chi-RT (includes 4 Chen style actions)	4 × 60 min: 40 min: 6 reps × 5 min exercise, 2 min rest (more details ng)	ng

Table 2 (continued)

First author Year	Study length (months)	Life style status	Major type of exercise	Exercise/strain composition Exercise frequency (*n*/week), duration of the session (min/week), type of exercise, sets/repetitions or duration of the exercise, exercise intensity	Attendance
Waltman 2022	12	n.g	Jogging, DRT (all main muscle groups) with machines	3 × ?min/w, Jogging with weighted vest, DRT: ?exercises, ?sets, 8–12 reps at 70 to 85% of 1RM (more details ng)	59%
Woo 2007	12	Sedentary	Tai Chi (Yang style)	3 × ?min/w: 24 forms of Yang-Style Tai Chi (more details ng)	81%
	12		DRT (arm-lifting, hip abduction, heel raise, hip flexion, hip extension, squat) using elastic bands	3 × ?min/w: 6 exercises, 30 reps (more details ng)	76%
Wu 2006	12	Sedentary	Walking	3 × 60 min: 45 min of walking with 5–6 km/h	ng
Yamazaki 2004	12	Sedentary	Walking	≥ 4 × 60 min: 8000 steps/session at 50% $VO_{2,max}$	100%

Composition of strain/exercise parameters per session: AET: frequency/week, exercise duration per session, exercise intensity; DRT: exercises/number of exercises; number of sets, number of repetitions; exercise intensity. Jumping: type of jumps, number of jumps and intensity of jumps. Tai Chi: style, number of forms

AET aerobic exercise training, *BSE* bone-specific exercise, *DRT* dynamic resistance training, *GRF* ground reaction forces, *H* high, *HE* home exercise, HR_{max} maximum heart rate, *JE* joint exercise program, *n.g.* not reported, *RPE* rate of perceived exertion, *S* supervised, *TUT* time under tension, $VO_{2,max}$ maximum oxygen uptake, *WB* weight bearing, *1RM* one repetition maximum, *?* no clear information

Table 3 Assessment of risk of bias for included studies

First author, Year	Eligibility criteria[1]	Random allocation	Allocation concealment	Inter group homogeneity	Blinding subjects	Blinding caregivers	Blinding assessors	participation≥ 85% allocation	Intention to treat analysis[2]	Between group comparison	Measure of variability	Overall Score
Adami 1999	+	−	−	+	−	−	−	+	−	+	+	4
Basat 2013	+	+	+	+	−	−	−	−	−	+	+	5
Bassey 1998	+	+	−	+	−	−	−	−	−	+	+	4
Bassey 1995	+	+	−	+	−	−	−	−	−	+	+	4
Bello 2014	+	+	−	+	−	−	−	−	+	+	+	5
Bemben 2010	+	−	−	+	−	−	−	+	+	+	+	5
Bemben 2000	+	+	−	+	−	−	−	−	−	+	+	4
Bergström 2008	+	+	+	+	−	−	−	−	+	+	+	6
Bloomfield 1993	+	−	−	−	−	−	−	+	+	+	+	4
Bocalini 2009	+	+	−	+	−	−	+	−	−	+	+	5
Bolton 2012	+	+	+	−	−	−	+	+	+	+	+	7
Brooke-Wavell 2001	+	−	−	+	−	−	−	+	+	+	+	5
Brooke-Wavell 1997	+	+	−	+	−	−	−	+	−	+	+	5
Caplan 1993	+	−	−	+	−	−	−	+	+	+	+	5
Chan 2004	+	+	−	+	−	−	−	−	+	+	+	5
Chilibeck 2013	+	+	+	+	−	−	+	+	+	+	+	8
Chilibeck 2002	+	+	+	+	+	+	−	−	+	+	+	8
Choquette, 2011	+	+	−	+	−	−	−	−	+	+	+	5
Chuin 2009	+	+	−	+	−	−	−	−	+	+	+	5
de Matos 2009	+	−	−	+	−	−	−	−	−	+	+	3
Deng 2009	+	−	−	+	−	−	−	+	−	+	+	4

Table 3 (continued)

de Oliveira 2018	+	+	+	+	−	−	+	+	+	+	+	8
Duff 2016	+	+	+	+	+	−	+	−	+	+	+	8
Ebrahim 1997	+	+	+	+	−	−	+	−	+	+	+	7
Englund 2005	+	+	−	+	−	−	−	−	−	+	+	4
Evans 2007	+	+	+	+	−	−	−	−	+	+	+	6
Going 2003	+	+	−	+	−	−	−	−	+	+	+	5
Grove 1992	+	+	−	+	−	−	−	+	+	+	+	6
Hans 2002	+	+	−	+	−	−	−	−	+	+	+	5
Hartley 2019	+	+	+	+	−	−	−	−	−	+	+	5
Hartard 1996	+	−	−	+	−	−	−	+	+	+	+	5
Hatori 1993	+	+	−	+	−	−	+	+	−	+	+	6
Hettchen 2021	+	+	+	+	−	−	+	−	+	+	+	7
Holubiac 2022	+	−	−	+	−	−	−	+	+	+	+	5
Iwamoto 2001	+	+	−	+	−	−	−	−	+	+	+	5
Jessup 2003	+	+	+	−	−	−	+	+	+	+	+	7
Karakiriou 2011	+	+	−	−	−	−	−	−	−	+	+	3
Kemmler 2013	+	+	−	+	+	−	+	−	+	+	+	7
Kemmler 2010	+	+	+	+	+	−	+	+	+	+	+	9
Kemmler 2004	+	−	−	+	−	−	−	−	+	+	+	4
Kemmler 1999	+	−	−	+	−	−	−	+	+	+	+	5
Kerr 2001	+	+	−	+	−	−	−	−	+	+	+	5
Kerr 1996	+	+	−	+	−	−	−	−	+	+	+	5
Kohrt 1997	+	−	−	+	−	−	−	−	+	+	+	4
Kohrt 1995	+	−	−	+	−	−	−	−	+	+	+	4
Korpelainen 2006	+	+	+	+	−	−	+	−	+	+	+	7
Kwon 2008	+	−	−	+	−	−	−	−	−	+	+	3
Lau 1992	+	+	+	+	−	−	−	−	+	−	+	5
Liu 2015	+	+	−	+	−	−	−	+	+	+	+	6

Table 3 (continued)

Lord 1996	+	+	−	+	−	−	−	−	+	+	+	5
Maddalozzo 2007	+	+	−	+	−	−	−	+	+	+	+	6
Marin-Cascales 2019	+	+	+	+	−	+	−	−	−	+	+	6
Marques 2011	+	+	+	+	−	−	−	−	+	+	+	6
Marques 2011	+	+	+	+	−	−	−	−	+	+	+	6
Martin 1993	+	+	−	+	−	−	−	−	+	+	+	5
Milliken 2003	+	+	−	+	−	−	−	+	+	+	+	6
Montgomery 2020	+	+	+	+	−	−	+	−	−	+	+	6
Nelson 1994	+	+	−	+	−	−	−	+	+	+	+	6
Nelson 1991	+	−	−	+	−	−	−	+	+	+	+	5
Nichols 1995	+	+	−	+	−	−	−	−	+	+	+	5
Nicholson 2015	+	+	+	+	−	−	−	+	+	+	+	7
Orsatti 2013	+	+	+	+	−	−	−	+	+	+	+	7
Park 2008	+	+	+	+	−	−	−	+	+	+	+	7
Prince 1995	+	+	+	+	−	−	−	−	+	+	+	6
Pruitt 1995	+	+	−	+	−	−	−	−	+	+	+	5
Pruitt 1992	+	−	−	+	−	−	−	+	+	+	+	5
Rhodes 2000	+	+	−	+	−	−	−	+	+	+	+	6
Ryan 1998	+	−	−	+	−	−	−	−	+	+	+	4
Sakai 2010	+	+	+	+	−	−	−	+	−	+	+	6
Silverman 2009	+	−	−	+	−	−	+	−	−	+	+	4
Sinaki 1989	+	+	−	+	−	−	−	+	+	+	+	6
Sugiyama 2002	+	−	−	+	−	−	−	−	−	+	+	3
Tartibian 2011	+	+	−	+	−	−	−	+	+	+	+	6
Tolomio 2009	+	+	−	+	−	−	−	+	−	+	+	5
Verschueren 2003	+	+	+	+	−	−	+	−	−	+	+	6
Waltman 2022	+	+	+	+	−	−	−	−	−	+	+	5
Wang 2015	+	+	−	+	−	−	−	+	+	+	+	6
Woo 2007	+	+	+	+	−	−	+	+	+	+	+	8
Wu 2006	+	+	−	+	+	−	−	−	+	+	+	6
Yamazaki 2004	+	−	−	+	−	−	−	−	+	+	+	4

[1]This item is not reflected in the calculation of the PEDro score

[2]The point is awarded not only for intention to treat analysis, but also when "all subjects for whom outcome measures were available received the treatment or control condition as allocated"

IVhet Analysis of Change of Bone Mineral Density of Lumbar Spine

	EG		CG		
	Mean	SD	Mean	SD	SMD (95%CI)
Adami (1999)	0.003	0.0491	-0.002	0.0554	0.10 [-0.15, 0.34]
Basat (2013S)	0.012	0.0195	-0.023	0.0181	1.76 [0.71, 2.81]
Basat (2013HI)	0.004	0.0123	-0.023	0.0181	1.80 [0.74, 2.86]
Bassey (1998)	-0.002	0.0260	-0.001	0.0390	-0.03 [-0.48, 0.42]
Bassey (1995)	-0.022	0.0580	-0.006	0.0630	-0.26 [-0.76, 0.24]
Bemben (2010)	-0.007	0.0230	-0.002	0.0270	-0.20 [-0.90, 0.51]
Bemben (2000HL)	-0.009	0.0453	-0.008	0.0362	-0.02 [-1.08, 1.04]
Bemben (2000HR)	-0.006	0.0412	-0.008	0.0362	0.05 [-0.92, 1.02]
Bergström (2008)	-0.003	0.0310	-0.007	0.0390	0.11 [-0.26, 0.49]
Bloomfield (1993)	0.042	0.0198	-0.025	0.0141	3.65 [1.94, 5.36]
Bocalini (2009)	-0.001	0.0125	-0.009	0.0222	0.48 [-0.23, 1.18]
Bolton (2012)	-0.003	0.0320	-0.008	0.0210	0.18 [-0.45, 0.81]
Brooke-Wavell (2001)	-0.003	0.0320	0.017	0.0260	-0.68 [-1.32, -0.03]
Brooke-Wavell (1997)	0.006	0.0240	-0.005	0.0250	0.44 [0.01, 0.88]
Caplan (1993)	-0.009	0.0573	-0.041	0.0350	0.62 [-0.14, 1.38]
Chan (2004)	0.001	0.0469	-0.007	0.0496	0.16 [-0.18, 0.51]
Chilibeck (2013)	-0.009	0.0330	-0.003	0.0300	-0.19 [-0.49, 0.11]
Chilibeck (2002)	-0.007	0.0423	-0.002	0.0396	-0.12 [-0.86, 0.62]
Choquette (2011)	-0.010	0.0593	0.020	0.0487	-0.55 [-1.10, 0.01]
Chuin (2009)	-0.001	0.0562	-0.014	0.0591	0.22 [-0.73, 1.17]
De Matos (2009)	0.010	0.0430	-0.018	0.0390	0.67 [0.15, 1.20]
Deng (2009)	-0.015	0.0380	-0.057	0.0390	1.08 [0.61, 1.55]
De Oliveira (2018)	0.020	0.0200	0.000	0.0100	1.23 [0.50, 1.97]
Duff (2016)	-0.003	0.0280	0.011	0.0350	-0.43 [-1.03, 0.16]
Ebrahim (1997)	0.017	0.0510	0.017	0.0540	0.00 [-0.31, 0.31]
Englund (2005)	0.030	0.1800	0.010	0.1500	0.12 [-0.45, 0.69]
Evans (2007)	-0.017	0.0751	-0.008	0.0516	-0.13 [-0.86, 0.59]
Going (2003)	0.000	0.0290	-0.006	0.0250	0.22 [-0.09, 0.53]
Grove (1992L)	0.000	0.0360	-0.070	0.0561	1.44 [-0.36, 3.25]
Grove (1992H)	0.020	0.0329	-0.070	0.0561	1.86 [0.16, 3.55]
Hartard (1996)	0.003	0.0687	-0.054	0.0495	0.92 [0.21, 1.63]
Hartley (2019)	-0.010	0.1440	-0.010	0.1440	0.00 [-0.47, 0.47]
Hatori (1993M)	-0.008	0.0593	-0.014	0.0494	0.10 [-0.89, 1.10]
Hatori (1993H)	0.009	0.0461	-0.014	0.0494	0.46 [-0.53, 1.46]
Hettchen (2021)	0.002	0.0180	-0.009	0.0180	0.60 [0.06, 1.15]
Holubiac (2022)	0.014	0.0200	0.001	0.0220	0.60 [-0.14, 1.35]
Iwamoto (2001)	0.025	0.0321	0.005	0.0157	0.91 [0.05, 1.76]
Jessup (2003)	0.110	0.0266	-0.003	0.1117	1.33 [0.36, 2.30]
Karakiriou (2011)	0.013	0.0221	-0.018	0.0279	1.18 [0.21, 2.16]
Kemmler (2013)	-0.001	0.0220	-0.019	0.0180	0.89 [0.44, 1.33]
Kemmler (2010)	0.017	0.0270	0.003	0.0280	0.51 [0.25, 0.76]
Kemmler (2004)	0.006	0.0220	-0.019	0.0190	1.19 [0.81, 1.56]
Kemmler (1999EPM)	0.028	0.0605	-0.008	0.0680	0.55 [-0.32, 1.42]
Kemmler (1999LPM)	0.019	0.0567	-0.008	0.0680	0.43 [-0.36, 1.22]
Kerr (2001F)	0.001	0.0395	-0.002	0.0565	0.06 [-0.46, 0.59]
Kerr (2001S)	-0.009	0.0527	-0.002	0.0565	-0.13 [-0.65, 0.40]
Kohrt (1997J)	0.013	0.0140	0.002	0.0170	0.71 [-0.21, 1.63]
Kohrt (1997G)	0.016	0.0220	0.002	0.0170	0.66 [-0.20, 1.51]
Kohrt (1995)	0.020	0.0190	-0.003	0.0150	1.27 [0.20, 2.34]
Kwon (2008)	0.010	0.0534	-0.010	0.0353	0.43 [-0.19, 1.06]
Lau (1992)	-0.013	0.0583	-0.016	0.0403	0.06 [-0.66, 0.77]
Liu (2015)	0.012	0.0086	0.002	0.0088	1.14 [0.71, 1.57]
Lord (1996)	0.012	0.0679	0.004	0.0657	0.12 [-0.17, 0.41]
Maddalozzo (2006)	0.002	0.0428	-0.042	0.0474	0.96 [0.47, 1.46]
Marín-Cascales (2019)	0.030	0.0715	-0.018	0.0685	0.66 [-0.19, 1.50]
Marques, Mota (2011)	0.011	0.0316	-0.005	0.0296	0.52 [0.00, 1.03]
Martin (1993,30 min)	-0.007	0.0429	-0.010	0.0621	0.06 [-0.62, 0.74]
Martin (1993,45min)	0.007	0.0568	-0.010	0.0621	0.28 [-0.41, 0.98]
Milliken (2003)	-0.002	0.0524	-0.002	0.0561	0.00 [-0.53, 0.53]
Montgomery (2020) C	-0.021	0.0610	-0.020	0.0454	-0.02 [-1.05, 1.02]
Montgomery (2020) I	-0.011	0.0567	-0.020	0.0454	0.16 [-0.96, 1.28]
Nelson (1994)	0.009	0.0330	-0.019	0.0350	0.81 [0.16, 1.45]
Nelson (1991)	-0.010	0.0480	0.017	0.0720	-0.43 [-1.05, 0.18]
Nichols (1995)	-0.011	0.0401	0.014	0.0555	-0.50 [-1.19, 0.18]
Nicholson (2015)	0.011	0.0400	-0.023	0.0497	0.74 [0.20, 1.28]
Orsatti (2013)	-0.005	0.0501	-0.010	0.0377	0.11 [-0.51, 0.73]
Park (2008)	0.007	0.0267	-0.072	0.0700	1.47 [0.84, 2.09]
Prince (1995)	0.014	0.0478	0.005	0.0501	0.18 [-0.25, 0.61]
Pruitt (1995HI)	0.007	0.0180	0.000	0.0200	0.36 [-0.59, 1.32]
Pruitt (1995LI)	0.005	0.0270	0.000	0.0200	0.19 [-0.78, 1.16]
Pruitt (1992)	0.012	0.0340	-0.023	0.0524	0.82 [0.01, 1.63]
Rhodes (2000)	0.020	0.0585	0.000	0.0600	0.33 [-0.26, 0.93]
Ryan (1998)	0.016	0.0436	-0.010	0.0577	0.50 [-0.17, 1.16]
Silverman (2009)	0.005	0.0627	0.002	0.0578	0.05 [-0.37, 0.47]
Sinaki (1989)	-0.015	0.0593	-0.011	0.0565	-0.07 [-0.54, 0.41]
Sugiyama (2002)	-0.019	0.0593	-0.008	0.0590	-0.18 [-0.95, 0.59]
Tartibian (2011)	0.050	0.0423	-0.060	0.0494	2.35 [1.52, 3.18]
Verschueren (2004)	0.001	0.0446	0.004	0.0516	-0.06 [-0.64, 0.52]
Waltman (2022)	-0.001	0.0213	-0.004	0.0264	0.12 [-0.16, 0.41]
Wang (2015TC)	0.010	0.0520	-0.003	0.0487	0.25 [-0.30, 0.80]
Wang (2015TCR)	0.018	0.0560	-0.003	0.0487	0.39 [-0.16, 0.93]
Woo (2007RE)	0.013	0.0395	0.007	0.0318	0.16 [-0.46, 0.78]
Woo (2007TC)	0.000	0.0296	0.007	0.0318	-0.23 [-0.85, 0.39]
Wu (2006)	-0.015	0.0402	-0.008	0.0459	-0.16 [-0.64, 0.32]
Yamazaki (2004)	0.015	0.1540	-0.016	0.1092	0.22 [-0.36, 0.80]
IVhet Model for All Studies (Q = 261.99, df = 84, p < 0.001; I^2 = 67.9%)					0.29 [0.16, 0.42]

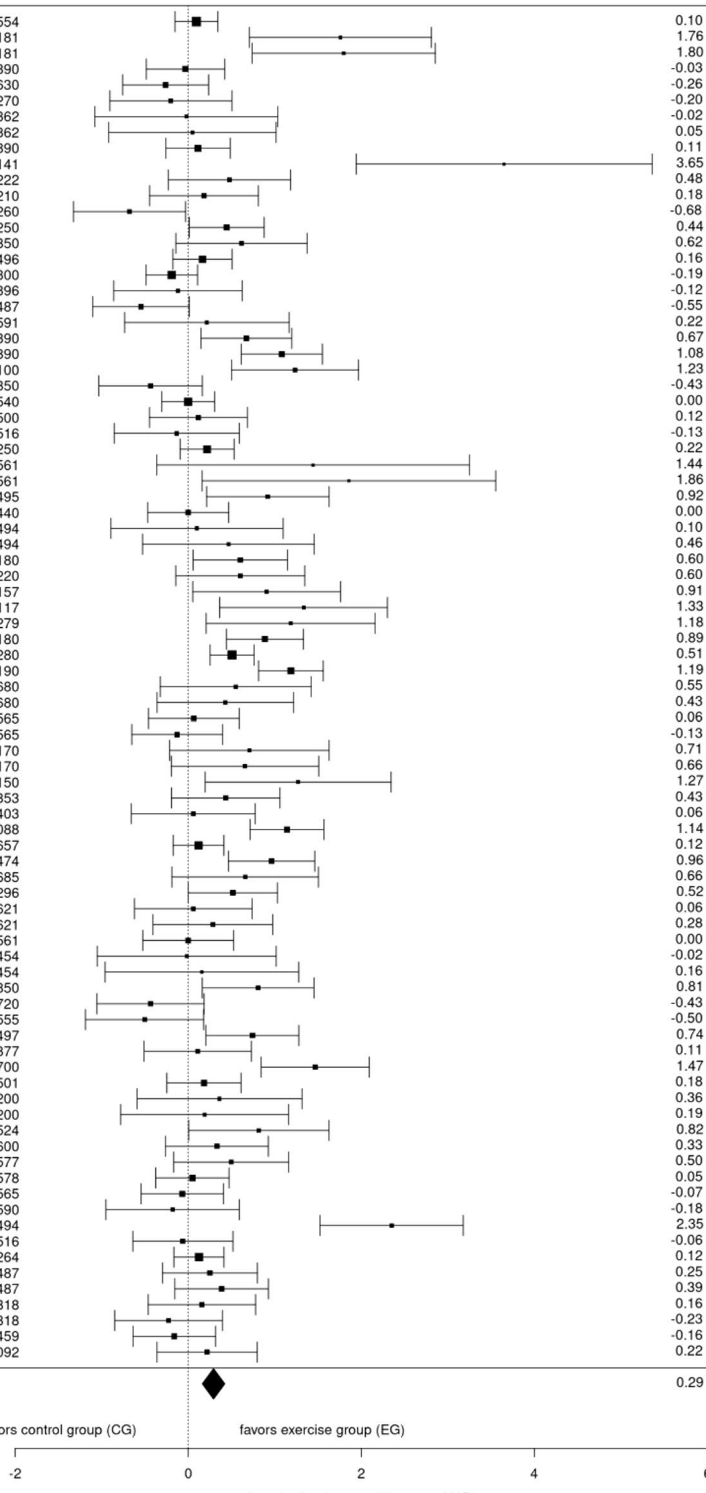

Fig. 2 Forest plot of meta-analysis results at the lumbar spine (IVhet model). The data are shown as pooled standard mean difference (SMD) with 95% CI for changes in the exercise (EG) versus control groups (CG). Imputation with mean correlation

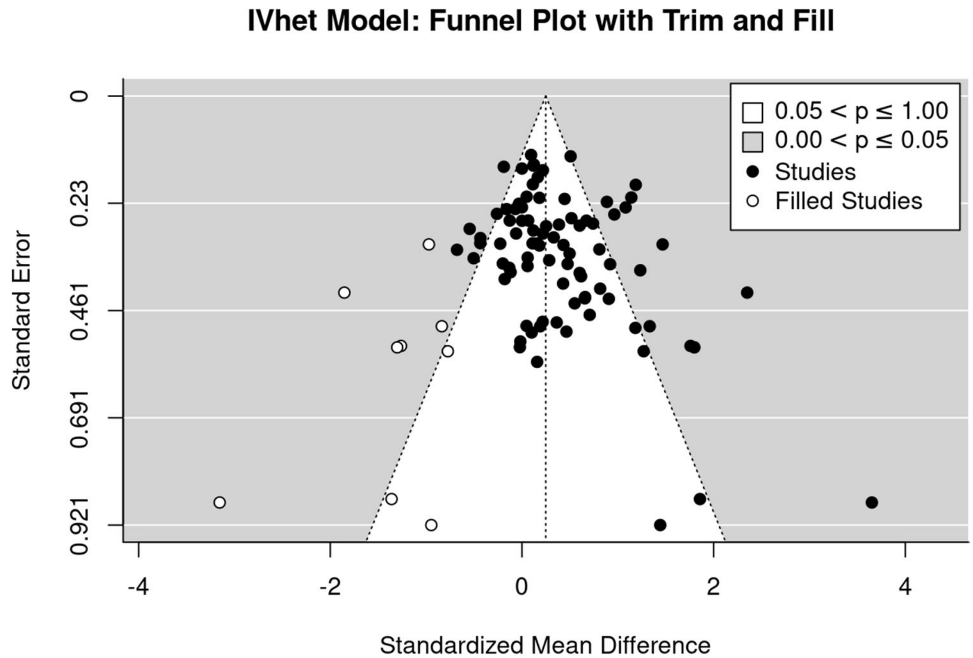

Fig. 3 Funnel plot with trim and fill on the effect of exercise on BMD at the lumbar spine

Inspecting the LFK Index (1.04), we observed minor asymmetry; results of the regression ($p = 0.068$) and rank correlation test ($p = 0.127$) were non-significant, however.

Effects of exercise on BMD at the total hip

Thirty comparisons addressed exercise effects for TH BMD (Fig. 6). The IVhet model (Fig. 6) with imputation of the mean correlation revealed a significant effect ($p < 0.001$) of exercise on BMD at the TH (SMD: 0.41; 95% CI: 0.30 to 0.52). Heterogeneity between the trial results ($I^2 = 20\%$) was low (Fig. 6). Applying sensitivity analyses with imputation with minimum correlation (SMD: 0.31; 95% CI: 0.22 to 0.42) or maximum correlation (SMD: 0.64; 95% CI: 0.44 to 0.83) led to diverging, but consistently significant ($p < 0.001$), results.

The funnel plot for TH BMD suggested evidence for a small study/publication bias (Fig. 7). The trim and fill model imputed three studies at the lower right-hand side (i.e., small-moderate sized studies with positive results). Considering these (imputed) data in the analysis, SMD increased slightly (0.43; 95% CI: 0.32–0.54). Funnel plot asymmetry was not confirmed by the LFK index (– 0.04), regression ($p = 0.47$), or rank test ($p = 0.57$).

Subanalyses on potentially modifying factors

Effect of bone status

Fourteen of 85 comparisons focused on BMD-LS in cohorts with osteopenia, osteoporosis, or a history of fractures (Table 1). The IVhet model determined no significant difference ($p = 0.094$) between the subgroups with (SMD: 0.54; 95% CI: 0.17 to 0.92) and without (SMD: 0.23; 95% CI: 0.08 to 0.38) osteopenia/osteoporosis on LS-BMD. Heterogeneity was substantial (I^2: 63% and I^2: 77%) in both subgroups. Ten versus 62 subgroups with and without osteopenia/osteoporosis were compared for FN. In summary, we observed slightly more favorable effects in the cohorts with osteopenia, osteoporosis, or a history of fractures; the between group differences were not significant ($p = 0.711$), however. The same was true for TH-BMD ($p = 0.453$) with 6 versus 25 comparisons.

Effect of menopausal status

In summary, we compared 7 early postmenopausal with 26 late postmenopausal study groups for LS-, 5 with 26 subgroups for FN-, and 5 with 9 subgroups for TH-BMD. In summary, we detected no significant BMD-difference at the LS ($p = 0.901$), FN ($p = 0.547$), or TH-BMD ($p = 0.824$).

Effect of supervision on exercise effects on BMD in postmenopausal women

Fifty-nine study groups that addressed LS-BMD applied a predominantly supervised exercise protocol, while 23 study arms focused on predominantly non-supervised exercise. In summary, the supervised exercise protocols revealed only tendentially ($p = 0.37$) higher effects compared with the predominantly unsupervised exercise protocols on LS-BMD (SMD: 0.19; 95% CI: – 0.03 to 0.41). In

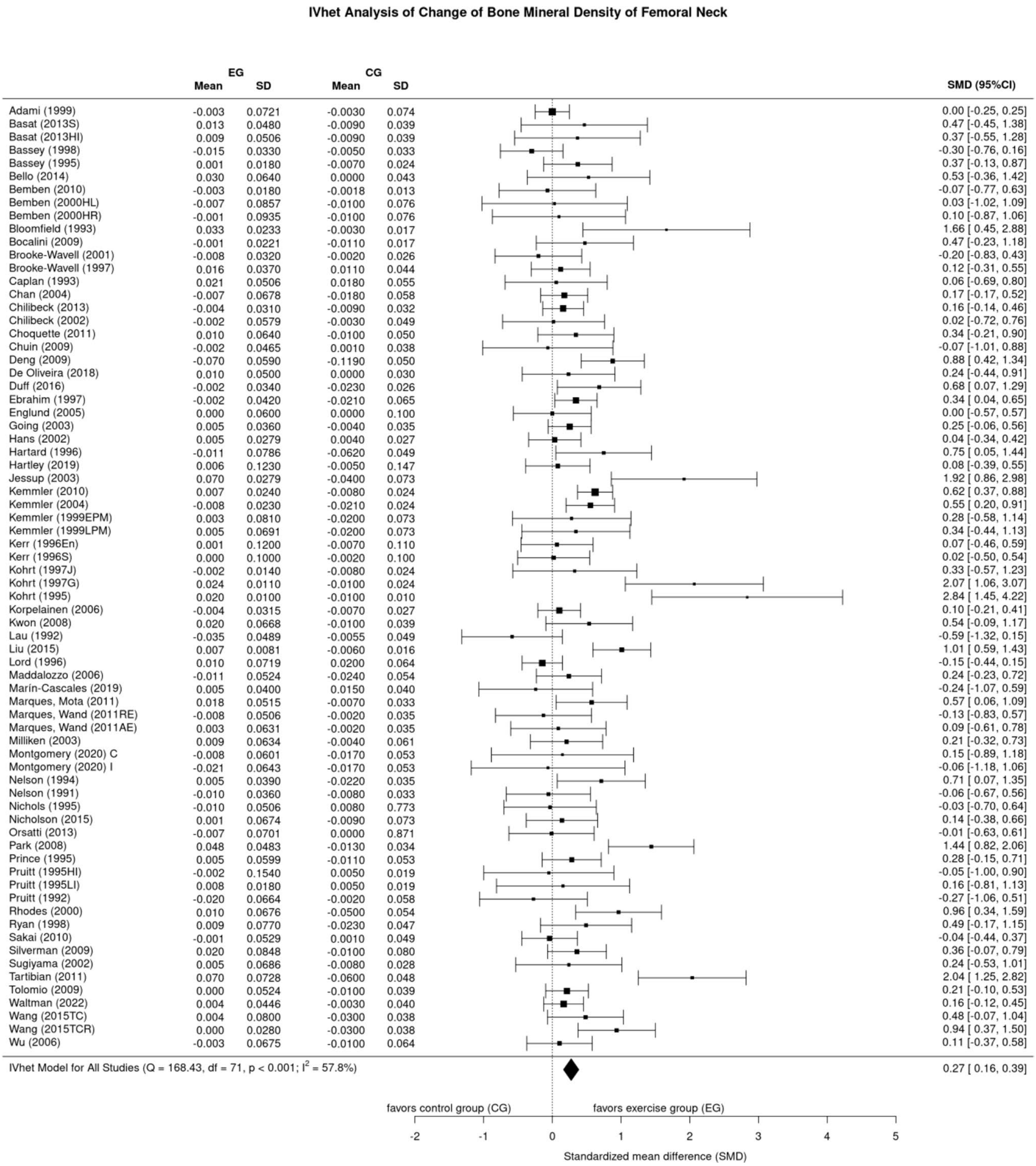

Fig. 4 Forest plot of meta-analysis results at the femoral neck (IVhet model). The data are shown as pooled standard mean difference (SMD) with 95% CI for changes in the exercise (EG) versus control groups (CG). Imputation with mean correlation

parallel, we observed no significant differences ($p = 0.549$) between predominantly supervised ($n = 50$) versus non-supervised ($n = 19$) exercise protocols for FN-BMD. However, the predominantly non-supervised exercise study groups per se did not show a significant exercise effect on BMD-LS and FN ($p = 0.09$ each). Finally, we observed no significant differences in TH-BMD ($p = 0.798$) for predominantly supervised ($n = 25$) versus predominantly non-supervised protocols ($n = 5$) with significant exercise effects for both subgroups.

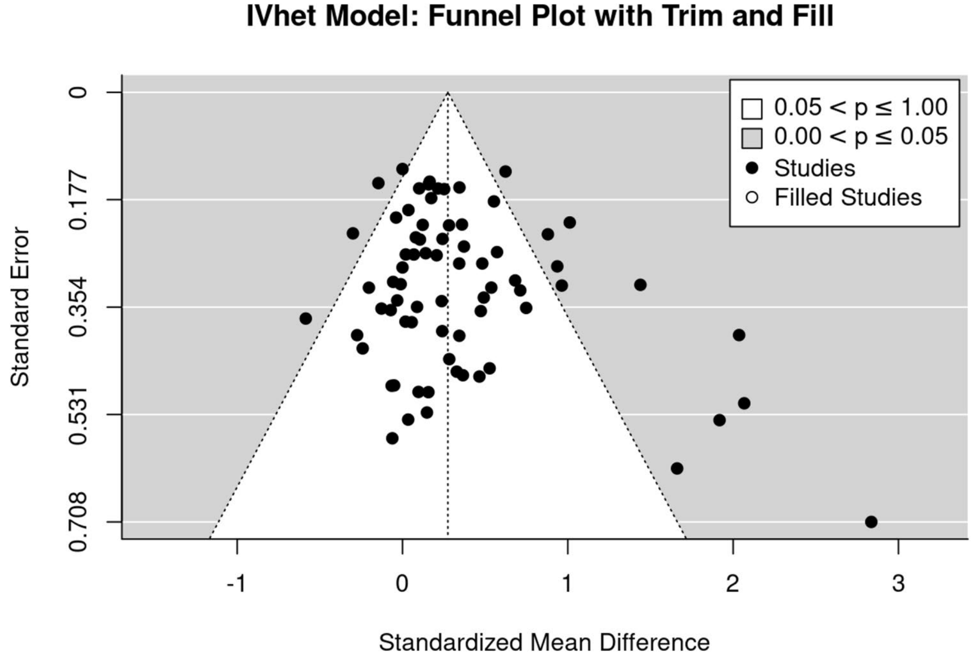

Fig. 5 Funnel plot with trim and fill on the effect of exercise on BMD at the femoral neck

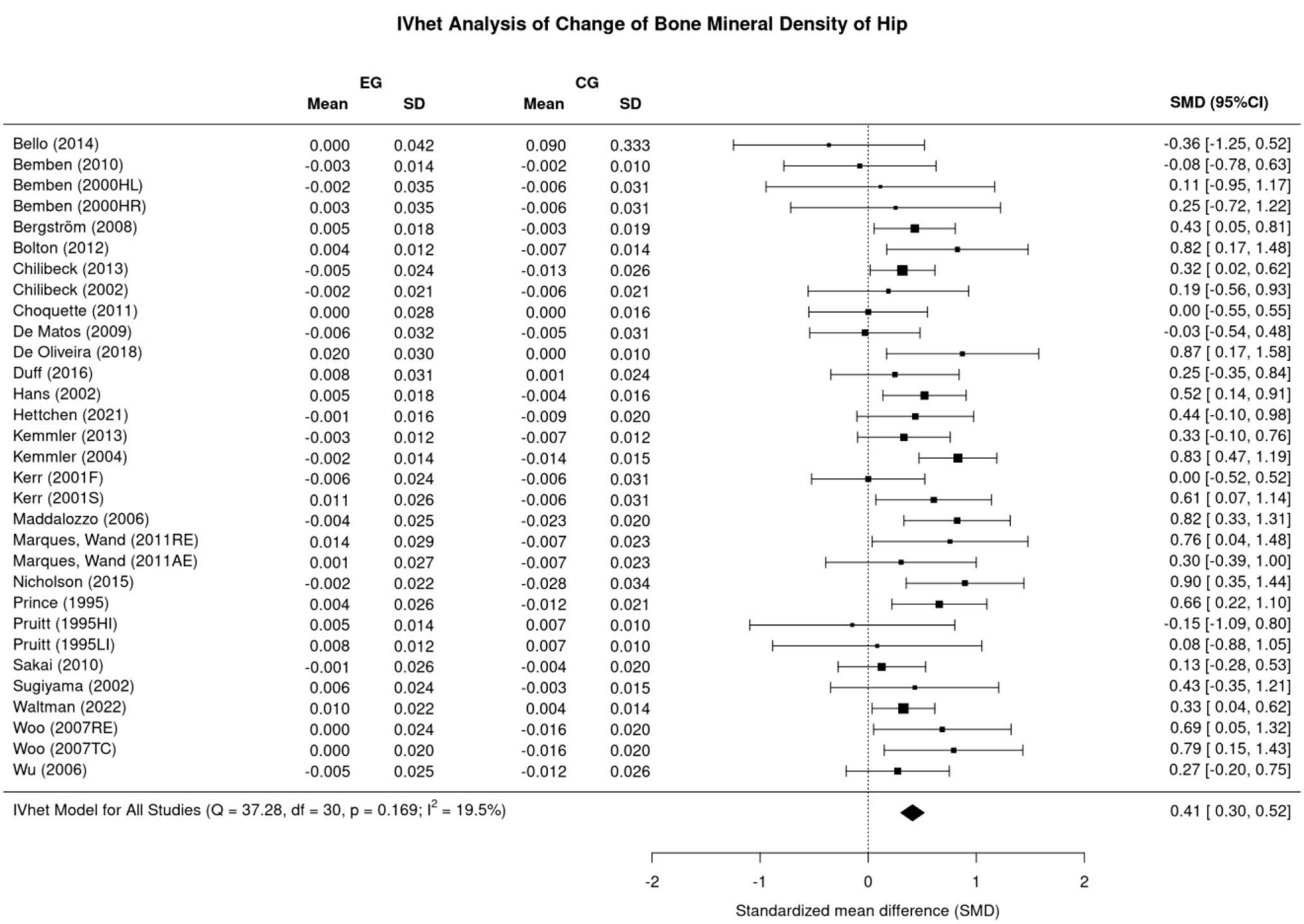

Fig. 6 Forest plot of meta-analysis results at the total hip (IVhet model). The data are shown as pooled standard mean difference (SMD) with 95% CI for changes in the exercise (EG) versus control groups (CG). Imputation with mean correlation

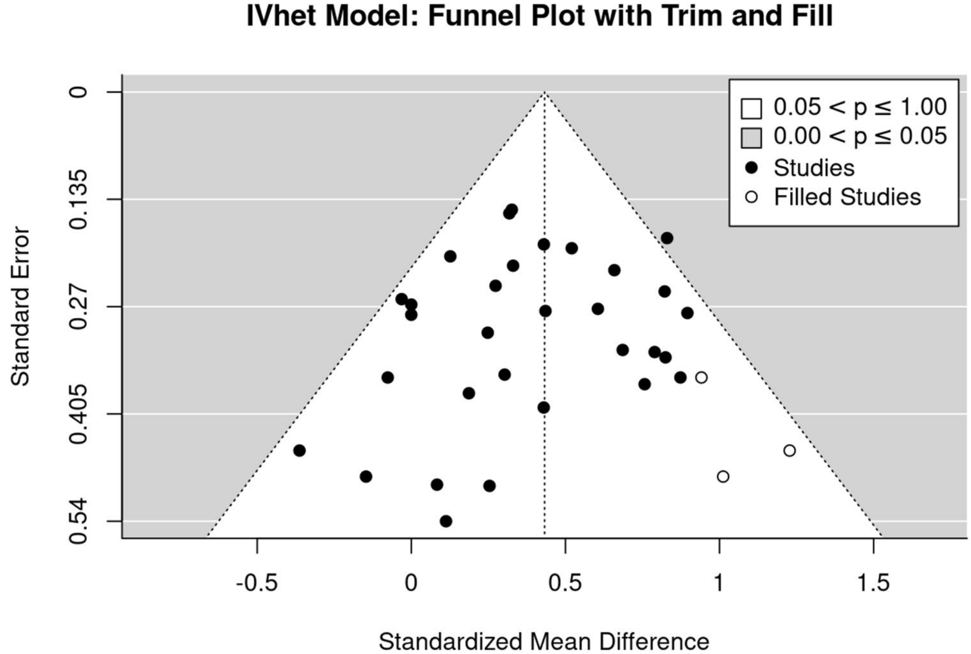

Fig. 7 Funnel plot with trim and fill on the effect of exercise on BMD at the total hip ROI

Discussion

In the present systematic review and meta-analysis, we provide further evidence for the favourable effect of exercise on BMD at LS, FN, and TH in postmenopausal women. However, since this 2022 update added six exercise trials [51, 53, 54, 72, 77, 96] while excluding one (aquatic exercise) trial [104], the result of significant but "small" exercise effects at LS (SMD: 0.29), FN (SMD: 0.27), and TH (SMD: 0.41) did not differ relevantly from our 2020 finding [1]. However, one main advantage of the present study is the application of the inverse heterogeneity model (IVhet) [9]. The IVhet approach is less susceptible to underestimation of statistical error in heterogeneous studies, i.e., results are more reliable in heterogeneous studies especially with respect to the coverage probability of confidence intervals [105]. Nevertheless, it would be a misconception to assume that the enormous heterogeneity between the trial results can be adequately addressed by statistical methods. Of course, other and our (e.g., [106–109]) meta-analytic results are simply the quintessence taken from a pool of studies with favorable and less favorable results. This is generally the case for meta-analyses; however, the situation in the field of exercise and (particularly) bone strength is much more complex than the sophisticated pharmacologic area, where this type of analysis was first applied. It is obvious that in contrast to pharmaceutic studies, the vast majority of exercise studies started immediately with the phase III study approach, without having addressed the general effectiveness of the exercise protocol in earlier pilot studies [110]. In some cases, one gains the impression that less promising interventions were applied to verify their ineffectiveness to favorably affect bone. Since there is no reliable rationale to exclude these "just look what happens trials," the dilution of the meta-analytic results is predictable.

Another enormous problem of systematic reviews and meta-analyses in the area of exercise and bone strength is the extreme variation among the participants and intervention characteristics of the individual trials. Considering the first aspect, bone [4, 111] and menopausal status [58] might be candidates with potentially moderating effect of exercise effect on BMD. In summary, we did not, however, observe any significant differences on BMD at LS, FN, and TH between the subgroups, be it for bone or for menopausal status. Of importance, with few exceptions (e.g., menopausal status: subgroup-analyses for TH-ROI), the number of studies included in the subgroups was high enough to exclude a predominate random effect. Nevertheless, there is some evidence that interaction effects between participant and exercise parameters in particular have affected our findings. As an example, it is plausible that more intense exercise protocols were applied in the younger, i.e., early postmenopausal cohorts or participants with a lower fracture risk, i.e., participants without osteopenia/osteoporosis. Reviewing the studies, however, we observed no striking differences in exercise intensity (or training frequency) between the cohorts with diverging bone or menopausal status. Even so, a simple adjustment of the subgroup analysis for exercise intensity is debatable, since the relevance of exercise intensity on a given outcome depends on other variables such as training frequency. The most successful approach for addressing the impact of participant characteristics such as bone or menopausal status on exercise induced BMD-changes might thus be to include participants with diverging characteristics but to apply the identical protocol.

While the effect of bone and menopausal status on exercise effect in middle aged-older women are "nice to know" for the exercise specialist, supervision of the exercise protocol is an issue with significant implications for various crucial elements of an intervention including setting, personal, finances, facilities, participants, and exercise protocol. This led us to the present approach of determining the effect of supervision on the exercise program on BMD. In a recent publication, we observed a significant superiority of supervision (versus predominantly non-supervised protocols) on overall and main osteoporotic fracture incidence in middle-aged to older adults [7]. This result was supported by findings [5, 112] which reported that supervised protocols demonstrate significantly higher effects on dynamic balance, strength, and power, i.e., parameters related to fall risk [113, 114] and bone strength [8]. Fisher et al. [5] postulated that the superiority of supervised (resistance) exercise programs might be related to higher adherence, motivation, intensity progression, and safety. Exercise programs on bone strengthening applied intensive resistance, weight bearing, and impact exercises [115, 116] which also underline the relevance of supervision for effective and safe exercise protocols, especially for older people. However, our approach does not determine a significant difference between predominantly supervised versus non-supervised exercise protocols, albeit with slightly higher effects of supervised protocols for BMD at the LS, FN, and TH. Again, we have to admit that in particular exercise parameters related to supervision (or not) diluted our result, e.g., some types of exercise (i.e. dynamic resistance exercise) need higher degrees of supervision compared to others (i.e. jumping protocols). Nevertheless, accepting this result as a reliable finding would simplify the broad implementation of exercise programs in the field of osteoporosis due to lower demands on personnel and — since most non-supervised protocols applied home exercise — locations. However, the decision about more or less supervision should ultimately be made in the light of the cohort addressed (e.g., fitness and health status), specific preventative/therapeutic aims and budget considerations in order to generate the safest and most effective/efficient training setting.

Apart from supervision, one may argue that comprehensive meta-analyses or their subanalyses on crucial exercise characteristics (i.e., type of exercise, strain intensity, exercise frequency, etc.) [1, 117] might be a smart solution for generating reliable recommendations on exercise protocols. In the meantime and in line with Gentil et al. [118], we do no longer agree with this idea. In fact, the close and inherent interactions within the given exercise protocol aggravate the addressing of isolated exercise parameters. For example, exercise intensity plays an important role for bone strengthening [117], but its relevance is (among other things) dependent on training frequency (once per day or once per week?) [119]. Bearing in mind that the effectiveness of continuously unchanged stimuli is limited [120], the aspect of progression is also crucial in particular when applying year-long exercise interventions [121]. One solution to this problem might be comparative meta-analyses that include trials with two study arms with diverging exercise parameters (e.g. intensity [122] or training frequency [119]) but otherwise identical protocols (… and participants).

At this point, we would like to briefly address some limitations and particularities of the present work. (1) Apart from the general limitation that quite heterogeneous exercise protocols have to be included in the analysis, some of our eligibility criteria might be also debatable. This refers to study length (≥ 6 months) and adjuvant pharmaceutic therapy with impact on bone metabolism (≤ 10% of participants — albeit only if the number of users was similar between exercise and control). Although evidence for additive effects of exercise and hormone replacement therapy [123] or bisphosphonates [124] is low, we tried to exclude such interactions. Furthermore, considering bone remodeling as the primary mode of bone renewal in adults [125, 126] and taking regular changes of exercise intensity into account, exercise studies shorter than 6 months might not have reached the full amount of mineralized bone and thus confound the BMD assessment. (2) In this context, a limitation to be mentioned was that only few data were available on the precision of DXA measurements and the calculated least significant change (LSC). The minimum acceptable precision for an individual technologist would be 1.9% (LSC = 5.3%) for BMD-LS, 1.8% (LSC = 5.0%) for BMD-TH and 2.5% (LSC = 6.9%) for BMD-FN [127]. (3) Another predominantly biometrical source of error was that SDs of the absolute change in BMD were not consistently available and thus had to be imputed. Although sensitivity analysis on imputation strategy consistently showed significant effects, outcomes for BMD at the LS, FN and TH varied considerably depending on whether imputation was conducted with mean, minimum, or maximum correlation. On the other hand, inspecting funnel and Doi plots, LFK indices, rank, and regression tests led to the conclusion that the probability of small study effects (publication bias, outcome reporting bias, dissemination bias, etc.) with confounding effects on our finding [128] is limited. (4) Our subgroup analyses on exercise-induced BMD changes focus on bone and menopausal status and supervision of the exercise session. We think that these are important aspects to be addressed, but other participant or study characteristics, i.e., baseline physical activity/exercise status or site specifity of the exercise might be equally or even more important and should be addressed by future studies. (5) Our subgroup analysis on menopausal status allocated study groups ≤ 5 years postmenopausal to the early and study groups > 8 years postmenopausal (or cohorts 60 years and older) to the late postmenopausal subgroup. Considering the considerable individual variation around the average time of menopause of 51 years [129], including study groups with a lower range of 60 years of age might slightly confound our analysis since few subjects of these cohorts might not fulfill the criteria of 8 years postmenopause. Nevertheless, an analysis with an alternative classification (i.e., ≤ 8 years postmenopausal: early versus > 8 years: late postmenopausal) results in similar non-significant group differences. (6) Although we carefully examined the studies, classification on "predominantly supervised" versus "predominantly non-supervised" based on attendance rates might be difficult and not always meaningful. This becomes more apparent where, for example, a study protocol that applied up to two supervised DRT and WB exercise sessions and three non-supervised walking sessions/week was classified as "predominantly non-supervised" by our procedure (5).

By applying robust statistical methods (i.e., the IVhet approach [9] which is less susceptible to underestimation of statistical error in the heterogeneous exercise studies), we provided further evidence for a positive effect of exercise on BMD at LS, FN, and TH in postmenopausal women. However, the average SMD for BMD effects on LS, FN, and TH can be classified as moderate at best (i.e., 0.2 to 0.5). Our subanalysis on bone and menopausal status and supervision effects did not indicate significant differences. Summing up our recent experiences and findings, we conclude that while comprehensive meta-analyses in the area of exercise and bone strength might be useful for a rapid (but rough) overview, their practical application for deriving dedicated and reliable exercise recommendations is rather limited.

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Data availability The data that support the findings of this study are available from the corresponding author (WK), upon reasonable request.

Declarations

Informed consent Not applicable.

Statement of human rights This article does not cover any studies with human participants with human participants or animals performed by any of the authors.

Conflicts of Interest None.

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