

Effects of Moderate- to High-Impact Exercise Training on Bone Structure Across the Lifespan: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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ABSTRACT

Moderate- to high-impact exercise improves bone mineral density (BMD) across the lifespan, but its effects on bone structure, which predicts fracture independent of areal BMD, are unclear. This systematic review and meta-analysis investigated effects of impact exercise on volumetric BMD (vBMD) and bone structure. Four databases (PubMed, Embase, SPORTDiscus, Web of Science) were searched up to March 2022 for randomized controlled trials (RCTs) investigating the effects of impact exercise, with ground reaction forces equal to or greater than running, compared with sham or habitual activity, on bone vBMD and structure. Bone variables were measured by quantitative computed tomography or magnetic resonance imaging at the tibia, radius, lumbar spine, and femur. Percentage changes in bone variables were compared among groups using mean differences (MD) and 95% confidence intervals (CI) calculated via random effects meta-analyses. Subgroup analyses were performed in children/adolescents (<18 years), adults (18–50 years), postmenopausal women, and older men. Twenty-eight RCTs ($n = 2985$) were included. Across all studies, impact exercise improved trabecular vBMD at the distal tibia (MD = 0.54% [95% CI 0.17, 0.90%]), total vBMD at the proximal femur (3.11% [1.07, 5.14%]), and cortical thickness at the mid/proximal radius (1.78% [0.21, 3.36%]). There was no effect on vBMD and bone structure at the distal radius, femoral shaft, or lumbar spine across all studies or in any subgroup. In adults, impact exercise decreased mid/proximal tibia cortical vBMD (−0.20% [−0.24, −0.15%]). In postmenopausal women, impact exercise improved distal tibia trabecular vBMD (0.79% [0.32, 1.25%]). There was no effect on bone parameters in children/adolescents in overall analyses, and there were insufficient studies in older men to perform meta-analyses. Impact exercise may have beneficial effects on bone structure and vBMD at various skeletal sites, but additional high-quality RCTs in different age and sex subgroups are needed to identify optimal exercise protocols for improving bone health across the lifespan. © 2023 The Authors. *Journal of Bone and Mineral Research* published by Wiley Periodicals LLC on behalf of American Society for Bone and Mineral Research (ASBMR).

KEY WORDS: AGING; BONE QCT/ μ CT; CLINICAL TRIALS; EXERCISE; RADIOLOGY

Introduction

Osteoporosis, defined as areal bone mineral density (aBMD) ≤ 2.5 SD below the reference mean,⁽¹⁾ is associated with a fivefold increased risk of fragility fracture.⁽²⁾ However, most low-trauma fragility fractures occur in older individuals with normal aBMD or osteopenia.^(3,4) This may in part be explained by age-related impairments in bone structure, quantified by

parameters such as cross-sectional area and microarchitecture, and volumetric bone mineral density (vBMD), which predict fractures independent of aBMD.^(5,6) The planar nature of dual-energy X-ray absorptiometry (DXA) limits the ability to assess material volume and individual cortical and trabecular compartments.⁽⁷⁾ Thus, three-dimensional (3D) imaging systems, such as quantitative computed tomography (QCT), peripheral QCT (pQCT), high-resolution pQCT (HR-pQCT), and magnetic resonance imaging

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(MRI), are increasingly used to evaluate vBMD and bone structure to predict fracture risk.^(8,9)

Approximately 40% to 60% of variation in bone structure and density is predetermined by genetic factors,⁽¹⁰⁾ indicating that modifiable environmental factors such as exercise can contribute to the development and maintenance of bone structure throughout the lifespan. In particular, animal studies have concluded that exercise with mechanical loading at magnitudes greater than a physiological threshold, and dynamically and rapidly applied, leads to significant improvements in bone health.⁽¹¹⁻¹³⁾ However, previous meta-analyses investigating effects of impact exercise on aBMD have reported inconsistent and modest changes in spine, femoral neck, and total hip aBMD in pre- and postmenopausal women.⁽¹⁴⁻¹⁹⁾ It is likely that bone strength improvements conferred by impact exercise occur independently of increases in aBMD via redistribution of bone mineral from the trabecular to cortical compartment or periosteal expansion of the bone,^(20,21) but effects of impact exercise on vBMD and bone structure have historically been less commonly examined in randomized controlled trials (RCTs) because of limited access to 3D imaging systems. A meta-analysis published a decade ago by Polidoulis and colleagues⁽²²⁾ reported small increases (0.9%) in trabecular and cortical vBMD at the distal tibia and tibial shaft, respectively, from exercise of all modalities compared with no exercise, among six studies in postmenopausal women. With the ascendancy of 3D skeletal imaging, many relevant trials have since been conducted, warranting an updated review on the topic. Furthermore, there is now increased recognition of the importance of conducting high-quality exercise interventions involving impact exercise of sufficiently high intensity for osteogenesis, as highlighted in a recent meta-analysis by Kistler-Fischbacher and colleagues.⁽¹⁸⁾

Given the higher prevalence of osteoporosis in women, the skeletal effects of exercise have been predominantly examined in pre- and postmenopausal women, and this evidence has formed the basis of impact exercise recommendations.^(12,23) However, it is unclear if these findings can be extrapolated across all age groups and both sexes. The osteogenic response to exercise is dependent on age, maturity status, and reproductive hormones,⁽²⁴⁻²⁶⁾ necessitating analyses of effects of impact exercise on bone structure in distinct populations. Impact exercise may be more effective in the prepubertal and peripubertal stages because of the rapid accrual of bone mass^(24,27) but may decline in effectiveness in adults who have stable bone mass.⁽²⁸⁾ Aging also dampens the adaptive skeletal response to mechanical loading due to age-related signaling disruptions to osteoblastic differentiations and structural changes to the lacuna-canalicular network.^(29,30) Sex-specific effects may also occur; unlike women, nonsignificant effects of impact exercise on lumbar spine aBMD have been reported in older men.^(31,32)

Thus, the aim of this systematic review and meta-analysis was to examine the effect of moderate- to high-impact exercise on changes in vBMD, bone structure, and strength at the tibia, radius, femur, and lumbar spine in children and adolescents (aged <18 years), adults (aged 18–50 years), postmenopausal women, and older men (aged >50 years).

Methods

This systematic review was performed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.⁽³³⁾ The study protocol was

registered a priori in the International Prospective Register of Systematic Review (PROSPERO; CRD42020184065) and deviations were documented.

Search strategy

Four electronic databases (PubMed, EMBASE, SPORTDiscus, and Web of Science) were searched from their inception to March 24, 2022. Titles, abstracts, and key words were searched using terms related to exercise (exercise; physical activity; training; sport; running; jumping; hopping), bone mineral density (bone; bone health; bone mass), three-dimensional scanning (pQCT; CT; structure; geometry; microarchitecture; cortical; trabecular), and study design (clinical trial; controlled trial). Boolean operators “OR” and “AND” were used within and between each search string, respectively. Hand searching was performed in bibliographies of relevant published literature. Forward citation searches of references citing the included studies were additionally conducted using Web of Science. No restrictions were placed for language or publication year. The search methodologies for each database are provided in Appendix A.

Eligibility criteria

Trials reported as peer-reviewed articles, abstracts, theses, and dissertations were included in this review. The following eligibility criteria were used:

1. Study population: Participants of any age, including those with diseases such as obesity, osteopenia, and osteoporosis, but without a physical disability that could limit exercise performance. We excluded patients recruited due to postoperative status and participants who were currently competing athletes.
2. Intervention: Moderate- to high-impact exercise interventions, such as hopping, dancing, and football, of any duration. For reference, activities with an effective load rating (indicating the peak vertical ground reaction force (GRF) and rate of force application) equal to or greater than 4.88, which reflects that of running, as previously determined by Weeks and Beck,⁽³⁴⁾ were included. Interventions that combined impact activities with other forms of exercise such as resistance training were also included. Exercise interventions with additional dietary weight loss interventions were excluded. Studies that provided participants with calcium or vitamin D supplementation were not excluded, but those that provided supplementation to only the exercise group were excluded.
3. Comparator: No exercise, or habitual recreational activities, or interventions not intended to influence bone structure (sham), such as stretching.
4. Outcomes: Evaluation of vBMD and bone structure using 3D scanning techniques, including computed tomography (CT), QCT, pQCT, HR-pQCT, and MRI, at the tibia, radius, femur, or lumbar spine.
5. Study type: RCTs and cluster RCTs

As the osteogenic response to impact exercise is dependent on age, maturity status, and reproductive hormones,^(23,24) studies were grouped by age groups (children and adolescents aged <18 years; adults aged 18–50 years; older adults aged >50 years). Studies in older adults were grouped separately for postmenopausal women and older men; postmenopausal women over the age of 50 years would have had marked bone deterioration and increased fracture risk.⁽³⁵⁾

Study selection

Two reviewers (CN and AG) independently screened titles and abstracts for eligibility using Covidence software (Veritas Health Innovation, Melbourne Australia). Full-text articles were obtained when the provided information was insufficient for a decision. Disagreement for article inclusion was resolved by reaching a consensus between the reviewers. Where necessary, discussion with a third reviewer (JM) resolved further conflicts. Covidence software was also used to remove duplicate publications, conduct full-text screening, and resolve conflicts.⁽³⁶⁾

Data collection

A single reviewer (CN) extracted data from each included article using Covidence software, and subsequent checking was performed by another reviewer (AG). A predefined data extraction form was used to collect study characteristics, which included study design; country; year of publication; participant eligibility criteria; age; sex; number of participants; intervention setting; study duration; exercise protocol details including the frequency, supervision, progression of exercise; imaging scan technique; machine producer; region of interest (ROI) assessed; study attrition; and exercise adherence.

Bone parameters of interest included total vBMD, total cross-sectional area; cortical vBMD, area and thickness; and trabecular vBMD, area, thickness, number, bone volume fraction and separation. Bone strength parameters, such as stress-strain index (SSI, mm³), bone strength index (BSI, mg²/mm⁴), and polar moment of inertia (m⁴), were additionally included.

Mean and SD percentage change values of bone parameters from baseline to follow-up were used in the meta-analysis, except for bone strength, where absolute mean and SD change was used. Missing data were obtained by contacting the authors via email a minimum of two times over a 4-week period. The authors of 16 studies were contacted,⁽³⁷⁻⁵⁵⁾ and five were able to supply the requested information.^(44-48,54) If data were still unavailable but absolute mean changes were provided, we converted these values into percentage mean change by dividing the absolute mean change by baseline mean values and multiplying by 100. Algebraic recalculation of missing SDs from between-group *p* values were performed according to the Cochrane reviewer's handbook.⁽⁵⁶⁾ Where data were only presented graphically, OriginPro version 2021b (OriginLab Corporation, Northampton, MA, USA) was used to extract values. If the SD for the change could not be derived, this was imputed using correlation coefficient (*r*) values calculated from the baseline and follow-up values from other studies included in this review.⁽⁵⁶⁾ *r* ranged from 0.91 to 0.99 for total vBMD, 0.93–0.99 for cortical vBMD, 0.97–0.99 for trabecular vBMD, 0.95–0.99 for total cross-sectional area, and 0.94–0.99 for cortical area depending on the population subgroup and ROI.

For clinical trials with more than one moderate- to high-impact exercise group, these groups were combined using the calculator function in RevMan version 5.4 (The Nordic Cochrane Centre, Copenhagen, Denmark) to form a single pair-wise comparison with the control.⁽⁵⁶⁾ If both intention-to-treat and per-protocol data were presented, the former was used. When multiple models were presented, unadjusted data were used. For factorial 2 × 2 RCTs examining the effects of both exercise and calcium and/or vitamin D supplementation, the exercise only and control groups were examined. The distal region was defined as ≤15% of the bone length from the distal endplate,

and the mid/proximal region was defined as sites >15% of the bone length. This threshold was chosen according to the location-specific effects of mechanical loading due to the anatomical variation of tissue distribution along the bone.^(57,58) For studies that reported two ROIs within the distal or mid/proximal regions, data for the ROI nearest to the average ROI of the remaining included studies in the analysis were used (eg, if the average mid/proximal region ROI of included studies in an analysis was 50%, for a separate study with 38% or 66% ROIs, only the 38% ROI data would be included in our analysis).

Quality assessment

Two reviewers (CN and JM) independently assessed the risk of bias of included studies using the Cochrane Risk of Bias 2 (RoB 2) tool.⁽⁵⁹⁾ Based on five domains (randomization; deviations from assignment to intended interventions; missing outcome data; outcome measurement; and selection of results), with an additional domain for timing of identification and recruitment for cluster RCTs, studies were classified as having low, unclear, or high risk of bias. Where a consensus could not be reached, a third reviewer (PO) resolved any disagreements.

Methodological quality of the studies was independently determined by two reviewers (CN and AG) using a seven-item rating list (Table 1). The tool was devised with guidance from a previously published grading system,⁽²⁷⁾ and evaluates the ability of an impact exercise trial to affect and assess 3D-imaged bone outcomes. All items were graded from one to three points, except for reporting of precision error of the imaging technique, which was graded from one to two points. The maximum quality score a study can obtain is 23. In this review, a score of <16 (third quartile) indicates a low study quality.

Statistical analysis

Effect sizes were presented as mean differences (MD), which were calculated as the mean percentage change in the exercise group minus that of the control group. Standardized MD (SMD) was used to compare changes in different bone strength measures between groups. Inverse variance weighted random-effects models were used to obtain summary estimates of the exercise effect with 95% confidence intervals (CI). Random-effects meta-analyses were used for all outcomes with a restricted maximum likelihood estimator for the between-study variance (T^2). We used the Hartung–Knapp–Sidik–Jonkman (HKSJ) method for estimating the variance of the pooled effect when meta-analyses had <5 studies (*k*)⁽⁶⁰⁾ as this method reduces type 1 error rates compared with the DerSimonian–Laird method⁽⁶¹⁾ if the number of included studies is small or there is substantial heterogeneity.⁽⁶²⁻⁶⁴⁾ In line with recommendations for meta-analysis of cluster randomized controlled trials,⁽⁶⁵⁾ we adjusted for the effects of clustering using a conservative intracluster correlation coefficient of 0.05 based on reported estimates from the included studies.^(37-39,42-47) Heterogeneity was tested using the Cochran *Q* statistic and presented with Tau^2 , Chi^2 , and I^2 . I^2 values of ≤25%, 25–50%, 50%–75% and ≥75% were indicative of low, moderate, high, and very high heterogeneity, respectively.⁽⁶⁶⁾ Subgroup analyses were performed according to population (children and adolescents; young adults; older men; and postmenopausal women). Meta-regression analyses on outcome data with at least 10 studies were performed to determine whether mean baseline age led to different treatment effects across studies. Meta-regression

Table 1. Criteria and Grading Used for Methodological Quality Assessment of the Studies

Criteria	Grade	Description
Consistency with guidelines for dose of osteogenic impact exercise ^a	1	2 or fewer completed sessions per week
	2	3 completed sessions per week
	3	4 or more completed sessions per week
Quantification of ground reaction forces (GRFs) produced from exercise intervention	1	No measure or estimation of GRF
	2	GRF was estimated based on previously published values
	3	GRF was objectively measured
Duration of trial	1	<6 months
	2	≥6 and <12 months
	3	≥12 months
Progression or periodization	1	No progression or not reported
	2	Progression or periodization of one component of the exercise intervention ^b
	3	Progression or periodization of more than one component of the exercise intervention
Supervision	1	No supervision during exercise sessions (not including the initial familiarization of the exercise program) or not reported
	2	Supervision during some exercise sessions
	3	Supervision during all exercise sessions
Precision error of imaging technique ^c	1	Not reported
	2	Short-term or long-term precision reported
Technical details of scan acquisition and analysis methods ^d	1	2 or fewer items reported
	2	3–5 items reported
	3	6–7 items reported

^aRecommendation based on the Exercise and Sports Science Australia position statement.⁽²³⁾

^bExamples of exercise components include frequency of exercise sessions, height of jumps, number of repetitions, and changes in core movements. An initial familiarization of the exercise program does not count as progression or periodization.

^cPrecision error may be reported as coefficient of variation (CV%) or least significant change.

^dProtocol details include the following seven items based on the International Society of Clinical Densitometry Official Position⁽¹⁰⁶⁾: imaging device model and manufacturer; bone length measurement methods if a percent rule was used and reference line selection; slice thickness; voxel size; scan acquisition parameters including QCT scanner's translation speed and MRI pulse sequence parameters; segmentation thresholds for image analysis; image quality grading or exclusion procedure due to poor image quality.

bubble plots were presented to display the relationship between effect sizes and baseline age. All analyses were conducted in Stata (v17, StataCorp, College Station, TX, USA). An α value of 0.05 was adopted for all analyses.

Sensitivity analyses were also conducted on studies without a high risk of bias; studies without a low methodological quality score; exercise protocols achieving sufficiently high impact of ≥ 4 bodyweights (BW) as recommended in the Exercise and Sports Science Australia position statement⁽²³⁾; combined impact and resistance exercise programs; studies of at least 6 months in duration; and by ROI at the tibia and radius. For studies that required imputation of SDs, we performed sensitivity analyses with correlation coefficients of 0.5 and 0.7. The pooled effect in sensitivity analyses had both adjusted and unadjusted standard errors applied, with the latter being interpreted due to HKSJ-adjusted standard errors having low empirical power, making it difficult to observe significant treatment effects in these exploratory analyses.⁽⁶⁷⁾

Results

Our search strategy identified 1438 study abstracts, of which 1297 were duplicates or irrelevant (Fig. 1). The full text of the remaining 141 articles were screened, with 31 articles fulfilling the eligibility criteria. There were two instances where a trial was reported in two relevant articles examining different bone structural parameters.⁽⁴⁰⁻⁴³⁾ The results for another relevant trial were reported in separate articles for girls and boys,^(46,47) which

was classified as one study. In total, 28 studies were included in this review.

Table 2 describes the characteristics of the included studies according to population subgroup.

Three of the 10 studies in children and adolescents only recruited girls,⁽³⁹⁻⁴³⁾ with the remaining studies recruiting both girls and boys.^(37,38,44-48,68) The five studies in adults only recruited women.^(49-51,69,70) Eight studies were in postmenopausal women^(52-54,71-75) and two were in older men.^(55,76) Results were combined for older men and women in one study,⁽⁷⁷⁾ for peri- and postmenopausal women in another,⁽⁷⁸⁾ and for pre- and postmenopausal women in another.⁽⁷⁹⁾ Six studies each were conducted in the United States,^(39,48-50,68,69) Australia,^(38,40,46,47,70,76,77) and Finland.^(51,52,72,74,75,79) Participants were predominantly White, and few studies reported participants of other ethnicities, including Asians^(38,39,44,46,47,49,69) and Blacks.^(39,45,47) Six studies excluded postmenopausal women with osteoporosis,^(71,72,74,76,77,79) and one study only included postmenopausal women with osteopenia or osteoporosis.⁽⁵³⁾

The duration of the trials ranged from 10 weeks to 7 years; 15 studies had a duration of >12 months^(38,39,44,48,49,51,52,55,72-77,79) and five studies had a duration of less than 6 months.^(45,50,53,54,68) Exercise protocols were also heterogenous in their impact intensity, frequency, level of progression, and supervision. Three studies involved two moderate- to high-impact exercise groups,^(40,50,72) for which results were combined. Jumping or hopping were implemented in most protocols, but some impact exercises were of an aerobic nature, such as running and dancing,^(50,53,78) and 14 studies added resistance training.^(38,44,45,49,50,52,54,69,72,73,75-79) Most

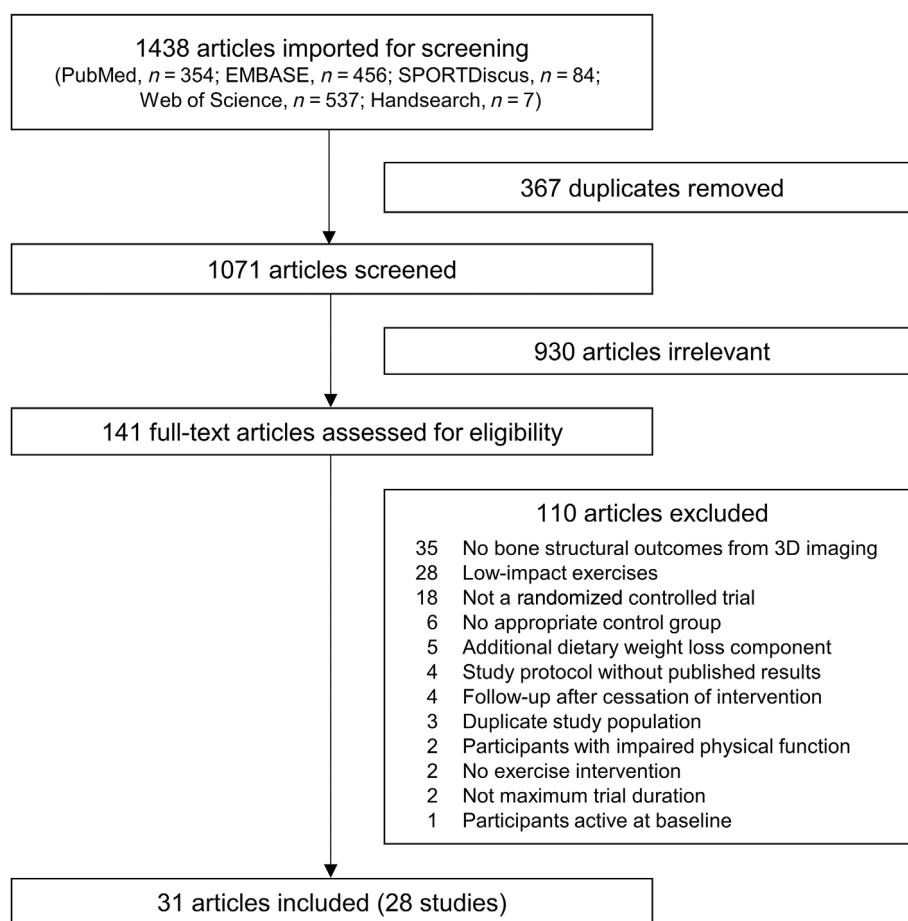


Fig. 1. PRISMA flow diagram of trial selection process.

protocols reported impact intensities in relation to forces exerted on the lower limb, whereas few described activities with upper limb impact, such as catching a weighted ball, performing cartwheels, or boxing.^(45-47,69,70) Fifteen studies reported exercise intensities of equal to or greater than four bodyweights and were thus classified as high-impact exercises,^(39-44,46,47,52-54,68,70,73,74,76,77,79) although these values were not quantitatively measured in four of the studies^(39,53,74,77) (Table 2).

A total of 1670 participants were allocated to exercise and 1315 to control. The differences in percentage change within and between the intervention and control groups for each bone parameter are reported in Supplemental Table S1. Seventeen studies utilized pQCT, where parameters from the 4% and 66% tibial and radial sites, and 38% tibial site, were mainly included in studies published after 2009.^(37-39,45-47,50) The radius was imaged in eight studies.^(38,46,47,53,54,69,70,72,78) Of these studies, upper-limb exercises had an impact component in three studies^(46,47,69,70) and a resistance component in another three,^(54,78,80) but it was not clear in two studies whether any activities involved the upper limbs.^(38,53) Lumbar spine was imaged by QCT in only three studies,^(49,73,76) whereas the femur was imaged by MRI,^(40,77) CT,^(52,55) QCT,^(51,76) and pQCT⁽³⁹⁾ at different sites in seven studies. HR-pQCT of the ultradistal tibia and radius was only used in two studies in postmenopausal women published in 2020.^(54,71)

Risk of bias summaries for each quality domain are reported in Figure 2 and Supplemental Figure S1. Seven studies were cluster RCTs, which were all based in schools,^(37-39,42-47) and all except one study had unclear timing of randomization.⁽³⁸⁾ Two studies used a within-participant unilateral design of an assigned exercise and control leg,^(55,71) which had unclear bias because of missing outcome data. Some studies invited a subset of the original study population for 3D imaging, but because of insufficient information pertaining to the subset, these studies had high risk of bias as a result of the randomization process and missing outcome data.^(42,43,46,47,53,71,77,79) Another potential area of bias arose from the fact that control groups continued habitual physical activity in most studies, rather than performing sham or non-osteogenic exercise interventions.^(37,43,48,49,53,70,73)

Scores from our assessment of methodological quality ranged from 10 to 19 (Table 2), with a higher score indicating better study quality and studies with scores <16 classified as low quality. Most studies that were assigned low quality scores had participants who completed two or fewer exercise sessions per week,^(37,38,42,43,45,49,53,69,70,72-79) did not measure or estimate exercise GRF values^(38,45-49,69,72,75,78) or had minimal or no exercise progression.^(38,40,44,45,48,49,54,68,69,73,78,79) Lower-quality studies also did not report a precision error for the imaging technique,^(37,46,47,54,75,77) but almost all the remaining studies reported precision ranges for multiple bone parameters instead

Table 2. Study Characteristics of the Included Trials Categorized by Population Group

Author, year, country	Design	Age in mean (SD) or range (years), n (analyzed/enrolled), sex	Follow-up duration	Frequency, duration, supervision	Exercise protocol	Intensity; mode of measurement	Exercise adherence	Quality score ^a (no. out of 23)
Children and adolescents Anliker, 2012, ⁽³⁷⁾ Switzerland	Cluster RCT	EX: 10.5 (1.2), n = 22/30 CON: 10.8 (1.1), n = 23/30 Girls and boys	36 weeks	2 d/wk 10 min/d All sessions supervised	Circuit of five jumping and sprinting exercises at start of PE. Includes two- and one-legged hopping, drop jumps, and multidirectional sprints. Progression: Intensity and repetitions increased every 6 weeks.	3.08–3.22 BW; Force plate	100%	15
Daly, 2016, ⁽³⁸⁾ Australia	Cluster RCT	Girls: EX: 8.1 (0.3), n = 132/192 CON: 8.1 (0.4), n = 112/170 Boys: EX: 8.1 (0.4), n = 149/206 CON: 8.2 (0.3), n = 112/159	4 years	2 d/wk 50 min/d All sessions supervised	Bluearth Foundation program with five activity types: coordination and agility activities; skill activities; dynamic movements; games; and core movements. Progression: Intervention teachers increased physical activity each year.	Not reported	Not reported	15
Farr, 2013, ⁽³⁹⁾ United States	Cluster RCT	EX: 10.6 (1.1), n = 109/292 CON: 10.7 (1.0), n = 98/217 Girls	2 years	3 d/wk 5–10 min/d Supervision not reported	40 jumps from boxes per session. Progression: Box height increased from 6 to 12 to 18 and finally to 24 inches over initial 8 weeks. Repetitions increased.	3–8 BW; Estimated	Not reported	16
Greene, 2009, ⁽⁴⁰⁾ Australia	RCT	Low-drop (LD): 7.8 (0.9), n = 13/14 High-drop (HD): 7.9 (1.1), n = 13/14 CON: 7.9 (0.8), n = 14/14 Girls	8 months	3 d/wk 8–22 min/d All sessions supervised	10 sets of single-leg drop-landing from 5-step benches. LD: 14 cm drop-landing HD: 28 cm drop-landing Progression: During week 1, sets increased per session from 3 to 9.	LD: 2.5–3.6 BW, HD: 2.9–4.4 BW; Pedar system	100%	17
Heinonen, 2001, ^(42,43) Canada	RCT	10.4 (0.5) EX: n = 8/93 CON: n = 8/98 Girls	7–8 months	3 d/wk 10–12 min/d All sessions supervised	Five 1.5–2 min circuit training stations, composed of jumping exercises (jumping jacks, lunge jumps, hopping, drop jumps). Progression: Three levels of difficulty at 2.5 and 3 months where height repetition and intensity of forces increased.	3.5–5 BW; Force platform	80%	16
Johannsen, 2003, ⁽⁶⁸⁾ United States	RCT	EX: 10.3 (5.3), n = 28/29 CON: 10.0 (5.1), n = 26/26 Girls and boys	12 weeks	5 d/wk Duration not reported All sessions supervised	25 two-legged jumps from a 45 cm box. Progression: -	4–4.3 BW; Force plate	76%	15

(Continues)

Table 2. Continued

Author, year, country	Design	Age in mean (SD) or range (years), <i>n</i> (analyzed/enrolled), sex	Follow-up duration	Frequency, duration, supervision	Exercise protocol	Intensity; mode of measurement	Exercise adherence	Quality score ^a (no. out of 23)
Macdonald, 2007, ⁽⁴⁴⁾ Canada	Cluster RCT	10.2 (0.6) EX: <i>n</i> = 281/359	16 months	Additional physical activities: 5 d/wk; 15 min/d Bounce at the Bell: 4 d/wk; 9 min/d	Two components: Additional 15 min of physical activities including skipping, dancing, and resistance exercises; Bounce at the Bell program three times for 3 min/d consisting of countermovement jumps and side-to-side jumps. Progression: Bounce at the Bell from 5 bilateral jumps or 10 unilateral jumps increased by 5 per session until a maximum of 36 jumps per day.	5 BW; Force plate	Teacher compliance 94% for additional activity; 74% for Bounce at the Bell	19
Meiring, 2014, ⁽⁴⁵⁾ South Africa	Cluster RCT	EX: 9.7 (1.2), <i>n</i> = 12/24 CON: 9.3 (0.9), <i>n</i> = 10/10	20 weeks	2 d/wk 45 min/d All sessions supervised	Five 5-min activities in an exercise circuit with warm-up, sprinting, running, jumping to catch 1 kg ball, ladder hopping, hopping over hurdles, and jump-rope. Progression: -	Not reported	78% completed all exercise sessions	12
Noqueira, 2015, ^(46,47) Australia	Cluster RCT	45 min/d Girls: EX: 10.5 (0.6), <i>n</i> = 71/76 CON: 10.7 (0.6), <i>n</i> = 67/75	9 months	3 d/wk 10 min/d	Capoeira-specific movements (Ginga, kicks, and defense movements with an emphasis on high-speed execution). Medium- to high-impact maneuvers such as jumps, hops, and cartwheels. Progression: Intensity and repetitions increased from 60 to 120–150 jumps, from 20 to 30–50 kicks and from 15 to 20–40 inverted movements such as handstands or cartwheels.	Mean of 1.3 BW (cartwheels)–5.4 BW (360° jumps); Force platform	90%	13
Specker, 2003, ⁽⁴⁸⁾ United States	RCT	Boys: EX: 10.5 (0.5), <i>n</i> = 104/107 CON: 10.7 (0.6), <i>n</i> = 68/76	1 year	All sessions supervised 5 d/wk 30 min/d Supervision not reported	5-min warm-up, 20-min of jumping, hopping, and skipping activities, 5-min of cool-down. 17 different weekly programs. Progression: -	Not reported	74%	14

Adults

(Continues)

Table 2. Continued

Author, year, country	Design	Age in mean (SD) or range (years), n (analyzed/enrolled), sex	Follow-up duration	Frequency, duration, supervision	Exercise protocol	Intensity; mode of measurement	Exercise adherence	Quality score ^a (no. out of 23)
Friedlander, 1995, ⁽⁴⁸⁾ United States	RCT	EX: 28.0 (6.8), n = 32/ CON: 30.1 (4.0), n = 31/ Women Total recruited n = 127	2 years	3 d/wk 60 min/d Supervision not reported	10-min warm-up and cool-down. One of three types of activities per week: Quickly alternating (1–2 min) cycles of push-up, sit-ups, high-impact aerobic activities, etc.; strengthening exercises with barbells, dumbbells, and weights; and vigorous high-impact aerobic workout of 70–85% maximal heart rate. Progression: During the second year, lifts were started from ground level and increased in load; step benches were added to vigorous high-impact workout program. Jumping performed with sun salutation postures. Backward jumps performed during stand-forward bend pose and plank pose. Forward jumps performed during downward facing dog pose and stand-forward bend pose. Progression: Number of jumps increased from 6 jumps per session in the first month to 14 jumps per session in the 8th month.	Not reported	61.3%	11
Kim, 2015, ⁽⁶⁹⁾ United States	RCT	EX: 45.7 (1.0), n = 16/27 CON: 43.2 (1.0), n = 18/20 Premenopausal women	8 months	2 d/wk 60 min/d All sessions supervised	Lower limb impact exercises included bilateral and unilateral versions of unidirectional and multidirectional jumps, and drop jumps. Upper limb impact exercise included punching combinations in both orthodox and southpaw positions. Progression: Height of drop jumps increased every 7 weeks from 15 cm to 80 cm; jumps and hops changed in directionality and force during landing; power and complexity of punching increased every 7 weeks	Not reported	≥80% for all included in analysis	14
Lambert 2019, ⁽⁷⁰⁾ Australia	RCT	EX: 22.1 (3.6), n = 10/17 CON: 23.1 (4.3), n = 10/17 Women	10 months	2 d/wk 40 min/d All sessions supervised	Mean of 4.70–6.79 BW across the seven progressive training stages; Force plate	Mean of 4.70–6.79 BW across the seven progressive training stages; Force plate	61.4%	15

(Continues)

Table 2. Continued

Author, year, country	Design	Age in mean (SD) or range (years), <i>n</i> (analyzed/enrolled), sex	Follow-up duration	Frequency, duration, supervision	Exercise protocol	Intensity; mode of measurement	Exercise adherence	Quality score ^a (no. out of 23)
Lester, 2009, ⁽⁵⁰⁾ United States	RCT	20.2 (1.7) Aerobic: <i>n</i> = 15/ CON <i>n</i> = 10/ Women no. recruited not reported	8 weeks	3 d/wk 30–90 min/d All sessions supervised	Aerobic: 5- to 10-min warm-up and cool-down. Steady-state or interval aerobic/running workouts at 75–85% HRmax. Combined: Aerobic and nonlinear periodized resistance program. Progression: For aerobic program, distance of runs and number of intervals increased or varied on one day every week. For resistance program, the load, repetitions, and exercise types varied per session	Mean weekly Osteogenic Index of 20.6 for aerobic group; and 36.9 for combined group; Estimated	Not reported	16
Vainionpaa, 2007, ⁽⁵¹⁾ Finland	RCT	EX: 38.2 (1.8), <i>n</i> = 39/64 CON: 38.1 (1.6), <i>n</i> = 41/60 Women	1 year	Supervised sessions: 3 d/wk; 60 min/d Home sessions: 7 d/wk; 10 min/d	High-impact training with step patterns, stamping, jumping, and running. Similar exercises at home. Progression: Intensity increased bimonthly. After 3 months, a 10 cm step bench was used, with the addition of another after 6 months.	1.2–5.6 g; Accelerometer	Ave 0.9 supervised sessions per week; Ave 2.2 home sessions per week	18
Older adults Daly, 2020, ⁽⁷⁷⁾ Australia	RCT	EX: 67.7 (6.5), <i>n</i> = 77/81 CON: 67.2, (5.5), <i>n</i> = 71/81 Men and women	18 months	3 d/wk 60 min/d Some sessions supervised	Battery of 27 weight-bearing exercises of three categories of directionality with three levels of difficulty each. 3 sets of 10–20 repetitions performed for 2–3 exercises per session. Also performed high-velocity progressive resistance training with machine and weights, and two high-challenge balance and mobility exercises. Progression: Every mesocycle, increased in intensity, repetitions and rate, and incorporated multidirectional movements.	1–9 BW; Estimated	55%	15

Postmenopausal women

(Continues)

Table 2. Continued

Author, year, country	Design	Age in mean (SD) or range (years), n (analyzed/enrolled), sex	Follow-up duration	Frequency, duration, supervision	Exercise protocol	Intensity; mode of measurement	Exercise adherence	Quality score ^a (no. out of 23)
Cheng, 2002, ⁽⁵²⁾ Finland	RCT	50–57 EX: n = 12/20	1 year	Supervised sessions: 2 d/wk Home sessions: 4 d/wk	10-min warm-up. Circuit-training with skipping, bounding over hurdles, drop-jumping, and single-legged hopping, with a total of about 200 jumps per session. 3–4 additional resistance exercises. Home exercise was a circuit of skipping, hopping, drop-jumping, and muscle strengthening. Progression: Hop height and repetitions increased over five periods. High-impact aerobic dance between periods.	3.4–5.2 BW; Force plate	Ave 1 supervised session per week	18
Du, 2020, ⁽⁷¹⁾ United Kingdom	RCT	63 (4), n = 10/11 EX and CON leg	6 months	3–7 d/wk <15 min/d Supervised sessions optional	3–5 sets of unilateral hops with 15 s of rest between sets. Progression: Individually increased in repetitions and intensity for first 10 weeks until performed 50 multidirectional hops daily after week 11.	2.15–2.37 BW; Force plate	80.4% during final 14 weeks	18
Karinkanta, 2007, ⁽⁷²⁾ Finland	RCT	Balance-jumping: 72.9 (2.3), n = 35/37 Combined: 72.9 (2.2), n = 36/38 CON: 72.0 (2.1), n = 36/37	1 year	3 d/wk 40–50 min/wk All sessions supervised	Balance-jumping: Static and dynamic balance, agility movements, jumps and other impacts, and direction changing exercises. Combined: Addition of progressive resistance training with machines and large muscle group exercises. Progression: Every 12 weeks, alternated between different aerobics and step-aerobics programs. Difficulty of movements, repetitions, and intensity of impact and resistance training increased. High-impact aerobic dance with step boards. 4 sets of 15–20 multilateral jumps added in subsequent sessions. High-intensity resistance training included functional gymnastics and dynamic resistance training. Progression: Intensity increased every 6–12 weeks	Not reported	56% for balance-jumping group, 67% for combined group	16
Kemmler, 2013, ⁽⁷³⁾ Germany	RCT	EX: 52.3 (2.3), n = 36/43 CON: 52.4 (2.7), n = 30/42	1 year	3 d/wk 60 min/d All sessions supervised	High-impact aerobic dance with step boards. 4 sets of 15–20 multilateral jumps added in subsequent sessions. High-intensity resistance training included functional gymnastics and dynamic resistance training. Progression: Intensity increased every 6–12 weeks	2.5–4 BW; Force plate	67%	16

(Continues)

Table 2. Continued

Author, year, country	Design	Age in mean (SD) or range (years), <i>n</i> (analyzed/enrolled), sex	Follow-up duration	Frequency, duration, supervision	Exercise protocol	Intensity; mode of measurement	Exercise adherence	Quality score ^a (no. out of 23)
Liu-Ambrose, 2004, ⁽⁶³⁾ Canada	RCT	EX: 78.9 (2.8), <i>n</i> = 34/36 CON: 79.5 (3.2), <i>n</i> = 32/34	25 weeks	2 d/wk 50 min/wk All sessions supervised	Agility training including dance movements, relay races, and practicing sudden starts and stops with various speeds and directions. Progression: Increased difficulty and challenges to sensory reactions and increased number of stimuli.	2–4 BW; Estimated	87%	15
Pinho, 2020, ⁽⁶⁴⁾ Brazil	RCT	EX: 66.9 (4.2), <i>n</i> = 21/21 CON: 65.0 (3.4), <i>n</i> = 17/17	20 weeks	3 d/wk 60 min/d All sessions supervised	14 exercise stations (drop jumps, squat jumps, muscle strengthening exercises etc), 3 sets of 10 repetitions per station. Progression: 9 cm step used for drop-jump exercise for first 6 weeks, then replaced with 18 cm step.	2.2–4.3 BW; Force plate	92%	14
Uusi-Rasi, 2003, ⁽⁷⁴⁾ Finland	RCT	EX: 53.3 (2.2), <i>n</i> = 37/41 CON: 53.2 (2.1), <i>n</i> = 39/41	1 year	3 d/wk 60 min/d All sessions supervised	15-min warm-up, 20-min multidirectional jump program (either aerobic jumping or step exercises), 15-min of calisthenics and 10-min cooldown. Progression: Height of jumps over foam fences and in step exercises increased from 10 to 25 cm.	2.1–5.6 BW; Estimated	Ave 1.6 sessions per week	17
Uusi-Rasi, 2015, ⁽⁷⁵⁾ Finland	RCT	EX: 74.8 (2.9), <i>n</i> = 91/103 CON: 73.8 (3.1), <i>n</i> = 95/102	2 years	1–2 d/wk 60 min/d All sessions supervised	10-min warm-up, then exercise sessions focused on agility, mobility, strengthening, weight-bearing change of direction, and balance. Resistance training additionally performed with gym equipment. Modified exercises were performed at home. Progression: Impact intensity increased using different surfaces, multidirectional movements, addition of weights and higher step boards.	Not reported	72.8% for supervised training, 66.1% for home training	14

Pre-, peri-, and postmenopausal women

(Continues)

Table 2. Continued

Author, year, country	Design	Age in mean (SD) or range (years), <i>n</i> (analyzed/enrolled), sex	Follow-up duration	Frequency, duration, supervision	Exercise protocol	Intensity; mode of measurement	Exercise adherence	Quality score ^a (no. out of 23)
Danz, 1998, ⁽⁷⁸⁾ Germany	RCT	EX: 51.9 (4.5), <i>n</i> = 46/60 CON: 51.5 (4.1), <i>n</i> = 37/61 Peri- and postmenopausal women	6 months	3 d/wk 60 min/d Supervision not reported Supervised sessions:	20-min gymnastics with ball games, aerobic dance, and upper body strengthening exercises. Followed by jogging. Progression: Increased duration of jogging from 3 to 40 min within 12 weeks.	Not reported	75%	10
Nikulan, 2012, ⁽⁷⁹⁾ Finland	RCT	EX: 53.7 (6.8), <i>n</i> = 37/40 CON: 52.6 (7.1), <i>n</i> = 30/37 Pre- and postmenopausal women	1 year	1 d/wk; 30–40 min/d Home sessions: At least 2 d/wk; duration not reported	Supervised sessions were alternate weeks of step aerobics or circuit training with a total of 150–180 jumps and leaps per session, and rest periods between consecutive movements. Home sessions comprised about 100 jumps and leaps. Progression: -	Up to 6 BW; Accelerometer	76% for supervised sessions, 60% for home sessions	15
Older men Allison, 2015, ⁽⁵⁵⁾ United Kingdom	RCT	70 (4), <i>n</i> = 34/50 EX and CON leg	1 year	3–7 d/wk 10 min/d Some sessions supervised	5 sets of 10 unilateral hopping with 15 s rest between sets. Progression: Increased in intensity and repetition and incorporated multidirectional hops.	2.7–3.0 BW; Force plate	92%	18
Kukuljan, 2011, ⁽⁷⁶⁾ Australia	RCT	EX: 60.7 (7.1), <i>n</i> = 46/48 CON: 59.9 (7.4), <i>n</i> = 44/46	18 months	3 d/wk 60–75 min/d Some sessions supervised	5–10 min warmup and cool-down, impact exercises (unilateral hops, tuck jumps and bench drop jumps), and progressive resistance training. Progression: Increased intensity, rate, and repetitions and incorporated multidirectionality over mesocycles and microcycles.	1.5–9.7 BW; Force plate	63%	16

Abbreviation: BW = bodyweights; CT = controlled trial; CON = control group; d/wk = days per week; EX = exercise group; HD = high-drop; HRmax = maximum heart rate; LD = low-drop; min/d = minutes per day; PE = physical exercise; RM = repetition maximum; RCT = randomized controlled trial; SD = standard deviation.

^aThe study quality score evaluates the ability of an impact exercise trial to affect and assess bone structural outcomes via the following criteria: impact exercise dose; intensity; duration; progression; supervision; imaging technique precision error; and scan acquisition and analysis techniques. A score of ≥ 16 indicates a high study quality.

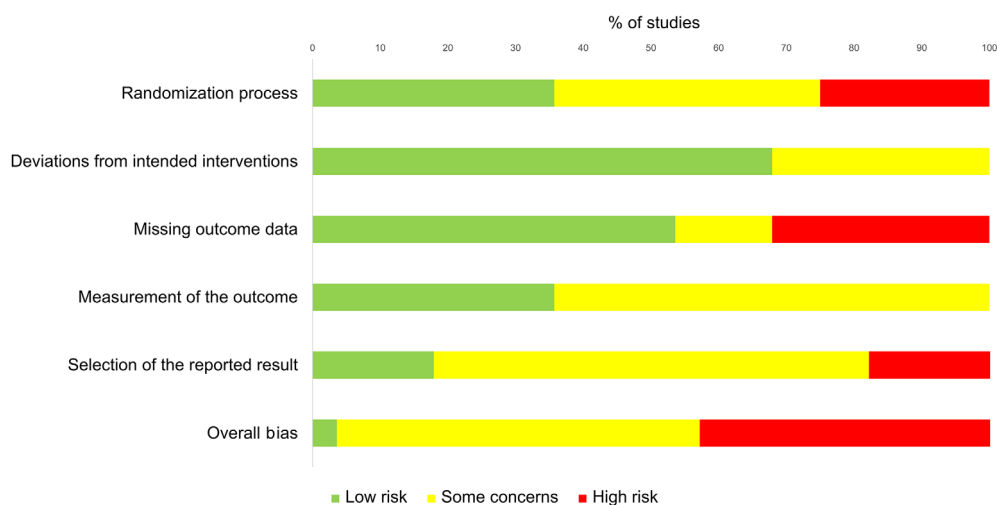


Fig. 2. Percentage of studies in each risk of bias domain.

of values specific to each parameter. Reporting of scan acquisition and analysis was heterogenous as well, with most studies not specifying the segmentation thresholds used in image analyses,^(37,40-43,46,47,49,50,54,68,71,72,74,75,78,79) any use of image quality grading,^(42-44,46,47,49,51,53,54,69,70,72-79) or scan acquisition parameters such as QCT scanner translation speed or MRI pulse sequence parameters.^(37,40-43,45-47,49,51-54,68,70,73,76,78)

Figure 3 provides a summary of impact exercise effects on vBMD and bone structure. Forest plots are presented in Supplemental Figures S2–S32. Overall, impact exercise improved trabecular vBMD (MD = 0.54% [95% CI 0.17, 0.90%], $p = 0.01$, $I^2 = 23.1%$, number of studies $k = 13$) at the distal tibia compared with controls (Fig. 4). When restricting the analysis to studies of high-impact exercise, the significant exercise effect on trabecular vBMD at the distal tibia increased in magnitude (0.69% [0.27, 1.10%], $p < 0.01$, $I^2 = 0%$, $k = 6$) (Supplemental

Table S3). When excluding studies of low methodological quality, there were positive exercise effects at the distal tibia for total vBMD (1.11% [0.37, 1.84%], $p < 0.01$, $I^2 = 0%$, $k = 3$) and bone strength (SMD = 0.36 [0.06, 0.66], $p = 0.02$, $I^2 = 68%$, $k = 5$). At the mid/proximal radius, impact exercise significantly improved cortical thickness (1.78% [0.21, 3.36%], $p = 0.04$, $I^2 = 0%$, $k = 3$) (Fig. 6), even after sensitivity analyses for high-impact exercise. Significant exercise effects were also observed for total vBMD at the proximal femur (3.11% [1.07, 5.14%], $p = 0.03$, $I^2 = 0%$, $k = 2$) (Fig. 7). Impact exercise did not significantly change bone parameters at the distal radius, femoral shaft, or lumbar spine across all studies and in subgroups (Figs. 8 and 9). Subgroup differences were present for changes in total vBMD and cortical vBMD at the mid/proximal tibia, trabecular vBMD at the distal radius, and cortical vBMD, cortical area, and bone strength at the mid/proximal radius. However, age-adjusted meta-regression on outcome data

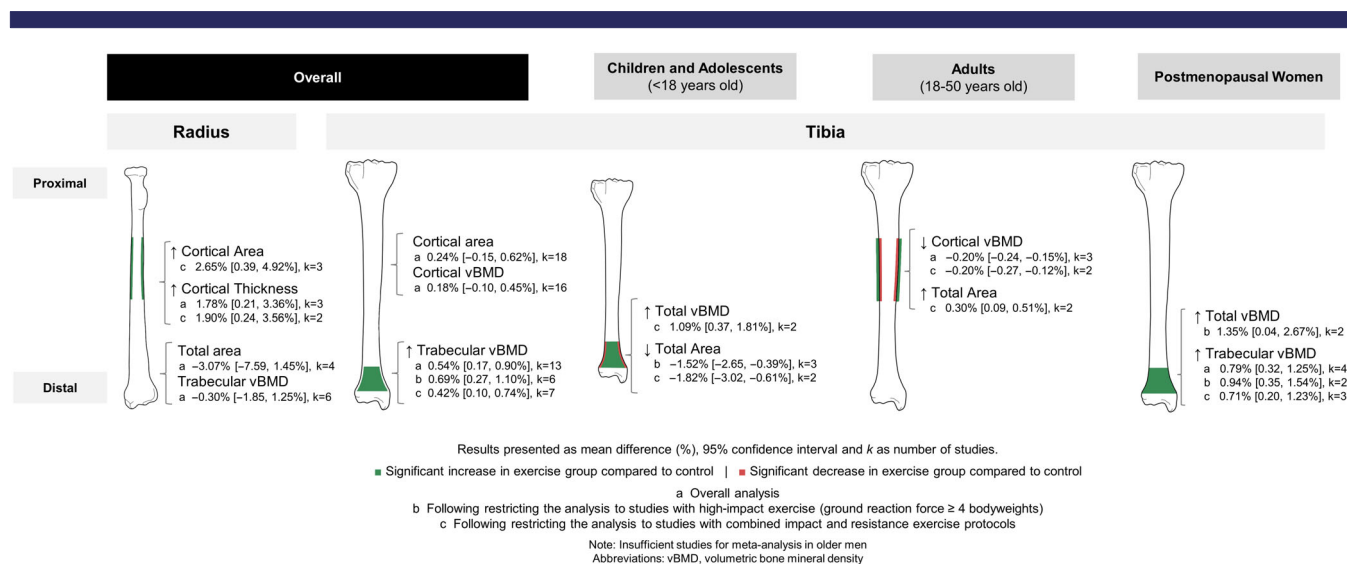


Fig. 3. A schematic diagram summarizing the main effects of moderate- to high-impact exercise on radial and tibial bone structure and volumetric bone mineral density (vBMD) across the lifespan.

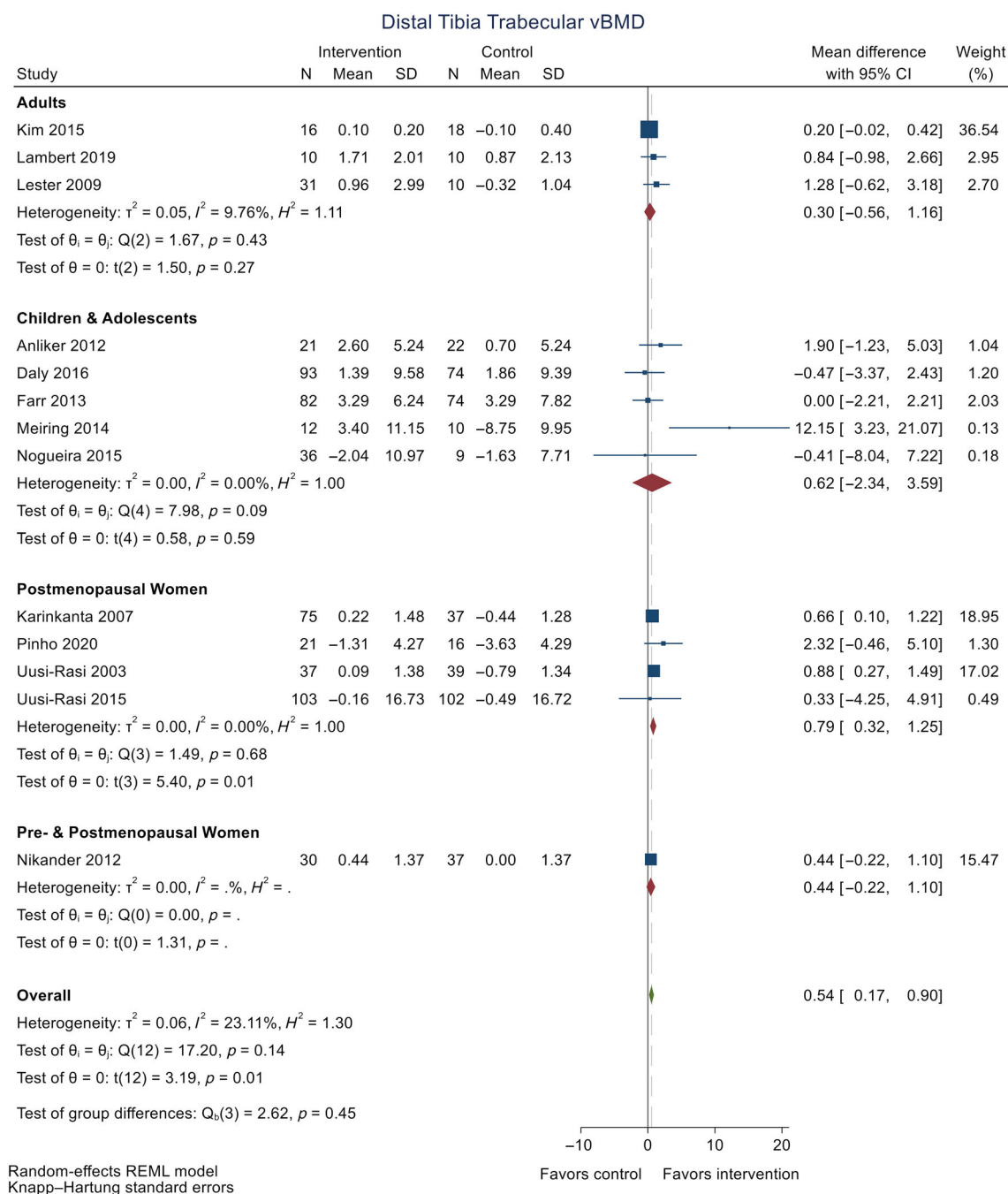


Fig. 4. Effects of impact exercise on trabecular volumetric bone mineral density (vBMD) at the distal tibia.

with at least 10 studies showed that age was unlikely to be a source of heterogeneity (Supplemental Table S5).

Children and adolescents

In children and adolescents, impact exercise led to a significant decrease in total area at the distal tibia after sensitivity analyses for risk of bias, combined impact and resistance exercise, and high-impact exercise (Supplemental Tables S2–S4). However, only one of the included studies were of sufficient methodological quality,⁽⁴⁴⁾ and when restricting the analysis to the 4% to 5% tibia

site, the effect on total area was nonsignificant (MD = 0.15% [-1.34, 1.64%], $p = 0.85$, $I^2 = 0\%$, $k = 5$). Impact exercise significantly improved total vBMD at the distal tibia in sensitivity analyses for combined impact and resistance exercise programs (1.09% [0.37, 1.81%], $p < 0.01$, $I^2 = 0\%$, $k = 2$) and interventions of at least 6 months (1.03% [0.37, 1.68%], $p < 0.01$, $I^2 = 0\%$, $k = 5$). No significant exercise effect was found at the mid/proximal tibia. At the 66% radial site, a significant positive exercise effect was observed for cortical vBMD (1.58% [0.81, 2.34%], $p < 0.01$, $I^2 = 0\%$, $k = 2$) and cortical area (5.32% [1.82, 8.81%], $p < 0.01$, $I^2 = 0$, $k = 2$). Impact exercise did not significantly change vBMD and bone

Mid Prox Tibia Cortical vBMD

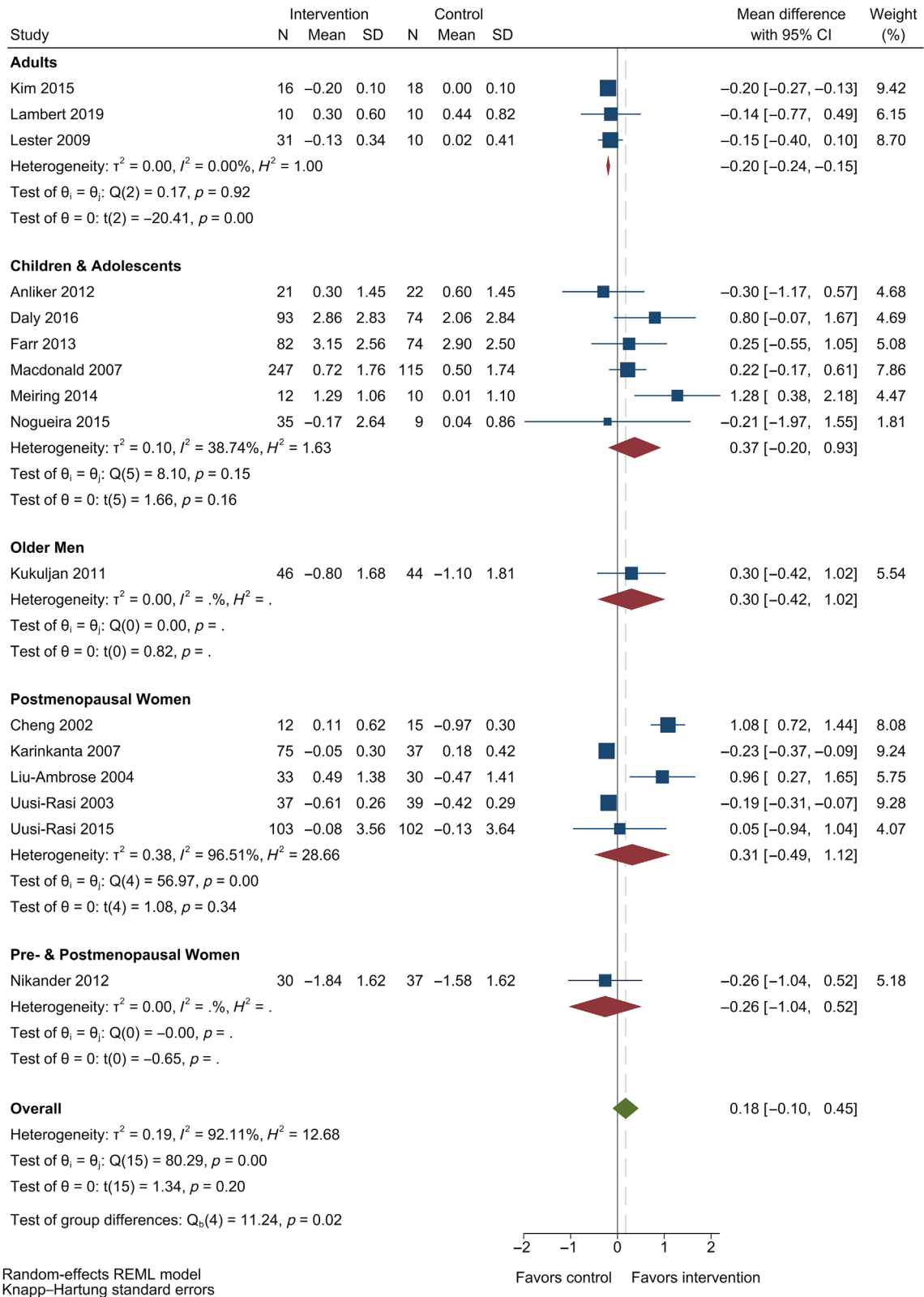


Fig. 5. Effects of impact exercise on cortical volumetric bone mineral density (vBMD) at the mid/proximal tibia.

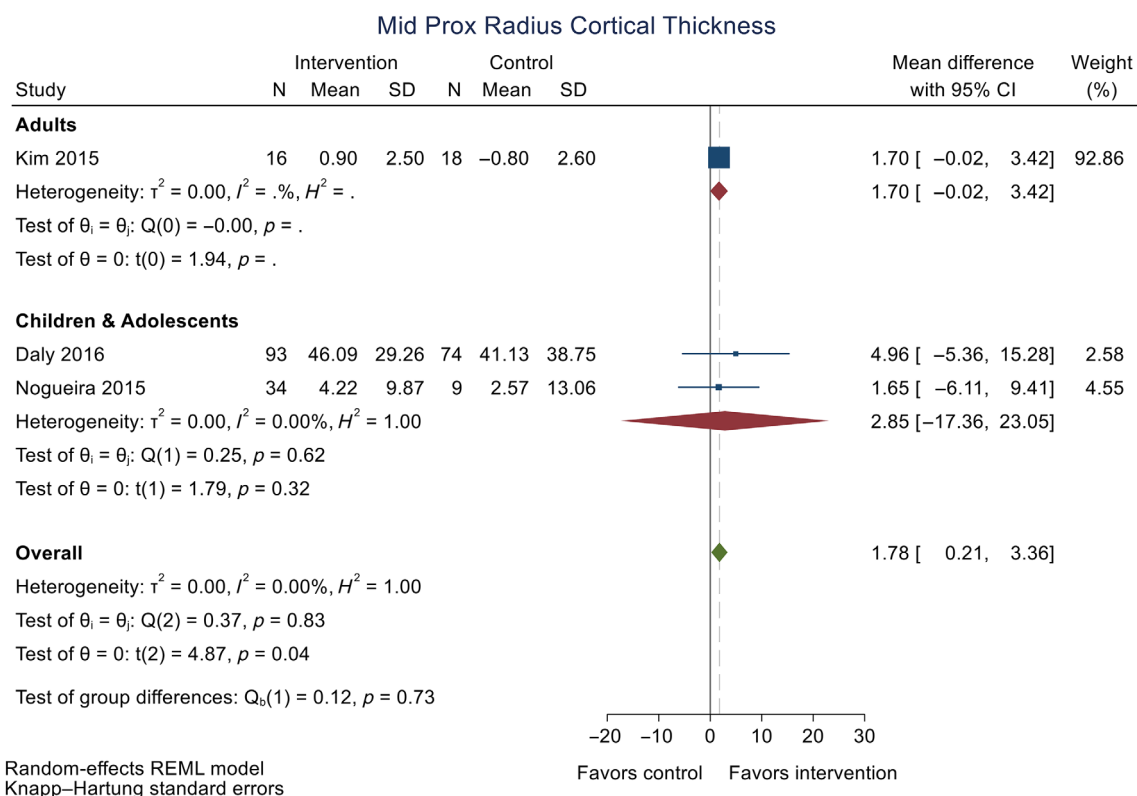


Fig. 6. Effects of impact exercise on cortical thickness at the mid/proximal radius.

structure at the femur. There were no studies in children and adolescents investigating the bone structural effects of impact exercise on the lumbar spine.

Adults

Impact exercise significantly decreased cortical vBMD at the mid/proximal tibia (MD = -0.20% [95% CI -0.24, -0.15%], $p < 0.01, I^2 = 0\%, k = 3$) in adults (Fig. 5), which remained

significant when separately analyzing the 38% and 66% tibial sites. The trial by Kim and colleagues⁽⁶⁹⁾ demonstrated the greatest significant decrease in cortical vBMD at the mid/proximal tibia (-0.20% [-0.27, -0.13%]) but also observed a positive increase in cortical area (0.20% [-0.01, 0.41%]). The only trial classified as high impact was by Lambert,⁽⁷⁰⁾ whereas other studies reported impact intensity using the osteogenic index⁽⁵⁰⁾ or in accelerations due to Earth's gravity.⁽⁵¹⁾ When correlation coefficients of 0.5 and 0.7 were used, a significant positive exercise

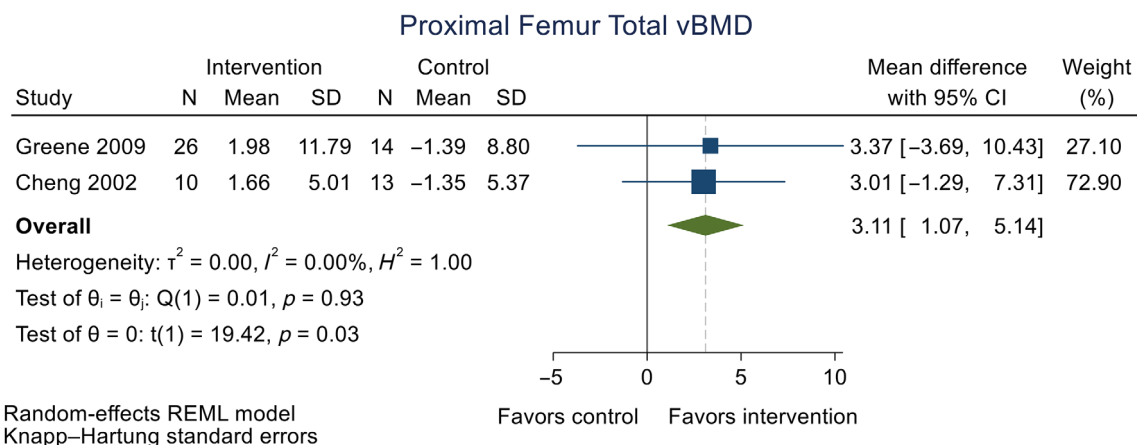


Fig. 7. Effects of impact exercise on total volumetric bone mineral density (vBMD) at the proximal femur.

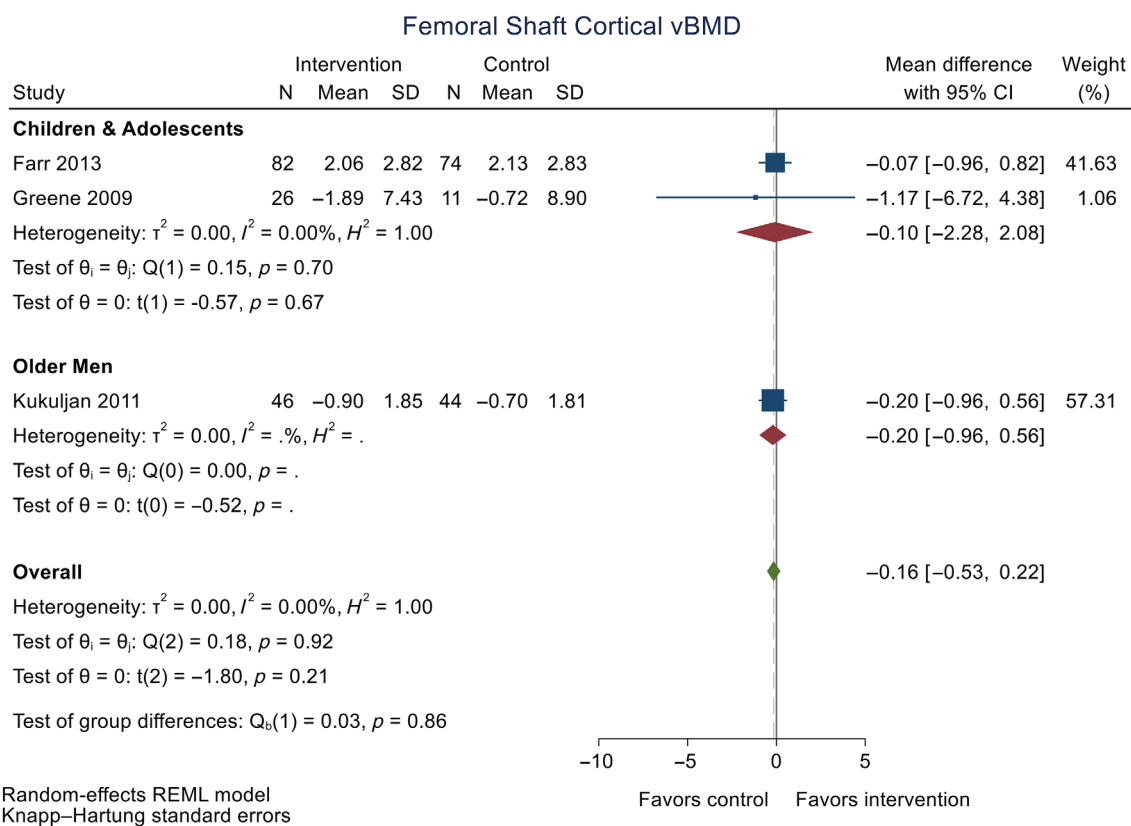


Fig. 8. Effects of impact exercise on cortical volumetric bone mineral density (vBMD) at the femoral shaft.

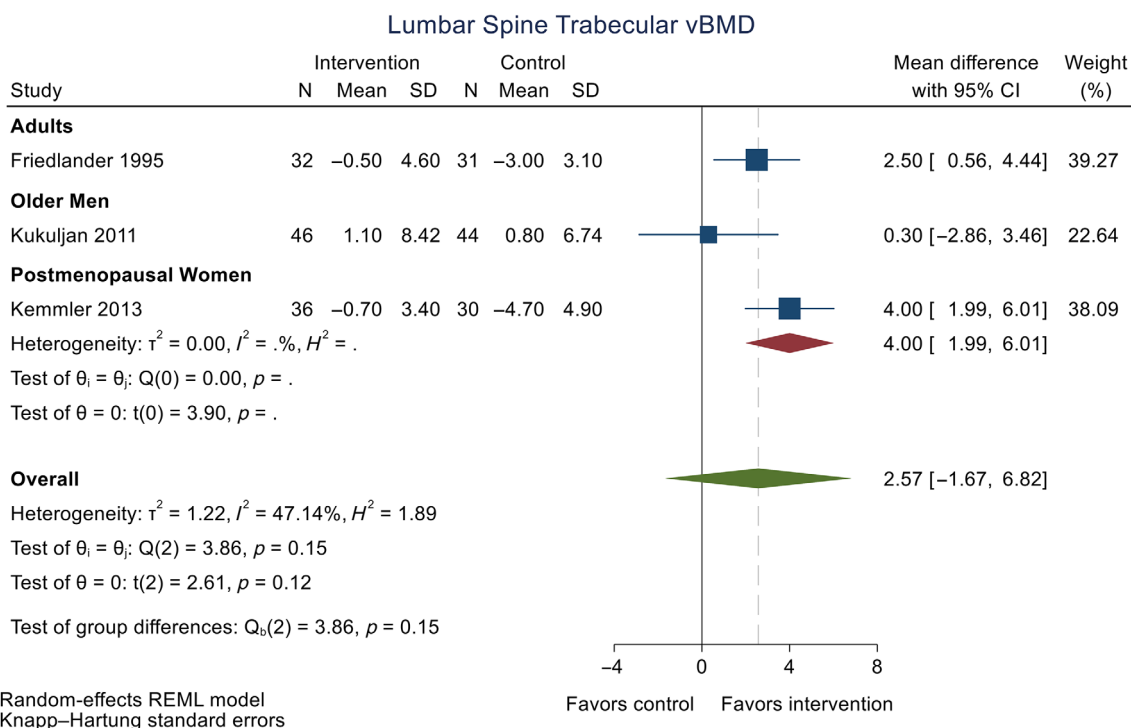


Fig. 9. Effects of impact exercise on trabecular volumetric bone mineral density (vBMD) at the lumbar spine.

effect was additionally observed for trabecular vBMD at the distal tibia (0.21% [0.00, 0.42%], $p < 0.05$, $I^2 = 0\%$, $k = 3$ for both).

There were insufficient studies examining the femur and lumbar spine to perform meta-analyses in adults. The RCT by Vainionpaa and colleagues⁽⁵¹⁾ revealed no significant changes in cortical thickness at the femoral shaft in both the exercise (−0.13%, SD = 2.17%) and control groups (−0.02%, SD = 2.4%) but increases in cortical area in both groups (0.23%, SD = 0.74% for exercise; 0.36%, SD = 0.9% for control) after a year of progressive high-impact training. At the lumbar spine, impact exercise significantly improved trabecular vBMD in the 2-year impact and aerobic exercise RCT by Friedlander and colleagues⁽⁴⁹⁾ (MD = 2.5%. [95% CI 0.57, 4.43%]).

Postmenopausal women

In postmenopausal women, impact exercise significantly increased trabecular vBMD at the distal tibia (MD = 0.79% [95% CI 0.32, 1.25%], $p = 0.01$, $I^2 = 0\%$, $k = 4$). Sensitivity analysis including only high-impact exercise trials displayed a significant positive exercise effect on total vBMD at the distal tibia (1.35% [0.04, 2.67%], $p = 0.04$, $I^2 = 0\%$, $k = 2$). There were no significant exercise effects on HR-pQCT-derived trabecular microarchitecture, and all results had moderate to high heterogeneity ($I^2 = 49.6$ –84.4%). When tibial ROIs were examined separately, impact exercise significantly improved cortical area at the 50% tibia (MD = 1.00% [95% CI 0.66, 1.34%], $p < 0.01$, $I^2 = 0\%$, $k = 4$).

One trial reported bone structural changes at the femur and one trial reported bone structural changes at the lumbar spine. Cheng and colleagues⁽⁵²⁾ reported no significant within- or between-group changes in total area at the mid-femur and total vBMD at the proximal femur, but these parameters increased in the exercise group (0.43% and 1.66%, respectively) and decreased in the control group (−0.42% and −1.35%, respectively). Kemmler and colleagues⁽⁷³⁾ reported reductions in total and trabecular vBMD at the lumbar spine for both exercise and control groups, but decreases were attenuated in the exercise group (MD = 1.80% [95% CI = 0.76, 2.84%] and 4.00% [1.92, 6.08%], respectively).

Older men

Both trials in older men were of sufficiently high quality, but there were insufficient data to conduct meta-analyses. The 18-month intervention by Kukuljan and colleagues⁽⁷⁶⁾ included a combination of progressive resistance training and high-impact exercise with GRF of up to 9.7 bodyweights. A greater increase in total vBMD and trabecular vBMD was observed at the lumbar spine in the exercise group (+0.7% and +1.1%, respectively) compared with controls (−0.1% and +0.8%, respectively), whereas cortical vBMD, cortical area, and polar moment of inertia at the 50% tibia and 50% femur declined to similar extents in both exercise and control groups. The 1-year within-participant unilateral trial by Allison and colleagues⁽⁵⁵⁾ involved a one-legged hopping program but recorded impacts that were not classified as high (≤ 3 bodyweights). Nonetheless, at the proximal femur, there was a greater increase in trabecular and cortical vBMD in the exercise leg (6.4% and 1.8%, respectively) compared with the control leg (4.5% and 1.6%, respectively).

Discussion

This systematic review of 28 RCTs showed varying effects of moderate- to high-impact exercise training on vBMD and bone structural compartments in population subgroups across the

lifespan. Impact exercise training increased trabecular vBMD at the distal tibia, total vBMD at the proximal femur, and cortical thickness at the mid/proximal radius across age and sex groups. In adults, impact exercise decreased cortical vBMD at the mid/proximal tibia but improved total area when combined with resistance exercise. In postmenopausal women, trabecular vBMD increased at the distal tibia. In older men, bone structural changes were not significantly different among exercise and control groups. Impact exercise had no effect on bone parameters at the distal radius, femoral shaft, or lumbar spine across all groups or in any subgroup, and meta-analysis was not possible for several bone parameters in the subgroups due to few studies. Nonetheless, age-adjusted meta-regression suggests that age was not a source of heterogeneity.

To our knowledge, this is the first systematic review examining the effects of impact exercise on vBMD and bone structure measured by 3D imaging techniques across the lifespan. Currently, systematic reviews and meta-analyses examining the effect of exercise on 3D bone parameters have been specific to children and adolescents,^(81,82) postmenopausal women,^(22,83) or adults at least 18 years of age.⁽¹⁶⁾ Additionally, as studies of all exercise types were included in these systematic reviews, it is difficult to ascertain the role of impact exercise on vBMD and bone structure. Several systematic reviews have investigated the skeletal effects of impact or weight-bearing exercise,^(14,15,18,27,84–87) but inconsistent or vague definitions for the inclusion of such exercises have been used. A meta-analysis by Kistler-Fischbacher and colleagues⁽¹⁸⁾ found moderate- to high-intensity impact and resistance exercise to be more effective for improvements in lumbar spine and hip aBMD than low-intensity impact and resistance exercise in postmenopausal women, highlighting the necessity of appropriately prescribing impact exercise of sufficient intensity to optimize osteogenesis. The current meta-analysis investigates the effects of impact exercise of sufficient intensity on vBMD and bone structural parameters at multiple sites across different populations.

Across age and sex groups, impact exercise significantly improved trabecular vBMD at the distal tibia. This result remained positive and significant in sensitivity analyses for high-impact exercise, combined impact and resistance protocols, and studies with sufficiently high methodological quality scores. This finding is consistent with a meta-analysis in postmenopausal women, which reported improvements in trabecular vBMD at the distal tibia (MD = 0.87%) from all exercise types, including low impact exercise.⁽²²⁾ Although meta-regression analyses showed that age did not appear to explain impact exercise-induced changes in trabecular vBMD at the distal tibia, the bubble plot suggests a U-shaped relationship (Supplemental Fig. S33), with stronger exercise effects among trials including younger or older individuals compared with trials including middle-aged individuals. Aging has indeed been shown to reduce loading-induced trabecular bone formation in animal studies.^(88,89) However, the principle of exercise training known as “initial values” suggests that individuals with lower initial values in a physiological system have a higher potential for improvement in response to training and could explain greater skeletal improvements in older adults with poorer bone health at baseline.⁽⁹⁰⁾

We observed an improvement in cortical thickness at the mid/proximal radius after impact exercise across age and sex groups. A recent meta-analysis of upper-limb targeted exercise interventions in adults at least 18 years old reported increases in aBMD and vBMD in the forearm.⁽¹⁶⁾ When including children and adolescents in our meta-analyses, we additionally observed subgroup differences for cortical area and vBMD, but not cortical thickness, at the mid/proximal radius, with the greatest increases

in cortical area and vBMD being among children. This trend is suggestive of periosteal apposition in response to impact exercise occurring before puberty and reduced endosteal resorption even after this “window of opportunity” during growth.^(81,91)

Children and adolescents

There was a negative exercise effect on total area measured at the distal tibia in studies with high-impact exercise and combined impact and resistance exercises. However, after excluding sites outside of the growth plate (ie, excluding sites $\geq 8\%$ of the bone length from the tibial endplate⁽⁹²⁾), this difference was not significant in the remaining studies. Indeed, the greatest decrease in total area was in Macdonald and colleagues' study⁽⁴⁴⁾ where the 8% site was examined. Although the reason for a decrease in total area in these sensitivity analyses is unclear, cortical area did not significantly change in our analyses, suggesting that the less-active control group may have instead experienced greater endocortical resorption,⁽⁹¹⁾ resulting in periosteal apposition in compensation.⁽⁹³⁾

The addition of resistance training to high-impact exercise for improving bone health in children may be warranted, as evidenced by increased total vBMD at the distal tibia in trials with combined impact and strength training. There was a trend toward a greater effect in combined exercise compared with studies of impact training without resistance training (data not shown). Of note, the two studies in this sensitivity analysis (Daly and colleagues⁽³⁸⁾ and Macdonald and colleagues⁽⁴⁴⁾) demonstrated the greatest increase in total vBMD and greatest decrease in total area at the distal tibia. As periosteal apposition is understood to be an adaptive response to mechanical loading,⁽⁹¹⁾ this paradoxical finding may be explained by partial volume effects in the presence of incomplete bone mineralization when obtaining pQCT scans in the bones of children.⁽⁹⁴⁾ Indeed, changes in cortical vBMD in the study by Daly and colleagues⁽³⁸⁾ were not significant after adjusting for potential partial volume effects.

Impact exercise significantly improved cortical vBMD and area at the 66% radial site. Although the exercise protocol listed more general activities in the study by Daly and colleagues,⁽³⁸⁾ such as coordination and agility activities (including rope-skipping and jumping), the capoeira-based exercise prescribed by Nogueira and colleagues^(46,47) described the incorporation of 15 repetitions of cartwheels and handstands each per session, suggesting the presence of site-specific exercise effects. Conversely, the current meta-analysis did not observe any significant change in trabecular bone among children and adolescents. This may be attributed to the younger ages of participants (<11 years old) among the included studies; most participants were classified as prepubertal,^(38,40-42) whereas growth in the trabecular compartments tends to occur between maturity stages three and four (10–18 years old).⁽⁸²⁾ However, different forms of bone structural adaptations may occur in the peri- or postpubertal period,^(95,96) emphasizing the need for RCTs in more mature populations and comparisons of exercise-induced structural changes between maturity stages.

Adults

We observed negative exercise effects on cortical vBMD at the mid/proximal tibia in premenopausal women. Of all the included studies, an 8-month yoga intervention that incorporated jumping displayed the greatest significant decrease in cortical vBMD,

but also the largest increase in cortical area at both sites.⁽⁶⁹⁾ The observed trade-off of an increase in bone size but small decreases in cortical vBMD may have been a specific adaptation to impact exercise, as similarly observed in adult male tennis players.⁽⁹⁷⁾ This is supported by our finding of an accompanying increase in total area at the mid/proximal tibia for combined impact and resistance exercises.

Notably, the magnitude of change in cortical vBMD was overall small (-0.20 to -0.67%) and all individual study changes were within the reported coefficient of variation. In our assessment of methodological quality, no study in adults described whether or how image quality was graded. In addition, it was difficult to ascertain if the magnitude of impact was sufficiently high in these interventions as this was either not measured or was reported using measures such as the osteogenic index⁽⁵⁰⁾ or g , the acceleration due to gravity,⁽⁵¹⁾ which have unknown osteogenic thresholds.

A previous meta-analysis in premenopausal women reported significantly increased lumbar spine and femoral neck aBMD from impact exercise.⁽¹⁵⁾ Although there were insufficient studies for meta-analyses to elucidate vBMD and structural changes at these sites, the study by Friedlander and colleagues⁽⁴⁹⁾ reported a significant increase in trabecular vBMD after 2 years of high-impact aerobic exercise with resistance exercises. Conversely, the 1-year supervised and home-based impact training trial by Vainionpaa and colleagues⁽⁵¹⁾ did not significantly improve femoral shaft area and thickness, which may emphasize the need for the addition of resistance training for osteogenesis in premenopausal women.⁽¹⁵⁾

Postmenopausal women

Impact exercise significantly improved trabecular vBMD at the distal tibia in postmenopausal women, which reliably predicts fractures at clinically relevant sites such as the hip and spine.⁽⁵⁾ This supports the potential benefits of impact exercise particularly when trabecular bone loss is common after postmenopausal declines in estrogen levels.⁽⁹⁸⁾ It is worth noting, however, that the increase in trabecular vBMD (95% CI 0.39, 1.18%) does not exceed the least significant change of 2.4%⁽⁵⁾ and so the observed effect did not exceed precision error. Changes in cortical vBMD at the mid/proximal tibia were mixed in the present analysis, with two studies reporting significant increases^(52,53) and another two studies reporting significant decreases.^(72,74) These latter studies excluded postmenopausal women who had osteoporosis,^(72,74) whereas one of the studies with significant increases specifically recruited women with osteopenia and osteoporosis.⁽⁵³⁾ Postmenopausal women with low bone mass usually experience greater exercise-related increases in BMD than counterparts with normal bone mass,^(16,99,100) but there were insufficient studies in such populations in the current analysis to draw these conclusions.

Sufficiently high-intensity impact exercise significantly improved total and trabecular vBMD at the distal tibia. Conversely, a recent meta-analysis reported non-significant changes in spine and hip aBMD in postmenopausal women for high-intensity impact-only training using a similar definition of GRF ≥ 4 BW). This indicates that potential structural adaptations from impact exercise of sufficient intensity may not be reflected in aBMD measurements.⁽⁶⁾ Physiologically, high-impact exercise would likely be required to compensate for the downregulation of estrogen receptor α , which mediates signaling pathways in mechanotransduction for bone adaptation.⁽¹⁰¹⁾

Older men

There have been consistent reports of significant improvements in femoral neck BMD, but not lumbar spine BMD, for exercise in older men.^(31,32,102,103) Although we did not examine aBMD in the current review, the included studies by Allison and colleagues⁽⁵⁵⁾ and Kukuljan and colleagues⁽⁷⁶⁾ both reported significantly increased femoral neck aBMD and cross-sectional area in the exercise group compared with controls, but this was not accompanied by significant structural bone changes at the femur. However, when the results were pooled with exercise and control group participants supplemented with calcium- and vitamin D₃-fortified milk in Kukuljan and colleagues⁽⁷⁶⁾ factorial RCT, lumbar spine trabecular vBMD significantly improved. Trabecular bone adaptations were also reported in a high-intensity resistance and impact exercise trial conducted by Harding and colleagues⁽¹⁰⁴⁾ in older men with lower than average aBMD, whereby pQCT-assessed total vBMD, area, and trabecular area at the distal tibia were significantly maintained in the exercise group, but this study was excluded from this review because the control group was not randomized.

Limitations

Our findings should be considered in the context of limitations of each individual study included. Many trials were powered to detect changes in aBMD or physical function rather than bone structural variables, which in some cases may require larger sample sizes. For example, the study by Daly and colleagues⁽³⁸⁾ recruited 365 boys, which only provided 53% statistical power to detect a 3% between-group difference for the change in cortical area. In comparison, sample sizes of <60 can yield an 80% to 95% power to detect a 1% to 2% difference for the change in femoral neck aBMD.^(77,105) Some studies also chose a subset of the original participants for 3D imaging, further decreasing statistical power and potentially causing biases to randomization. Because of the lack of standardization of ROI, these results were broadly classified into the distal and mid/proximal regions to improve statistical power, but this led to the elimination of one set of results for studies that reported two ROIs within the distal or mid/proximal regions. We also included cluster RCTs in our review, which may not have randomized factors such as socioeconomic status and ethnic background, but these were common because of their lower costs and potentially greater protocol compliance when incorporating exercise into school activities. Almost all studies in children included multiple pubertal stages (except for two studies^(40,48)), and there were insufficient results reported separately for sex and pubertal stages for meta-analyses. Our classification of moderate- to high-impact exercise was limited by the lack of GRF measurement in some studies, and the use of exercise protocols descriptions in our decisions may not account for the different osteogenic thresholds across populations. Regardless, excluding these studies without GRF measures did not significantly change our results (data not shown). We did not exclude bone outcomes that were not specific to the bone loaded in the intervention, and some studies incorporated upper-limb resistance training,^(54,78,80) which may limit our ability to identify site-specific effects of impact exercise. Nonetheless, the studies contributing to our findings at the radius described exercises contributing to impact at the upper limb. Our analyses utilized percentage changes in bone parameters to describe the proportion of change, but this may not reflect the actual magnitude of change and may be

influenced by bone status at baseline.⁽⁹⁰⁾ Interpretation of our sensitivity analyses was based on a less conservative statistical approach that provides more statistical power than the more conservative approach, so these findings should be interpreted with caution. Additionally, effect sizes were small, and as most studies did not report the long-term precision error of specific bone parameters, it is difficult to ascertain if these changes were true or clinically meaningful.

This systematic review and meta-analysis investigated the effects of moderate- to high-impact exercise on bone structure and vBMD. Notably, impact exercise appears to support improvements in the trabecular compartment for postmenopausal women. However, we are unable to conclusively determine sex-, age-, and skeletal site-specific effects of impact exercise because of limitations in statistical power and heterogeneous protocols. Additional high-quality RCTs including different age and sex groups, as well as analyses for these distinct subgroups, are required to explore the potential benefits of adjunct therapies and identify optimal exercise protocols for improving bone health across the lifespan.

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Author Contributions

Carrie-Anne Ng: Conceptualization; methodology; formal analysis; investigation; writing – original draft; writing – review and editing; data curation; visualization. **Anoohya Gandham:** Methodology; validation; investigation; data curation; writing – review and editing. **Jakub Mesinovic:** Methodology; writing – review and editing; validation; data curation; investigation. **Patrick J Owen:** Methodology; investigation; writing – review and editing; visualization; formal analysis. **Peter R Ebeling:** Supervision; writing – review and editing. **David Scott:** Conceptualization; supervision; writing – review and editing.

Peer Review

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Disclosures

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