Osteoporos Int. Author manuscript; available in PMC 2017 January 11.

Published in final edited form as:

Osteoporos Int. 2010 December ; 21(12): 1969–1980. doi:10.1007/s00198-010-1228-z.

Effect of whole-body vibration on BMD: a systematic review and meta-analysis

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Abstract

Summary—Our systematic review and meta-analysis of randomized controlled trials (RCTs) examining whole-body vibration (WBV) effect on bone mineral density (BMD) found significant but small improvements in hip areal BMD (aBMD) in postmenopausal women and in tibia and spine volumetric BMD in children/adolescents, but not in other BMD measurements in postmenopausal women and young adults.

Introduction—Animal experiments report anabolic bone changes in response to WBV, but data in humans are limited. Our objective is to conduct a systematic review and meta-analysis of RCTs examining WBV effect on BMD.

Methods—Eligible RCTs included randomized or quasi-randomized trials, with follow-up of ≥6 months, examining WBV effects on BMD in ambulatory individuals without secondary causes of osteoporosis. The weighted mean differences between WBV and control groups in absolute pre-

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Conflicts of interest None.

post change in spine and hip aBMD, and in spine and tibia trabecular volumetric BMD (vBMD) were calculated.

Results—Eight RCTs in postmenopausal women (five RCTs), young adults (one RCT), and children and adolescents (two RCTs) were included. The regimens were heterogeneous, study durations were relatively short, and available data was mostly per-protocol. In postmenopausal women, WBV was found to significantly increase hip aBMD (0.015 g cm^{-2}; 95% confidence interval (CI), 0.008–0.022; n=131) versus controls, but not spine aBMD (n=181) or tibia trabecular vBMD (n=29). In young adults, WBV did not increase spine or hip bone mineral content, or tibia trabecular vBMD (n=53). In children and adolescents, WBV significantly increased spine (6.2 mg cm^{-3}; 95% CI, 2.5–10.0; n=65) and tibia (14.2 mg cm^{-3}; 95% CI, 5.2–23.2; n=17) trabecular vBMD.

Conclusions—We found significant but small improvements in BMD in postmenopausal women and children and adolescents, but not in young adults. WBV is a promising new modality, but before recommendations can be made for clinical practice, large-scale long-term studies are needed to determine optimal magnitude, frequency, and duration.

Keywords

Bone mineral density; Meta-analysis; Quantitative computed tomography; Whole-body vibration

Introduction

Whole-body vibration (WBV) has received much attention as a potential antiosteoporotic intervention in recent years [1, 2]. In experimental animal models, WBV was found to lead to anabolic bone changes [3–11]. Based on these data and the availability of many different WBV platforms in North America and Europe, optimistic claims that these benefits may translate to humans have been made within the scientific community [12] and in the media [13]. Such claims quickly proliferated to today's information savvy general population [14] and has left many clinicians and patients wondering about the role of WBV in osteoporosis prevention and/or treatment.

The intervention involves an individual standing on a vibrating platform. Through ground-based vertical accelerations starting at the plantar surface of the feet, the mechanical vibration is transmitted through the weight-bearing muscles and bones [15, 16]. The intensity of WBV is defined by its frequency (hertz) and magnitude, where magnitude is expressed as vertical acceleration (g; 1g= 9.8 m/s^2 acceleration due to gravity) or vertical displacement (millimeters). A hypothesized mechanism through which WBV is believed to exert its anabolic effects on the skeleton is via activation of the musculature, which results in mechanotransduction of vibration strains within the bone [2, 17]. Another hypothesis is that these high frequencies but low-magnitude WBV signals become amplified within the bone tissue by stress-generated fluid flow, and thereby activate bone cells which act as mechanosensors [2, 17].

In spite of the plausible physiological mechanism and the promising results obtained in experimental animal models, effects of WBV on the human skeleton remain uncertain.

Although different reviews have attempted to summarize the existing body of clinical evidence, none of them has performed a systematic evaluation [1, 2, 18]. Therefore, to more objectively advance our knowledge of the role of WBV in clinical practice, we conducted a systematic review and a meta-analysis of WBV effect on bone mineral density (BMD) in humans.

Methods

We followed the procedures for conducting systematic reviews as defined by the Cochrane Collaboration [19] and reporting guidelines of the QUOROM statement [20]. Data sources, study selection, data extraction, and quantitative data synthesis were specified a priori. Study selection and data extraction were conducted independently by two authors (LS and SMHA) using the same data forms, and disagreements were resolved by consensus. Subgroup and sensitivity analyses were modified post hoc due to the small number of eligible randomized controlled trials (RCTs).

Data sources

One reviewer (LS) performed a search strategy, screened the titles and abstracts, and identified references potentially appropriate for inclusion. With assistance from an experienced research librarian, a broad search strategy was performed without language restriction, from the earliest available date, using relevant electronic databases (MEDLINE, EMBASE, Cochrane, CINAHL, SportsDiscus, ProQuest Dissertations, and Theses Canada Portal). The following medical subject headings terms were used: (*vibration*, *mechanical stress*, *physical stress*, *physical activity*, *or weight-bearing*) and (*bone and bones*, *bone density*, *or muscles*) and (*clinical trial*, *meta-analysis*, *or multicenter study*). Finally, we performed a hand search of bibliographies of the publications that were retrieved. Unpublished trials were searched using clinical trials registries (http://ClinicalTrials.gov and http://controlled-trials.com) and by enquiring experts in the area of WBV.

Study selection

We included randomized and quasi-randomized trials examining the effects of WBV on BMD in humans, with a minimum follow-up period of 6 months, as it takes six or more months for BMD to show a significant response. Eligible study populations were not restricted based on age, sex, race, or physical activity levels. Blinding of participants and study staff was not an eligibility requirement. WBV therapy was defined as mechanical vibration, performed with a straight body (standing or lying), with no restriction on the frequency (hertz), amplitude (millimeters), magnitude (vibration acceleration due to gravity, *g*), and cumulative dose (total number of minutes per study duration; most WBV platforms have a sensory device that monitors the adherence) of WBV. Localized mechanical vibration (e.g., vibration pads) or ultrasound and electrical stimuli were not recognized as WBV. Vibration signals that were not received through a completely straight body (e.g., sitting on a vibrating chair) were also excluded. Acceptable control interventions types included no treatment, sham vibration (audible sound with no mechanical vibration), and exercise interventions. Trials which included participants with secondary causes of osteoporosis (e.g., glucocorticoids therapy or hemodialysis) or those with causes for non-ambulatory status

(e.g., paraplegics) were also excluded. We also excluded RCTs in which participants were taking antiosteoporotic medications if they were *not* distributed equally between study arms, but we included trials in which antiosteoporotic co-interventions were matched between trial arms. Finally, trials with more than two study arms were included in the analysis without eliminating any of the arms; relevant study arms were combined to create a single pair-wise comparison as recommended in the Cochrane Handbook for Systematic Reviews of Interventions version 5.0.1 [19].

Data extraction

The extracted data included any relevant information regarding the trials' characteristics, BMD outcomes, and methodological quality. Per-protocol and not intention-to-treat (ITT) data were preferentially extracted for primary analysis. We chose per-protocol over ITT data because the majority of the included RCTs reported per-protocol and not ITT analysis. Also, adherence to prescribed cumulative dose of WBV ranged considerably between the included trials. Hence, using per-protocol data allowed us to minimize the clinical heterogeneity between trials, as well as enabled us to better examine the effectiveness of WBV due to higher overall adherence. A major drawback of per-protocol analysis is that it produces attrition bias, reduces the methodological quality of the results, and thus increases the type I error.

Data was extracted separately for postmenopausal women, young adults, and children and adolescents, so that separate analyses can be performed for each population. Pooling these populations would introduce unwanted clinical heterogeneity, because physiologically different bone metabolic processes occur in these populations. In children and adolescents, bone is being accrued, and their BMD typically increases over time and in response to effective therapies [21]. In young adults, BMD generally plateaus and would be expected to also increase in response to effective interventions [21]. Finally, postmenopausal women typically lose BMD over time and would be expected to experience a reduction in the decline of BMD in response an effective therapy [22].

Methodological quality was assessed in terms of the different components that make up trial quality as opposed to using the currently available quality scales, due to the advantages that this approach offers in comparison to the scale approach [23]. As such, we identified the presence of the following types of study bias via a standardized but *not validated* checklist (see "Appendix"): selection bias (lack of true randomization and concealment of allocation), performance bias (lack of matching based on relevant baseline characteristics), detection bias (lack of blinding of outcome assessors), and/or attrition bias (lack of ITT data).

Sensitivity and subgroup analyses

Per-protocol data were replaced with ITT data for those trials that made both types of data available, in order to examine whether the different analytic approach influenced our primary results. The influence of methodological quality on the robustness of the results was assessed by excluding trial(s) with the greatest number of biases. For the areal BMD (aBMD) analysis of the hip, trials that obtained the femoral neck measurements were analyzed separately from those that obtained the total hip measurements.

We performed separate subgroup analyses for each population type (postmenopausal women, young adults, and children and adolescents). A priori specified sources of clinical heterogeneity were analyzed in the following subgroup analyses: (1) control intervention type (no treatment or sham vibration versus exercise interventions; excluded RCTs where bone medications were used as a co-intervention), (2) magnitude of WBV (low magnitude [<1*g*] versus high magnitude [≥1 *g*]), and (3) actual cumulative dose of WBV (at or below median versus above median).

Quantitative data synthesis

The effect measure was a weighted mean difference between the WBV and control groups (WBV group minus control group) in absolute pre-post change in aBMD in the spine (L1–L4 or L2–L4) and hip (femoral neck or total hip), as measured by dual energy X-ray absorptiometry (DXA), and in the trabecular volumetric BMD (vBMDt) in the spine (lumbar) and tibia (distal or proximal), as measured by quantitative computed tomography. Values were considered statistically significant if $p<0.05$. Fixed effect models were reported, unless statistically significant heterogeneity was found, in which case, random effects models were used. The Cochrane Q test for heterogeneity was performed and considered statistically significant if $p \leq 0.10$. Heterogeneity was also quantified with the I^2 statistic, where 0–40%, 30–60%, 50–90%, and 75–100% is generally defined as unimportant, moderate, substantial, and considerable heterogeneity, respectively [19]. All analyses were performed using RevMan version 5.0.16. For included trials with missing information, two reviewers (LS and AMC) contacted the original authors. Where the original data were no longer available, estimations and/or statistical inferences were used to obtain the BMD outcomes (see "Appendix"); also, estimations were made to determine the cumulative dose of WBV based on the duration per session and number of days used.

Results

Study characteristics

From 1,302 potentially relevant titles and abstracts identified, eight RCTs were deemed eligible (Fig. 1 [24–31]). The majority of identified studies were excluded because they were not RCTs and/or the experimental treatment did not fit our criteria of WBV. The remaining RCTs were then primarily excluded because they did not obtain BMD measurements and/or their study duration was too short. The RCTs included in our systematic review involved the following study population types: postmenopausal women (*n*=210, five RCTs, [25–28, 30]), young adults (*n*=53, one RCT [29]), and children and adolescents (*n*=65, two RCTs [24, 31]). All included trials were of relatively short duration (6–12 months) and small sample size (17 to 70 participants) and included at least one type of study bias (Table 1). The control intervention types included no treatment, sham vibration, and exercise regimens. The WBV regimens varied between the included trials in terms of the WBV frequency and magnitude and the cumulative dose (Table 1). Four studies ensured adequate calcium intake either through diet [26, 29] or supplementation [24, 28], but only one trial also ensured adequate vitamin D intake [28]. Two RCTs measured dietary calcium but not vitamin D intake at baseline, but did not report whether the average intake was adequate and/or matched between the study groups [25, 27].

Postmenopausal women

There were five trials in postmenopausal women: four using high-magnitude WBV [25, 26, 28, 30] and one using low-magnitude WBV [27]. Study participants included women with osteopenia and osteoporosis, aged 47–88 years, of Caucasian and Southeast Asian origin, and with low to moderate physical activity levels (Table 1). Most participants did not take bone medication as a co-intervention, except for one RCT in which 50 osteoporotic Japanese women received the same alendronate treatment in both the WBV and the control arms [26]. In another trial, eight out of 29 women were on hormone replacement therapy and were matched between the trial arms [28]. Where two control arms were included [30], we combined them in the primary analysis to create a single pair-wise comparison (n=45) and then entered them separately in a subgroup analysis of the control intervention type (no treatment, n=23; exercise, n=22). Four RCTs obtained spine aBMD measurements (L1–L4, two RCTs [26, 30]; L2–L4, two RCTs [25, 27]), three hip aBMD (femoral neck, two RCTs [25, 27]; total hip, one RCT [30]), and one tibia vBMDt measurements (Table 2 [28]).

The difference in the hip aBMD change between the WBV and control groups was statistically significant (0.015 g cm^{-2} [95% confidence interval (CI), 0.008 to 0.022] $p<$ 0.0001, n=131; Fig. 2). No significant effects of WBV on spine aBMD (−0.003 g cm^{-2} [95% CI, −0.012 to 0.005] p= 0.44, n=181; Fig. 2) and tibia vBMDt (−2.2 mg cm^{-3} [95% CI, −10.0 to 5.7] p=0.58, n=29) were found.

When we analyzed BMD outcomes according to ITT analysis, there was no effect of WBV on hip aBMD (0.014 g cm^{-2} [95% CI, −0.003 to 0.031] p=0.12, n=168; Fig. 3) and spine aBMD (−0.003 g cm^{-2} [95% CI, −0.011 to 0.005] p=0.43, n=218; Fig. 3). When we excluded the lowest quality trial [25], our results remained the same as in the primary analysis (difference in hip aBMD, 0.014 g cm^{-2} [95% CI, 0.006–0.021] p=0.0002, n=103; difference in spine aBMD, −0.003 g cm^{-2} [95% CI, −0.012 to 0.005] p= 0.42, n=153; Fig. 3). Finally, after separating the hip aBMD measurements into total hip (one RCT [30]) and femoral neck (two RCTs [25, 27]) aBMDs, the results remained significant for the total hip (0.014 g cm^{-2} [95% CI, 0.007–0.021] p=0.0002, n=70) but not for the femoral neck (0.023 g cm^{-2} [95% CI, −0.009 to 0.055] p=0.17, n=61).

In all subgroup analyses of spine aBMD, our results remained nonsignificant. In a subgroup analysis of hip aBMD based on different control intervention types, results remained statistically significant when WBV was compared to no treatment or sham vibration (0.013 g cm^{-2} [95% CI, 0.005–0.021] p=0.001, n=81; Fig. 4), but became nonsignificant when WBV was compared to exercise interventions (0.023 g cm^{-2} [95% CI, −0.003 to 0.048] p=0.08, n=75; Fig. 4). Hip aBMD subgroup analyses of the magnitude and actual cumulative dose involved the same division of trials. The aBMD results were neither significant for RCTs examining WBV at $\geq 1g$ magnitude and at or below median cumulative dose (0.023 g cm^{-2} [95% CI, −0.001 to 0.047] p=0.06, n=98; Fig. 4) nor for a trial examining WBV at $<1g$ magnitude and above median cumulative dose (0.007 g cm^{-2} [95% CI, −0.019 to 0.033] p=0.60, n=33; Fig. 4).

Children and adolescents

There were two trials in children and adolescents [24, 31]. Both used low-magnitude WBV. Study participants included ambulatory boys and girls aged 4–20 years with limited mobility due to disabled conditions [31] and healthy girls aged 15–20 years with low BMD and a history of at least one fracture (Table 1 [24]). As part of their per-protocol analysis, one trial [24] excluded the lowest adherence quartile of WBV participants (n=6) from the WBV vibration group (n=18) and included it in the control group (n=30). A significant difference in the tibia vBMDt was observed between the control and WBV groups (14.2 mg cm^{-3} [95% CI, 5.2–23.2] p=0.002, n=17) in one RCT [31]. A significant difference in the spine vBMDt (L2 [31] and L1–L3 [24]) was also found (6.2 mg cm^{-3} [95% CI, 2.5–10.0] p=0.001, n=65; Fig. 5). In addition to per-protocol data, one trial also reported the ITT data which involved the original allocation of WBV (n=24) and control (n=24) participants in their respective arms [24]. This allowed us to perform a sensitivity analysis of the influence of different analytical approaches, in which the spine vBMDt results remained significant (4.2 mg cm^{-3} [95% CI, 0.4–8.1] p= 0.03, n=65; Fig. 5). No additional sensitivity analyses were performed, because the methodological quality was similar, and no hip aBMD outcomes were reported in the two included RCTs. Finally, no subgroup analyses were performed due to insufficient number of eligible trials.

Young adults

There is only one trial using high-magnitude WBV in young adults [29]. Study participants were healthy, nonathletic European men and women aged 19 to 38 (Table 1). Bone mineral content (BMC, in grams) versus aBMD was reported in one eligible trial, and aBMD was not available to the original authors [29]. However, since bone size would not be expected to change in a young adult population over the study duration of 8 months, BMC changes were included in our analysis to approximate aBMD changes (Table 2). No significant between-group differences in the change in L2–L4 BMC (0.428 g [95% CI, −1.291 to 2.147], p=0.63, n= 53), femoral neck BMC (0.004 g [95% CI, −0.120 to 0.128] p=0.95, n=53), and tibia vBMDt (−0.7 mg cm^{-3} [95% CI, −5.7 to 4.3] p=0.78, n=53) were observed [29]. No subgroup or sensitivity analyses were performed due to insufficient number of eligible trials.

Adverse events

Only one included RCT, examining postmenopausal women, reported non-serious adverse events (AEs) that were possibly caused or exacerbated by WBV [28]. Lower leg itching and erythema was reported in six of 17 participants receiving high-magnitude WBV, which disappeared after the first three vibration sessions [28]. Possible knee pain exacerbation was also reported in two overweight WBV participants with pre-existing knee osteoarthritis, which subsided after a few days of rest [28]. Based on an 8-month follow-up magnetic resonance imaging examination, the trial which examined young adults did not observe any changes in the articular cartilage or bone tissue of the ankle joint [29]. The remaining trials reported no AEs that could be possibly related to WBV use [24–27, 29–31]. Positive health-related outcomes were reported in one trial which examined 50 Japanese postmenopausal, osteoporotic women receiving alendronate therapy [26]. As part of the trial's inclusion criteria, all of the included participants were experiencing chronic back pain at baseline, as

evaluated by face scale score [26]. After 12 months of high-magnitude WBV, most of the treatment-arm participants "felt refreshed in the leg and back muscles" immediately after the vibration session. Further, the chronic back pain of the WBV participants was significantly less when compared to the controls [26].

Discussion

Our systematic evaluation of WBV found statistically significant improvement in hip aBMD in postmenopausal women and in spine and tibia vBMDt in children and adolescents. No significant effects were found on spine aBMD and tibia vBMDt in postmenopausal women and on BMC and vBMDt in young adults. Although statistically significant, the effect size in postmenopausal women was small. The between-group difference in the hip aBMD change of 0.015 g cm^{-2} is comparable to the effect size expected in response to adequate calcium and vitamin D supplementation [32]. Further, this magnitude is approximately one half of the least significant change in hip aBMD as detectable by current DXA instruments in the clinical settings [33].

Compared to postmenopausal women, the effect size observed in children and adolescents was greater. The magnitude of the effect for vBMDt in children and adolescents was 14.2 mg cm^{-3} in the tibia and 6.2 mg cm^{-3} in the spine. An RCT examining the effect of adequate calcium supplementation in normal children found a between-group difference of approximately 6.0 mg cm^{-3} in the tibia vBMDt [34]. This comparably larger effect size existed even though children and adolescents were relatively less adherent to WBV than the other two populations (Table 1). Therefore, it would seem that a growing skeleton in children and adolescents with a compromised bone mass is more sensitive to WBV than that of postmenopausal women or young adults.

There may be differential effects of WBV on different bone sites, because of the variability in the transmission of WBV signals. The transmissibility of WBV signals varies significantly from one anatomical site to another due to the nonlinearities of the musculoskeletal system (e.g., joint angle and soft tissue distribution) and the differences in body positions (e.g., bent knees versus straight knees) [15, 16]. This may explain the discrepancy between the hip versus spine aBMD findings in postmenopausal women. However, the discrepancy between the hip aBMD versus tibia vBMDt results in postmenopausal women was probably due to inadequate sample size, leading to inadequate statistical power in the vBMDt analysis.

In contrast to postmenopausal women and children and adolescents, we did not find a significant effect of WBV in healthy young adults. Some clinical [27] and experimental [3, 35] evidence suggests that there is an inverse relationship between the skeleton's sensitivity to WBV and the initial BMD. Young adults may be less sensitive to WBV, because their baseline BMDs are generally higher than those in postmenopausal women and children and adolescents. Also, young adults' skeleton is less metabolically active than children's and adolescents', and thus may be less sensitive to mechanical stimuli such as WBV. Another plausible reason for not observing a significant effect in young adults is insufficient sample size and statistical power in this population.

There are current controversies as to the optimal frequency and magnitude of WBV. According to Wolff's law of bone remodeling, only large-magnitude strains (such as those arising from high-intensity impact activities) are capable of new bone formation, and the greater the magnitude, the greater the effect [8, 36]. For WBV, this conventional premise was challenged by the experimental animal models, which showed that exposures to low-magnitude but high-frequency vibration can also enhance bone accrual [3–11]. These high-frequency, low-magnitude vibration signals are believed to piezoelectrically, or by stress-generated fluid flow, stimulate bone cells [2, 17], with the bone anabolic effect increasing with increasing frequency [27, 31]. We were unable to examine the differential effect of various frequencies (12–90 Hz) because of the small number of RCTs included. However, we grouped the magnitudes of WBV into two relevant categories ($<1g$ and $\geq 1g$) for hip aBMD analysis and found no significant differences (Fig. 4).

There are several limitations to our study, including the small number of RCTs available, and the small sample sizes, short durations, and methodological issues of the included trials. The small number of RCTs was especially true for the adult (one RCT, n=53 [29]) and children and adolescent (two RCTs, n=65 [24, 31]) populations in comparison to the postmenopausal women (five RCTs, n= 210 [25–28, 30]). At least one study bias was present in each trial, and calcium and vitamin D intakes may have been insufficient in study subjects. Our primary analysis was not according to ITT, because of the lack of ITT data in the original trials. This may bias our results to show more favorable outcomes.

In conclusion, this is the first systematic review and meta-analysis of the effect of WBV on BMD in humans. We found statistically significant but clinically small effects in postmenopausal women, and moderate effects in children and adolescents, but not in young adults. We also found WBV to be well tolerated and safe. While WBV is a promising new modality for improving bone health in certain populations, larger and well-designed RCTs are needed before recommendations can be made for clinical practice. In addition to examining safety and efficacy of WBV on BMD, these future RCTs should also compare different frequencies, magnitudes, and cumulative doses of WBV, as well as examine other bone quality parameters as measured by newer techniques such as high resolution peripheral quantitative computed tomography. Whether WBV can exert effects in addition to other simultaneous bone therapies such as calcium and vitamin D supplementation, exercise, and pharmacological interventions should also be further examined.

Acknowledgments

L. Slatkovska is supported by a Canadian Institutes of Health Research/Ontario Women's Health Council doctoral research award; Dr. Shabbir M. H. Alibhai is supported by a Research Scientist Award from the National Cancer Institute of Canada; Dr. AM Cheung is supported by a Canadian Institutes of Health Research/Ontario Women's Health Council Mid-Career Scientist Award. This study was in part supported by the Ontario Premier's Research Excellence award presented to Dr. Angela M. Cheung for innovations in postmenopausal osteoporosis.

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Appendix

Study bias determination

The methodological quality assessment involved identifying the presence of different types of study biases based on the information provided in the included trials (i.e., as published or as reported via email communications). The following types of study biases were identified using an *invalidated* checklist:

☐ Selection bias present (check as present if at least one "no" or "unclear" is present)			
Yes	No	Unclear	True r*andom* study-arm allocation performed
Yes	No	Unclear	*Concealed* study-arm allocation performed
☐ Performance bias (check as present if at least one "no" or "unclear" is present)			
Groups were matched baseline based on minor confounders			
Yes	No	Unclear	Calcium intakes
Yes	No	Unclear	Age at baseline
Yes	No	Unclear	Menstrual status at baseline
Yes	No	Unclear	BMD at baseline
Yes	No	Unclear	Body mass at baseline
☐ Detection bias present (check as present if at least one "no" or "unclear" is present)			
Yes	No	Unclear	Blinding of those assessing BMD outcomes
☐ Attrition bias present (check as present if at least one "no" or "unclear" is present)			
Yes	No	Unclear	Only intention-to-treat analysis performed

Handling of BMD outcomes

Contacting the original authors

We contacted the original authors of all of the included trials to obtain missing information, and we obtained 100% response rate. The mean absolute change in BMD was not reported in a number of original publications [26–30]. After contacting all of the original authors, Iwamoto et al. [26] and Verschueren et al. [30] provided us with the missing mean absolute change in BMD. However, since the original data were no longer available to Rubin et al. [27], Russo et al. [28], and Torvinen et al. [29], some estimations and statistical manipulations were performed to obtain the correct BMD outcome.

Estimations

Where BMD data were reported only as the baseline and final means [28, 29], the mean absolute change in BMD was obtained by subtracting the final from the baseline mean. The standard deviation (SD) corresponding to the absolute BMD change was estimated using the Follmann's method as described in the Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1 [19]. The correlation coefficient value (r) of 0.95 was used in all Follmann's calculations. Based on the 12-month follow-up data collected in our laboratory, we obtained r values ranging from 0.94 to 0.97 for the total hip, femoral neck, and L1–L4 aBMD change in 440 postmenopausal women receiving either placebo or vitamin K

treatment [38]. Prior meta-analysis utilized an even higher correlation coefficient value (r=0.99) in their Follmann's calculations [39]. Therefore, an r of 0.95 seemed to be a conservative value to use in our calculations.

A trial of Rubin et al. [27] required special attention in the determination of the aBMD outcomes. Neither the absolute mean change in aBMD nor the final aBMD was available to us. Instead, baseline aBMD was reported for 56 participants with all follow-up data out of the 70 originally enrolled participants. Also, the mean percent change in aBMD for the ITT (n=70) and per-protocol data was reported. The mean percent change for the per-protocol data was only reported for different adherence groups but not for the 56 participants with the baseline aBMD. The adherence group with the largest sample size (n=33) consisted of at least 60% adherent participants. Therefore, for our primary analysis of the per-protocol data, we utilized the baseline aBMD data (n=56) and the percent change aBMD data (n= 33) to estimate an absolute change in BMD. Alternatively, for our sensitivity analysis of the ITT data, we utilized the baseline BMD data (n=56) and the percent change aBMD data (n=70) to estimate an absolute change in aBMD. Finally, the SD corresponding to the mean absolute change in aBMD was imputed from another trial [25] for each study group (i.e., control and vibration) and each measurement site (i.e., L2–L4 and femoral neck). This trial [25] was used, because it is the most similar to the Rubin's et al. [27] trial in terms of its study sample size, population type, and measurement type.

Other statistical manipulations

When CIs [25] or standard errors [28] were reported only, statistical formulas were used to convert these measurements to SDs. When BMD data for more than one arm were pooled into one arm [30], the mean absolute change was obtained using the "weighted mean" formula, and the corresponding SD was obtained using the "pooled or weighted SD" formula. When raw data were provided in the original publication [31] or in our email communication with the original authors [26], appropriate descriptive statistics were used to obtain the mean absolute change and the corresponding SD.

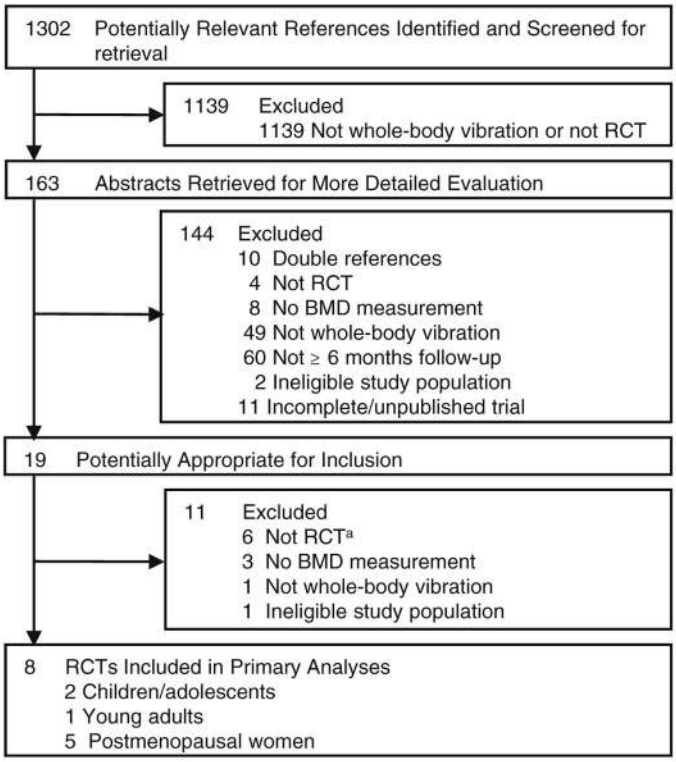

Fig. 1.

QUOROM flow diagram showing systematic literature search summary. [a]One study, "potentially appropriate for inclusion," was later excluded because it was not a true randomized controlled trial. This study examined postmenopausal Chinese women with osteoporosis who received either whole-body vibration or no treatment [37]. After contacting the original authors, it was confirmed that the group allocation did not involve randomization or quasi-randomization but instead it involved a convenience-based assignment

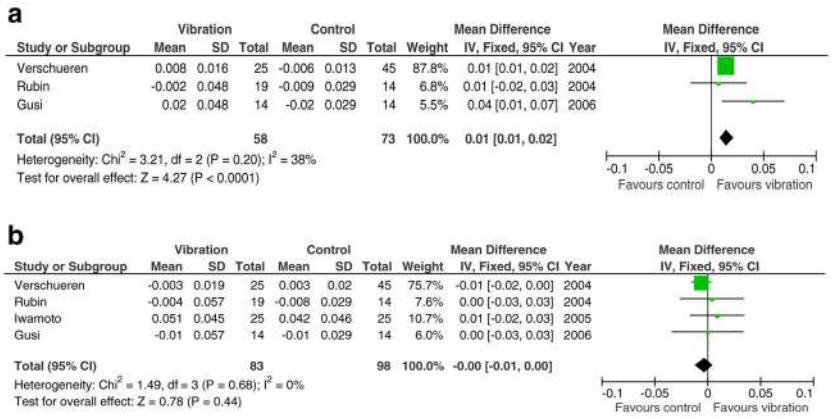

Fig. 2.

Primary analyses of whole-body vibration effect on bone mineral density in postmenopausal women. **a** Hip areal bone mineral density (g cm^{-2}). **b** Spine areal bone mineral density (g cm^{-2}). Forest plots show the weighted mean difference between the whole-body vibration and the control groups in absolute pre-post change. *Squares* and *diamonds* represent the effect sizes for each trial and for all trials, respectively. *Lines crossing the squares* represent confidence intervals. When the *line crossing the square* does not touch the *middle vertical line*, the trial results are statistically significant. When the *black diamond* does not touch the *middle vertical line*, the pooled results are statistically significant. Trials were listed by year of publication starting with the earliest trial. Note: The RevMan 5.0.16 software reported all bone mineral densities in terms of two decimal places in the forest plots. In the text and tables, areal bone mineral densities and trabecular volumetric bone mineral densities are reported in terms of three and one decimal place(s), respectively

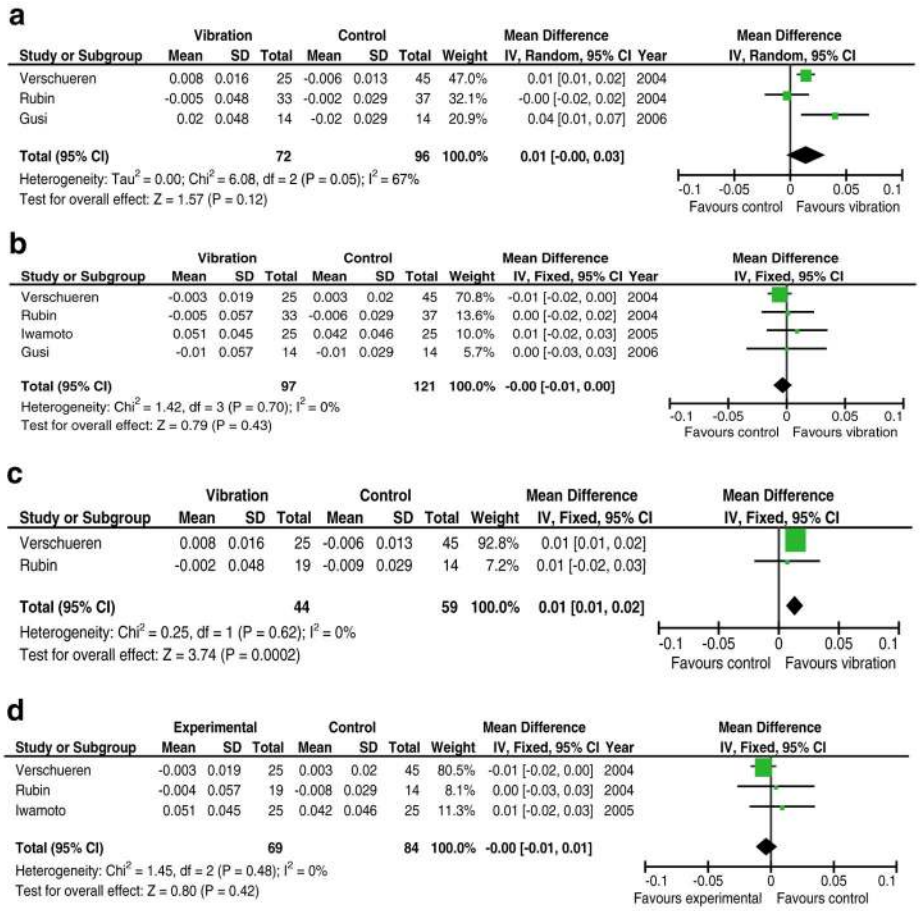

Fig. 3.

Sensitivity analyses of whole-body vibration effect on bone mineral density in post-menopausal women. **a** Hip areal bone mineral density (g cm^{-2})—intention-to-treat data included. **b** Spine areal bone mineral density (g cm^{-2})—intention-to-treat data included. **c** Hip areal bone mineral density (g cm^{-2})—trial with largest number of bias excluded. **d** Spine areal bone mineral density (g cm^{-2})—trial with largest number of bias excluded. Note: Refer to Fig. 2 for further legends

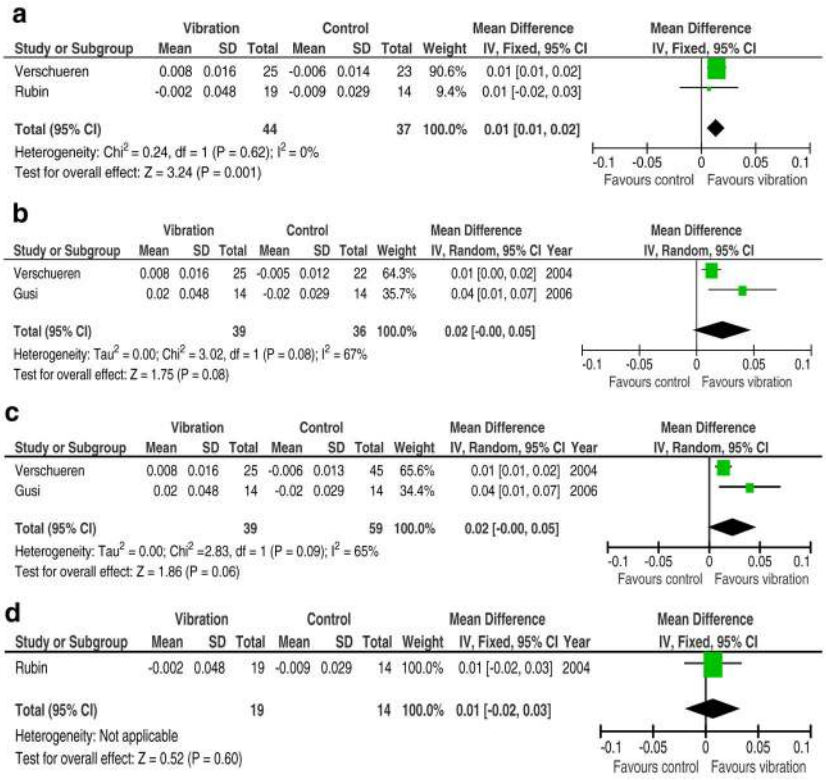

Fig. 4.

Subgroup analyses of whole-body vibration effect on hip areal bone mineral density (g cm $^{-2}$) in postmenopausal women. **a** Sham whole-body vibration or no treatment control groups without bone medications used as a co-intervention. **b** Exercise intervention control groups. **c** High magnitude and at/below median cumulative dose of whole-body vibration. **d** Low magnitude and above median cumulative dose of whole-body vibration. Note: Refer to Fig. 2 for further legends

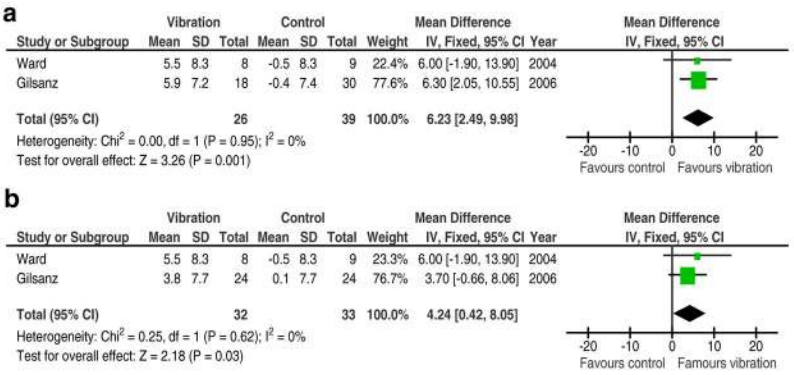

Fig. 5.

Primary (**a**) and sensitivity (**b**) analyses of whole-body vibration effect on the spine trabecular volumetric bone mineral density (mg cm^{-3}) in children and adolescents. Note: Refer to Fig. 2 for further legends

Table 1

Characteristics of randomized controlled trials included in the systematic review

Source	No. of participants enrolled	No. of participants analyzed	Age (range, years or mean ± SD)	Participants	Control intervention	Follow-up (months)	WBV frequency (hertz)	WBV magnitude (*g*)	Prescribed mean cumulative volume (minutes)	Actual mean cumulative volume (minutes)[a]	Calcium requirements	Vitamin D requirements	Study bias
Postmenopausal women													
Russo et al. 2003 [28]	33	29	61±7	Healthy European women	No treatment	6	12–28	≥1	240	200	1,000 mg supplement	0.25 μg supplement	S, D, A
Verschueren et al. 2004 [30]	89	70	58–74	Healthy European women	No treatment and resistance training	6	35–40	≥1	1134	1,021	None	None	S, A
Rubin et al. 2004 [27]	70	33	47–64	Healthy North American women	Sham vibration	12	30	<1	7,300	5,840	Measured intake	None	P, A
Iwamoto et al. 2005 [26]	50	50	55–88	Osteoporotic Japanese women on alendronate (5 mg per day)	No treatment	12	20	≥1	208	208	>800 mg through diet	None	S
Gusi et al. 2006 [25]	36	28	66±5	Healthy European women	Walking	8	12.6	≥1	549	494	Measured intake	Measured intake	S, P, A
Young adults													
Torvinen et al. 2003 [29]	56	53	19–38	Healthy nonathletic European men and women	No treatment	8	25–45	≥1	354	330	>800 mg through diet	None	S, A
Children/adolescents													
Ward et al. 2004 [31]	20	17	4–19	Ambulatory North American boys and girls with limited mobility due to disabled conditions	Sham vibration	6	90	<1	1,300	568	None	None	P, A
Gilsanz et al. 2006 [24]	48	48	15–20	Healthy North American Caucasian girls with low BMD	No treatment	12	30	<1	3,650	2,124	500 mg supplement	None	S, A

WBV whole-body vibration, *SD* standard deviation, *g* acceleration due to gravity, *S* selection bias, *P* performance bias, *D* detection bias, *A* attrition bias

[a]Actual cumulative dose was derived from the mean percent adherence and the prescribed cumulative dose

Table 2

Bone mineral density data extracted for all analyses

Source	Data type available for extraction	Study group	No. participants extracted	Absolute pre-post change in BMD (mean ± SD)			
				Hip aBMD (g cm^{-2})	Spine aBMD (g cm^{-2})	Tibia vBMDt (mg cm^{-3})	Spine vBMDt (mg cm^{-3})
Postmenopausal women							
Russo et al. 2003 [28]	Per-protocol	Vibration	14			−3.5±12.9	
		Control	15			−1.3±7.9	
Verschueren et al. 2004 [30]	Per-protocol	Vibration	25	0.008±0.016[b]	−0.003±0.019		
		Control	45	−0.006±0.013	0.003±0.020		
Rubin et al. 2004 [27]	Per-protocol	Vibration	19	−0.002±0.048	−0.004±0.057		
		Control	14	−0.009±0.029	−0.008±0.029		
	(ITT)	Vibration	(33)	(−0.005±0.048)	(−0.005±0.057)		
		Control	(37)	(−0.002±0.029)	(−0.006±0.029)		
Iwamoto et al. 2005 [26]	ITT	Vibration	25		0.051±0.045		
		Control	25		0.042±0.046		
Gusi et al. 2006 [25]	Per-protocol	Vibration	14	0.020±0.048[b]	−0.010±0.057		
		Control	14	−0.020±0.029	−0.010±0.029		
Young adults							
Torvinen et al. 2003 [29]	Per-protocol	Vibration	27	0.033±0.219[a]	0.454±3.064[a]	4.2±8.3	
		Control	26	0.029±0.240[a]	0.026±3.312[a]	4.9±10.1	
Children/adolescents							
Ward et al. 2004 [31]	Per-protocol	Vibration	8			8.5±8.2[b]	5.5±8.3
		Control	9			−5.7±10.7	−0.5±8.3
Gilsanz et al. 2006 [24]	Per-protocol	Vibration	18				5.9±7.2[b]
		Control	30				−0.4±7.4
	(ITT)	Vibration	(24)				(3.8±7.7)
		Control	(24)				(0.1±7.7)

Brackets indicate intention-to-treat data that was used as part of the sensitivity analysis only

ITT intention-to-treat, *aBMD* areal BMD, *vBMDt* trabecular volumetric BMD, *SD* standard deviation

[a] aBMD change reported in bone mineral content units (grams)

[b] Significant effect of the whole-body vibration group compared to the control group, as reported in the original publication