Vibration Therapy to Prevent Bone Loss and Falls: Mechanisms and Efficacy

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Abstract A considerable volume of evidence has accumulated to suggest that whole-body vibration (WBV) may have a therapeutic role to play in the prevention of osteoporotic fracture, particularly for individuals who are unable to tolerate vigorous exercise interventions. There is moderate to strong evidence that WBV will prevent falls (likely due to enhanced neuromuscular function), but also some indication that the effects of WBV do not outstrip those of targeted exercise. Animal data indicates that WBV will also improve bone mass, including preventing loss due to hormone withdrawal, disuse and glucocorticoid exposure. Human trials, however, have produced equivocal outcomes for bone. Positive trends are apparent at the hip and spine, but shortcomings in study designs have limited statistical power. The mechanism of the vibration effect on bone tissue is likely to be mechanical coupling between an oscillating cell nucleus and the cytoskeleton. More robust dose-response human data are required before therapeutic guidelines can be developed.

Keywords Whole-body vibration · Osteoporosis · Neuromuscular function · Balance · Fracture

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Introduction

Why Vibration?

It is well recognised that the risk of osteoporotic fracture increases with age-related loss of bone mass [1]. In fact, for every standard deviation decrease in femoral neck bone mineral density (BMD), there is an almost threefold increased risk of hip fracture [1]. Of even greater significance, over 90 % of hip fractures occur as a direct result of a fall [2] which also increase with age, largely reflecting a deterioration in neuromuscular function [3]. Thus, preventing age-related loss of bone and enhancing lower extremity muscle strength and balance to decrease falls [4] are both vital strategies to reduce the risk of osteoporotic fracture.

Pharmacological interventions are the most recognised and accepted therapies for osteoporosis, by virtue of their ability to induce the most marked improvement in bone mass and to reduce fractures [5]. However, adoption is low, non-response and side effects are common and compliance after 1 year is very poor [6–9]. Furthermore, while anti-resorptive treatment has been associated with a 42 % overall reduced risk for hip fracture [10], only a 26 % reduction in rate of *recurrent* fractures has been observed [11]. As medications do not maintain or enhance muscle strength or balance [12], they offer no protection from falls. There is, therefore, a clear need to identify alternative treatments to drug therapy in order to address the growing burden of osteoporotic fractures in ageing populations.

Animal models have shown that exercises involving high magnitude loads are anabolic to bone. The translation from 'bench to bedside' has been somewhat disappointing however, as the response of the ageing human skeleton to exercise is often quite modest. The latter situation may be a function of both reduced capacity and inclination of the elderly to tolerate the requisite loading intensity for exercise benefits to be realised. A

less physically intense or passive source of mechanical stimulation of the skeleton would therefore be advantageous for those most at risk of osteoporotic fracture. For this reason, whole-body vibration (WBV), a low-magnitude but high-frequency form of mechanical stimulation, has been examined as a potential therapy to enhance bone mass and improve neuromuscular function.

What Exactly Is Whole Body Vibration?

It is difficult, if not impossible, to actively apply mechanical loads at very high frequency to the whole human body. To illustrate, the world 100-m sprint record holder Usain Bolt ran at a step frequency of only 4.49 Hz to clock a time of 9.58 s (Berlin 2009). Clearly then, vibration loads must be externally applied. For the 'whole body' to be stimulated, a person must stand on a floor-mounted vibrating plate. (As the upper extremity does not receive a weight bearing vibration, the *whole* body is not technically affected by the same stimulus.) WBV can be produced by the plate in a number of ways (e.g. Fig. 1): by alternate direction movements in a vertical plane, by alternating elevations of the right and left sides around a central axis or by a combination of movements in the horizontal, vertical and oblique planes (sometimes referred to as tri-planar vibration) [13]. Vertical vibration has been shown to transmit 85 % of a 0.2 g, 30 Hz vibration stimulus at the feet during standing to clinically relevant skeletal sites (hip and spine) [14]. Others have also demonstrated strong transmissibility of a broad range of vibration stimuli [15]. Some report considerable damping of the signal (reduced transmission) if joints are flexed rather than fully extended in standing [16], but others have observed the opposite effect in a semi-squat position [17].

Vibration intensity is best described in terms of acceleration, in g-forces. A g is calculated by dividing maximum acceleration by gravity ($a_{max}/9.81$ ms^{-2}); therefore, 1 g is equal to the acceleration of gravity. Acceleration can be modulated through the frequency (f) of plate movements per second (in Hz), or the amplitude (a) of plate movement (displacement of the plate from equilibrium, measured in mm), or both (Fig. 2). Increasing vibration amplitude most notably increases acceleration forces [17]. A vibration stimulus of <1 g is considered to be low intensity, whereas a stimulus if ≥1 g is considered high intensity.

There are now many WBV devices commercially available, producing a wide range of accelerations; from 0.3 g to more than 10 g. Depending on device, frequency and amplitude can be fixed by the manufacturer, or varied by adjusting a dial and/or foot placement (if the plate oscillates around a central fulcrum). Of concern, vibration intensity is frequently omitted from device specifications, as is the degree of change in intensity per unit adjustment on a control panel. As a consequence, it is likely that many devices operate at vibration intensities above the safety limits determined by the International Organisation for Standardisation (ISO 2631/3) (discussed below).
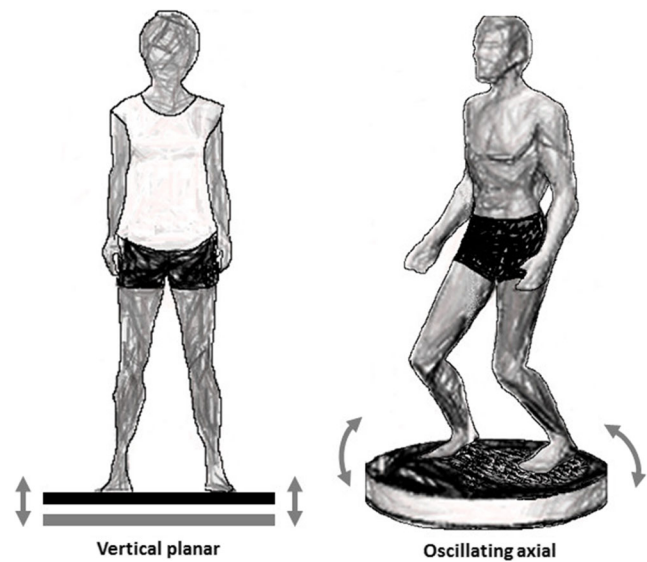
Fig. 1 Two methods to apply vibration: vertically and alternating side perturbations

Efficacy and Mechanisms

What Is the Evidence for Efficacy?

Bone Response

Animal Data A considerable volume of evidence from well-controlled animal studies is available to suggest a beneficial effect of vibration on bone. For example, decreased osteoclastic resorption [18] and improved tibial metaphyseal geometry
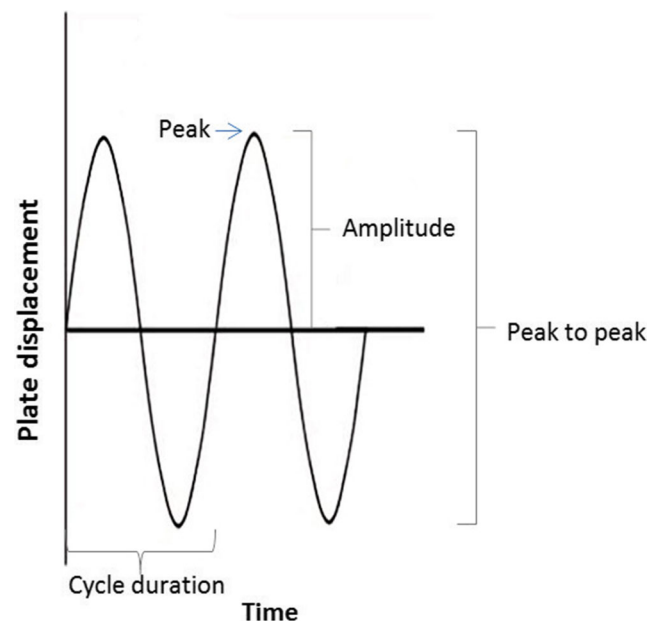

Fig. 2 Vibration parameters and terminology. Displacement can be described as amplitude (distance from plate equilibrium, in mm), or peak-to-peak distance (in mm), which, when combined with the sinusoidal cycle duration (frequency, in cycles per second, or Hz), can be described in terms of acceleration (g-force, ms^{-2})

and strength were observed in a murine model following 6 weeks of vibration [19]. 'Postmenopausal' bone loss was prevented in ovariectomised (OVX) rats exposed to 2 g acceleration at 50 Hz for 30 min/day, 5 days/week [20]. The addition of vibration enhanced the effect bisphosphonate treatment in one rat study [21] but not another [22]. Vibration at 90 Hz for 10 min/day prevented the decline in bone formation associated with disuse (hind limb suspension) in female rats, an effect that was not matched by 10 min/day weight bearing [23]. A protocol of 1 g at 60 Hz for 30 min/day, 5 days/week for 9 weeks, prevented glucocorticoid-induced bone loss [24]. Murine cell cultures subjected to 0.1–0.4 g at 30 Hz for 10–60 min/day also maintained bone formation and mineralisation during disuse with potentially enhanced preosteoblast differentiation [25]. Intriguingly, low-intensity vibration appears to stimulate preferential differentiation of mesenchymal stem cells into bone rather than fat cell precursors [26]. The first large-animal trial (20 min, 0.3 g vertical vibration at 30 Hz, 5 days/week for 12 months) increased trabecular bone in the proximal femora of sheep by 34.2 % [27]. Those trabeculae changed from rod to plate shaped in the plane of weight bearing, an effect that created a stiffer bone, less prone to fracture for a given load [28].

Human Data—Low-Intensity Vibration Human trials of WBV have produced results that do not entirely reflect the animal findings. Twelve months of 20 min/day, 0.2 g at 30 Hz, in postmenopausal women produced no significant difference between treatment and control groups from intention to treat analysis, but WBV maintained femoral neck and lumbar spine BMD of those who complied 86 % or more, and the lightest women improved the most [29]. A recent similar but larger trial also observed no significant between-group differences at the same sites at 12 months; however, large variability reduced statistical power and notable trends for a beneficial effect of WBV were observed [30]. Another group reported no effect of a similar WBV protocol at 30 or 90 Hz on volumetric BMD from high-resolution peripheral quantitative computed tomography (HR-pQCT) [31]. Findings were arguably confounded by simultaneous supplementation of the whole sample with high doses of calcium and vitamin D, now considered to be a non-trivial independent intervention. A report that a 12-month daily 0.3 g protocol at 30 or 90 Hz tended to reduce calcaneal BUA in postmenopausal women with osteopenia [32], must also be interpreted with caution in light of the recognised low precision of quantitative ultrasound (QUS) measures. In the latter trial, the reported changes for all groups were considerably lower than the LSC calculations for short-term QUS measurement reproducibility.

Younger cohorts at risk of low bone mass have also been treated with low-intensity WBV. A 12-month trial of 15–20-year-old young women with low bone mass found a 0.3 g stimulus at 30 Hz increased lumbar spine trabecular bone

2.1 % and femoral mid-shaft cortical bone 3.4 %. Cross-sectional area of paraspinal musculature also improved 4.9 % more in the treatment group than in the controls [33]. A 6-month RCT of the same low-intensity protocol markedly improved trabecular bone volume at the proximal tibia and spine of 20 pre- and post-pubertal, disabled, ambulant children [34].

Human Data—High-Intensity Vibration An 8-month high-intensity WBV intervention examined the effect of 4 min/day, 3–5 days/week vibration plus light exercise at 25 to 45 Hz, for maximum vertical accelerations of 2 to 8 g on young, healthy adults [35]. No effect on mass, structure or estimated strength of bone was observed at any skeletal site. The lack of effect in the young healthy cohort may reflect the diminishing returns of mechanical stimuli on an already robust skeleton. Untrained postmenopausal women increased hip BMD 4.3 % and balance 29 % after 8 months of 3 days/week, 6× 1 min sessions of side-to-side oscillating WBV compared with walking [36]. Six months of 5 mm, 30 Hz, 10 min/day, 5 days/week WBV stimulated improvements in femoral neck and lumbar spine BMD and reduced chronic back pain in postmenopausal women with osteoporosis [37]. While 6 months of 5 min of 3.2 g vibration at 30 Hz 3/week improved lumbar spine BMD >2 % in postmenopausal women [38], 12 months of 10×1 min, 20 Hz (3–4 mm) vibration at 30° knee flexion 2–3/week produced no discernible change in indices of bone quality from HR-pQCT [39]. Interestingly, results of a high-protein diet study indicated 5 days of 3.5 g vibration at 30 Hz 10 min/day counteracted diet-induced increased excretion of bone resorption markers in young men and women [40].

High-intensity vibration protocols that have been combined with exercise (6 months 35–40 Hz, 2.3–5.1 g, 20 min/day and 12.6 Hz, 2 g, 3/week) have shown improvements in hip BMD 0.93–4.3 % and balance 29 % in postmenopausal women [36, 41], but study designs prevent the examination of WBV in isolation.

A direct comparison of two different vibration regimes of twice weekly low-level WBV (15 min, 30 Hz, 0.3 g) versus higher-level WBV (6 min, 12.5 Hz, 1 g) against a control group found that both forms of WBV preserved bone mass at the hip and spine compared to losses in controls (with no notable differences between) and enhanced lower extremity muscle function and mobility [42].

Systematic reviews of WBV effects on bone have reported that less than 1 % of potentially relevant studies are eligible for inclusion due to methodological shortcomings and that cohort and stimulus heterogeneity limit the ability to make strong conclusions from remaining data [43–46]. While the most recent meta-analysis concluded that WBV has no effect on BMD, each BMD analysis included only two or three trials [46]. All reviews identify a need for future trials to be of more robust design, with larger cohorts and longer interventions.

Muscle Response

Muscle weakness not only increases the risk of falling [47] but also minimises loads on bone which may contribute to disuse osteopenia. Conversely, increased muscle strength is typically associated with improvements in bone. Thus, enhancement of neuromuscular performance likely provides dual benefits for fracture prevention.

Vibration loading enlarges fast and slow twitch muscle fibres [48] and increases lower extremity muscle activation during squatting [49]. Larger displacements (4 mm) will activate muscles more and induce greater muscle fatigue than smaller displacements (1 mm) [50].

A systematic review of the scientific support for effects of WBV on muscle strength and jump performance concluded there is moderate to strong evidence that long-term WBV improves lower extremity muscle performance, but that the effect is primarily observed in the untrained and/or those who cannot exercise at a high level of intensity such as the elderly [51]. In young, healthy [52] and postmenopausal cohorts [53, 54], improvements in muscle strength and performance following WBV training are often similar to those derived from exercise alone; however, there is some evidence that even when WBV-induced strength gains do not exceed those derived from resistance training, functional performance (e.g. counter movement jump height) may be enhanced [35, 55–57] or falls reduced [58]. The most recent meta-analysis concluded that WBV improves lower extremity muscle strength and function, an effect that can be achieved in 6–10 weeks [46].

While there is inadequate evidence in the literature to determine the optimum WBV dose for muscle strength outcomes, two and three training sessions a week are reportedly more effective than one [59]. It is possible that an individualised vibration frequency is required to produce an optimum neuromuscular response [60].

Balance and Fall Response

There is evidence to suggest that WBV may minimise fracture risk by improving balance, thereby reducing the risk of falls [3]. During vibration, small changes in muscle length are elicited that enhance the excitability of the spinal reflex [61]. Experiments in anaesthetized cats indicate that single 1a afferents can respond on a 1:1 basis to up to 150 Hz vibration [62]. Hypothetically then, neuromuscular adaptation to WBV may improve postural control and prevent falls when balance is perturbed.

While WBV does not appear to improve balance performance in young, healthy adults [35], the results for older cohorts are more consistently positive. A range of trials testing WBV interventions for balance-related outcomes over periods ranging from 6 weeks to 8 months have reported improvements in timed up and go and balance scores [56], walking speed, step length and balance [63], balance and stability [64], risk of falls and improved quality of life [65] and ankle joint range of motion and improved foot plantar surface sensation [66] of nursing home residents, untrained postmenopausal women and elderly community-living, non-exercising women compared with walking [36], exercises alone and physiotherapy. A number of well-designed trials comparing WBV plus exercise training versus exercising controls report beneficial effects such as reduced sway in response to stance perturbation [67] and improved balance, gait and functional mobility [68], but that WBV effects are not greater than exercise alone.

Importantly, a large trial examining the efficacy of 18 months of 20-min low-intensity vibration, 5 days/week, in elderly men and women reported significantly fewer falls or fractures in the treatment group [69•]. A simultaneous improvement in reaction time, muscle strength and movement velocity may explain the reduction in falls. Fracture rate was also lower in the WBV group but did not reach significance.

Authors of systematic reviews frequently conclude that while there may be evidence from a number of acceptable quality studies that WBV benefits balance, mobility and muscle function, many other studies have been insufficiently robust to differentiate the influence of WBV from exercise [43, 70, 71]. A 2012 meta-analysis suggests simple balance abilities and mobility (but not gait) may be improved by WBV and that a reduction in falls may be evident in the most frail [72].

What Is the Mechanism of Action?

The transduction of large exercise-induced mechanical loads into a biological signal for bone adaptation is thought to be a function of the tissue deformation-induced fluid flow that occurs during relatively large bone strain events [73]. Beyond strain magnitude, however, the response of bone to mechanical loads is governed by a complex interaction of strain parameters including frequency, rate and cycle number [74–76]. For example, as vibration frequency increases, strain magnitude necessarily falls as peak velocity of each vibration cycle decreases [77]. Intuitively, if vibration loads are small in magnitude, the mechanism of action on bone is unlikely to be related to tissue deformation, and recent evidence confirms that to be the case [78]. In fact, vibration at 0.6 g that induced cortical surface strains of only 10 microstrain ($\mu\varepsilon$) increased bone formation rates in the proximal tibiae of mice [79•]. Further, the mere oscillation of a limb in anaesthetised mice at 0.3 g and 45 Hz for 10 min/day enhanced trabecular bone formation rate, percent of mineralising surface and morphology, as well as cortical thickness and area [80, 81].

The results of a microscale model of vibration loading of a vertebral body suggested that fluid shear stress on trabecular surfaces due to marrow movement governs the anabolic

response of bone to a vibration stimulus [82]. However, others conclude, from finite element modelling, that vibration causes larger relative displacements of osteocyte-like cell nuclei than fluid shear and that gap junctional intracellular communication increases by 25 %, independent of vibration-induced fluid shear [83••]. The same group has now demonstrated that mesenchymal stem cell (MSC) response to vibration is may be driven by mechanical coupling between the cytoskeleton and the nucleus, inducing actin remodeling at the perinuclear domain [84]. It has also been reported that osteocytes respond to vibration by producing or downregulating soluble factors (COX-2, RANKL and PGE_2) that result in the inhibition of osteoclast formation which reduces bone resorption [85].

While muscle activation may be enhanced by certain vibration protocols, there is considerable evidence to suggest that the response of bone to vibration is not dependent on a muscle response [78].

As is often the case in biological systems, it is possible that the mechanism of action of vibration on bone is driven through a number of parallel or serial pathways.

What Are the Applications and Indications?

Up to 85 % of nursing home residents may suffer from osteoporosis [86]. Female nursing home residents with low BMD have over twice the risk of osteoporotic fracture than those with higher BMD, and those independent in transfer have three times the risk [87]. Although the initial cost of an individual WBV device is not inconsequential, a single WBV device may be installed in a nursing home and utilised by many. The cost and risks of WBV are also considerably less than chronic drug therapy for osteoporosis.

Any therapy is only as effective as its adoption and adherence. A study of satisfaction and preference for low-magnitude WBV versus medication suggested that 95 % of elderly women (mean age 86) living in a Continuing Care Retirement community were satisfied or very satisfied with vibration therapy and that over half (57 %) of the sample preferred vibration treatment to medication (24 %) [88]. Compliance was 83 % over 6 months [88]. A separate cohort of 24 elderly nursing home residents demonstrated 96 % compliance with a WBV plus exercise protocol versus 86 % compliance with exercise alone [56].

Nursing home residents and others for whom physical disability limits exercise feasibility are therefore particularly suited to the application of WBV therapy for musculoskeletal outcomes.

What Dose Is Best?

It is apparent that increasing the magnitude of vibration acceleration beyond a recognised effective dose will not enhance the effect and may be unsafe (in other words, more is not

better); however, only animal studies have examined dose-response to any appreciable degree. Bouts of 30 and 60 min of 0.3 g at 45 Hz were more effective for improving bone formation rate in mice than 15-min bouts, but increasing the number of bouts a day or partitioning a single daily bout into multiple shorter duration bouts did not improve the response [79•]. Others have also reported that the insertion of rest intervals does not potentiate the bone response to 15 min/day, 0.3 g, 45 Hz vibration in mice [18]. There is some evidence that a genetic predisposition to low bone mass may coincide with a greater response to vibration [89].

As animal observations cannot be directly applied to the human condition, considerably more data is required before therapeutic recommendations can be developed. Most human trials have been conducted using low to moderate vibration intensities (≤1 g) at or around a frequency of 30 Hz, for 10–20 min, 5–7 days a week, based on efficacy in animal studies and safety concerns. As results from those trials have been mixed, it remains unclear if such a dosage is optimal, and if not, which dosing parameters will be most efficacious or safe to modify. Minimal exposure appears to be required to stimulate a response, with benefits observed after as little as 2 min of daily exposure (15–20-year-old young women with low BMD and fracture) [90], or 15 min twice weekly in postmenopausal women [42].

It is important to note that there may be marked individual variations in response to different vibration frequencies [91], an effect that may reflect individual differences in transmission of the vibration stimulus to the body [17]. For this reason, the development of safe and effective dosimetry is unlikely to be straightforward, particularly for the frail elderly.

What Are the Risks?

As certain forms of occupational vibration are considered to be hazardous to the health [92–95], it is important to ensure that therapeutic applications do not replicate similar harmful vibration characteristics. In order to minimise occupational risk, the ISO has determined that a threshold of 0.3 g in the 20–50 Hz range is safe for human tolerance for up to 4 h at a time. Not all therapeutic devices have been developed to deliver vibration stimuli within those parameters.

Important differences exist between typical occupational and therapeutic vibrations however. Occupational exposures are normally less than 1 g but in the range of 3–10 Hz and can be very long duration. There is evidence from animal studies that deleterious bone effects (stimulation of resorption, impaired osteoid maturation) tend to occur at such frequencies (less than 10 Hz) [96••]. The effect may be a function of amplification of similar resonance frequencies of body segments of the small animals tested. In a human study of frequency-dependent transmissibility of vibration to ankles, knees and hips, frequencies of 10–90 Hz and accelerations

of 0.04–19.3 g were examined [15]. It was observed that transmission of vibration to joints was virtually 100 % at resonant frequencies (ankle 10–40 Hz, knee 10–25 Hz, hip 10–20 Hz). Others have reported the highest vibration accelerations in the human body to occur at 20 Hz compared with 10 or 30 Hz [17]. The greatest accelerations will be observed at anatomical sites in the closest proximity to the vibration surface and when plate amplitudes are greatest (including when feet are positioned farthest away from the central axis of the teeter plate) [17].

A recent computational analysis of stress dispersion on a femur with multiple vibration displacements and frequencies concluded that stress levels during most vibration protocols are likely to be equivalent to walking and stair climbing [97]. The authors indicate, however, that as vibration displacement increased, so too did the peak stress on the femur suggesting displacement ranges between 2 and 12 mm may not be safe for individuals with low bone strength. Their lack of consideration of the influence of muscle loads on the model and the lack of data pertaining to other clinically relevant bones (spine) suggests their findings are less than conclusive with respect to the safety of all vibration loads.

It is important to note that WBV has been used with some success to treat low back pain [98], and reports of side effects from therapeutic WBV are uncommon. It is reasonable to conclude that at low intensity, WBV is safe, as the magnitude of forces are orders of magnitude below those that induce damage; however, more exposure-response data is needed for higher-intensity vibration [99], including long-term effects on multiple systems. Although ISO standards can provide some guidance, they do not specifically address the exposures and durations of vibration typically applied during therapeutic or training-related WBV.

Where to from Here?

The next steps in the field of vibration therapy is for the conduct of rigorously designed randomised controlled trials to determine optimum dose-response guidelines on which future vibration device development and therapy should be based. Those studies must include larger samples sizes, both sexes and relevant cohorts (those at increased risk of fracture) and utilise clearly described vibration protocols based on the prevailing best evidence.

At the very least, it will be important for researchers to speak the same language. Current terminology includes WBV, low-magnitude mechanical signals, non-invasive micromechanical stimulation, plantar-based vibration and vibration exercise. Many trials vary with respect to vibration protocol and the details reported (e.g. treatment time, number, frequency, amplitude, peak-to-peak displacement, maximum acceleration) and do not distinguish vibration from simultaneous exercise intervention. Without systematic testing of a variety of protocols, it will not be possible to develop optimal therapeutic guidelines, including the determination of minimum effective dose.

More quality human data is needed in virtually every area of this field.

Conclusions

There is preliminary evidence that WBV will improve bone mass and reduce risk of osteoporotic fracture by improving neuromuscular function. Regrettably, much of the human research on WBV has been of inadequate rigor, or so heterogeneous, that the ability to form strong conclusions with respect to efficacy or dose is limited. It must be assumed that the designs of many of the devices in the rapidly growing commercial market of WBV have therefore not been informed by a robust evidence base of safety and efficacy. While low-intensity vibrating plates (<1 g) appear to be safe, individuals with very low bone mass and prior fractures should exercise caution when considering the use of devices that deliver higher vibration accelerations.

Compliance with Ethical Standards

Conflict of Interest   Dr. Beck states that this article has no conflicts of interests.

Human and Animal Rights and Informed Consent   This article contains no studies with human or animal subjects performed by the author.

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• Of importance
• • Of major importance

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