Biological mechanisms underlying the effects of low-magnitude mechanical stress in osteoporosis (Review)

ZHI LIU[1], DAN HAN[1], YANFEI WANG[2], HONGFAN LI[1], XUEDONG PEI[1] and ZHIJING SONG[1,3]

[1]Clinical College of Chinese Medicine, Gansu University of Chinese Medicine, Lanzhou, Gansu 730000, P.R. China; [2]College of Acupuncture-Moxibustion and Tuina, Gansu University of Chinese Medicine, Lanzhou, Gansu 730000, P.R. China; [3]Key Laboratory of Dunhuang Medicine, Ministry of Education, Lanzhou, Gansu 730000, P.R. China

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Abstract. Osteoporosis is characterized by reduced bone strength and an increased risk of fracture. Low-magnitude mechanical stress (LMMS) has been investigated as a non-invasive stimulus capable of modulating mechanotransduction in bone cells. This review synthesizes evidence concerning integrin-cytoskeletal signaling, linker of nucleoskeleton and cytoskeleton-mediated nuclear force transmission, connexin 43-mediated intercellular communication and the downstream regulation of bone marrow mesenchymal stem cells, osteoblasts and osteoclasts. Preclinical studies indicate that LMMS can activate the Wnt/β-catenin, MAPK/ERK, PI3K/AKT and receptor activator of nuclear factor-κB ligand/osteoprotegerin pathways in a context-dependent manner. However, clinical responses to whole-body vibration remain heterogeneous, vary according to the applied dose and skeletal site, and have not yet demonstrated fracture-prevention efficacy. Pulsed electromagnetic fields and therapeutic exercise are therefore discussed as related biophysical or mixed-magnitude interventions rather than as forms of LMMS itself. The present review highlights the gap between simplified cellular models and the three-dimensional bone microenvironment and proposes priorities for reporting standards and trial design to facilitate clinical translation.

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Correspondence to: Professor Zhijing Song, Clinical College of Chinese Medicine, Gansu University of Chinese Medicine, Wulipu Campus, 35 Dingxi East Road, Chengguan, Lanzhou, Gansu 730000, P.R. China
E-mail: songzhijing2020@163.com

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1. Introduction

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and deterioration of the bone microarchitecture, resulting in increased bone fragility and fracture risk (1). It represents a major global public health concern, affecting hundreds of millions of individuals, particularly postmenopausal women and older adults, and is associated with substantial morbidity, mortality and economic burden (2,3). The pathophysiology of osteoporosis primarily involves an imbalance in bone remodeling, in which osteoclast-mediated bone resorption exceeds osteoblast (OB)-mediated bone formation (4). The mainstay of clinical management includes antiresorptive agents, such as bisphosphonates and denosumab, and anabolic agents, such as teriparatide and romosozumab (5). Although effective, these pharmacological interventions have several limitations. Long-term bisphosphonate use has been associated with rare but serious adverse events, including osteonecrosis of the jaw and atypical femoral fractures (6). Furthermore, concerns regarding patient adherence, treatment costs and contraindications in certain populations underscore the need for alternative or adjunctive therapeutic strategies (7). Mechanical loading is a fundamental regulator of skeletal homeostasis. According to Wolff's law, bone adapts its mass and architecture in response to the mechanical demands imposed upon it (8). Importantly, the osteogenic response is not determined solely by high-magnitude strain. Pioneering studies have demonstrated that mechanical signals of low magnitude-several orders of magnitude lower than those generated during strenuous exercise-can exert potent anabolic effects on bone when delivered at high frequencies (9,10). This phenomenon provides the basis for low-magnitude mechanical stress (LMMS), also referred to as low-intensity vibration. The therapeutic appeal of LMMS lies in its non-invasive nature, the localized concentration of mechanical strain at structurally vulnerable sites, and its potentially self-optimizing

effect, whereby newly formed bone reduces local strain and consequently attenuates the mechanical stimulus (11,12). The signals generated are physiologically relevant and resemble those produced by postural muscle contractions (10). For many patients with osteoporosis, particularly frail older adults, conventional high-impact exercise may be impractical or contraindicated because of the elevated risk of fracture (13). LMMS-based interventions, including whole-body vibration platforms, may therefore provide a passive, low-risk and easily administered means of stimulating bone formation and limiting bone loss (14,15). Over the past two decades, extensive preclinical and clinical research has helped elucidate the complex biological mechanisms through which LMMS influences bone metabolism.

This review aims to synthesize current knowledge of the biological mechanisms linking LMMS to the prevention and treatment of osteoporosis. First, the fundamental principles of mechanotransduction in bone cells are outlined. The review then examines how LMMS regulates the fate and function of bone marrow mesenchymal stem cells (BMSCs), OBs and osteoclasts, with particular attention to major signaling pathways, including Wnt/β-catenin, MAPK and PI3K/AKT. The central role of osteocytes as mechanosensory cells is also highlighted. Finally, translational applications, the current clinical evidence and future directions for the development of LMMS as a mechanotherapeutic approach to osteoporosis are discussed.

To perform this narrative review, PubMed (https://pubmed.ncbi.nlm.nih.gov/) and Crossref (https://search.crossref.org/) were searched until 11 July 2026 using combinations of the following terms: 'low-magnitude mechanical stress', 'low-intensity vibration', 'whole-body vibration', 'osteoporosis', 'bone mechanotransduction', 'osteoblast', 'osteoclast', 'RANKL', 'OPG' and 'bone marrow mesenchymal stem cell'. Priority was given to recent systematic reviews, randomized controlled trials and mechanistic studies, while classic studies were retained when they established foundational mechanisms. The evidence was synthesized narratively because the intervention protocols, experimental models and reported outcomes were too heterogeneous to permit quantitative pooling within the scope of this review.

2. Biological mechanisms of LMMS

The anabolic effects of LMMS on bone are mediated by a sophisticated mechanotransduction cascade through which physical forces are converted into biochemical signals that ultimately regulate gene expression and cellular behavior. This process depends on the coordinated actions of cellular mechanosensors, the cytoskeleton and nuclear structures.

Mechanosensing and initial signal perception. The perception of LMMS begins at the plasma membrane and the cell-extracellular matrix (ECM) interface. Integrins, particularly αVβ3 and α5β1 in osteocytes and OBs, function as major mechanoreceptors (16,17). These transmembrane receptors bind to specific ECM proteins, including fibronectin and vitronectin, and form focal adhesions that physically connect the extracellular environment to the intracellular actin cytoskeleton. Mechanical stimulation induces integrin clustering and conformational changes, thereby activating associated kinases, such as focal adhesion kinase and Src-family kinases, and initiating downstream signaling cascades (18). The distinctive dendritic morphology of osteocytes within the lacunar-canalicular network acts as a biological amplifier of low-level mechanical strain. The 'tethering elements' connecting osteocyte processes to the canalicular walls concentrate mechanical signals, enabling osteocytes to detect subtle stimuli that might otherwise fall below the mechanosensory threshold (19,20).

Cytoskeletal remodeling and force transmission. Following mechanosensing, mechanical forces are rapidly transmitted through the actin cytoskeleton, which undergoes dynamic reorganization. LMMS has been shown to upregulate the expression and modify the spatial organization of key cytoskeletal and adaptor proteins, including α-actinin, vinculin (VCL) and cadherin-11 (5,21). This remodeling increases intracellular tension and cytoskeletal stiffness, thereby enhancing the capacity of cells to withstand and transmit mechanical loads. Rather than functioning merely as a passive structural scaffold, the cytoskeleton serves as an active signaling platform that regulates mechanosensitive proteins and transcription factors.

Nuclear mechanotransduction and gene regulation. Mechanical signals are ultimately transmitted to the nucleus, where they influence chromatin organization and gene transcription. This critical step is mediated by the linker of nucleoskeleton and cytoskeleton (LINC) complex, which comprises SUN and nesprin proteins spanning the nuclear envelope (4,22). By physically coupling the cytoskeleton to the nuclear lamina, the LINC complex enables the direct transmission of mechanical forces to the nucleus. It has been demonstrated that the structural integrity of the LINC complex is essential for the osteogenic response to LMMS, as disruption of this complex abolishes the mechanically induced expression of osteogenic genes such as RUNX family transcription factor 2 (Runx2) and Osterix (23). Force-induced alterations in nuclear morphology and chromatin accessibility further modulate transcriptional programs, thereby promoting a pro-osteogenic cellular state (24).

Intercellular communication via gap junctions. Mechanical signals are propagated throughout the bone multicellular unit through gap junctional intercellular communication. Connexin 43 (Cx43) is the predominant gap junction protein expressed in bone cells. LMMS upregulates Cx43 expression and promotes the formation of functional gap junctions, facilitating the direct transfer of ions, small metabolites and second messengers, including Ca^{2+} and inositol trisphosphate, among neighboring osteocytes, OBs and bone-lining cells (6,25). This communication network is essential for coordinating cellular responses and distributing anabolic and catabolic signals across extensive regions of bone tissue. In addition, unopposed Cx43 hemichannels located on the cell surface may open in response to mechanical stimulation, allowing the release of paracrine factors such as prostaglandin E_2 and ATP, both of which are potent mediators of bone formation (9,26). The opening of these hemichannels involves an integrin αVβ3-PI3K-AKT signaling

axis, linking primary mechanosensing to the amplification of paracrine signaling (10).

Interface between mechanosensing and cell-specific responses. The membrane, cytoskeletal and nuclear mechanosensors described above converge on several major signaling pathways, including PI3K/AKT, MAPK/ERK, Wnt/β-catenin and ras homolog family member A/Rho associated coiled-coil containing protein kinase 1-Yes1-associated transcriptional regulator/transcriptional co-activator with PDZ-binding motif signaling. To avoid repetition of cell-specific evidence, these downstream pathways are examined in section 3 in relation to BMSC lineage commitment, osteoclastogenesis and OB function (27-32).

Restoration of mechanosensitivity in osteoporotic bone. A defining feature of osteoporosis is the diminished skeletal response to mechanical loading. This mechanosensory impairment is associated with dysfunction in the pathways described above, including defective integrin signaling, altered cytoskeletal organization and increased sclerostin expression (33,34). LMMS interventions may help counteract these abnormalities. Preclinical studies indicate that LMMS can accelerate the recovery of bone mechanical properties, including ultimate load and stiffness, in osteoporotic models. These effects may be mediated in part by the restoration of angiogenic-osteogenic coupling and improvement of the bone vascular supply, which is frequently compromised in osteoporosis (11,12,35). In summary, LMMS coordinates a multistage mechanotransduction program extending from integrin-mediated sensing at the cell periphery to force-dependent transcriptional regulation within the nucleus. This process is integrated through cytoskeletal remodeling and intercellular communication. Together, these mechanisms enable bone tissue to adapt its structure and mass efficiently in response to subtle, high-frequency mechanical signals and provide the mechanistic basis for the potential therapeutic application of LMMS in osteoporosis. A schematic overview of these principal mechanisms is presented in Fig. 1.

3. Regulatory mechanisms linking low mechanical stress to osteoporosis

Effects of low mechanical stress on BMSCs. BMSCs can differentiate into osteogenic and adipogenic lineages. During aging and osteoporosis, the balance between RUNX2-driven osteoblastogenesis and peroxisome proliferator activated receptor (PPAR)γ-driven adipogenesis shifts toward increased marrow adiposity (36,37).

Promotion of osteogenic differentiation. Low-magnitude vibration may promote osteogenic commitment by increasing RUNX2 expression and suppressing PPARγ2 through ERK-dependent signaling (38). Cellular senescence is increasingly recognized as a contributor to age-related osteoporosis (39,40). In naturally aged rats, low-magnitude vibration partially restored osteogenic-cell function and was associated with increased sirtuin 1 (SIRT1) expression and reduced p53/p21 signaling. Importantly, the source study compared 22-month-old and 3-month-old Sprague Dawley rats rather than rats and mice (41). A separate study compared 20-month-old rats with 6-month-old rat controls and demonstrated that vibration-induced microRNA (miR)-378a-3p suppressed growth factor receptor bound protein 2 expression and increased osteogenic-marker expression in BMSCs derived from aged rats (42). Although these findings provide useful mechanistic insights, they remain limited to preclinical models.

Suppression of adipogenic differentiation. Mechanical loading reduces PPARγ signaling and may redirect mesenchymal lineage commitment away from adipogenesis (38). The p38 MAPK pathway has also been implicated in osteoporosis-related lineage regulation (43). Before vibration treatment, BMSCs from aged rats exhibited fewer mineralized nodules and greater lipid-droplet accumulation. The intervention partially corrected this imbalance through changes associated with the SIRT1/p53/p21 pathway (41). In ovariectomized models, estrogen receptor (ER)α/Wnt signaling has also been implicated in the suppression of adipogenic commitment (44). However, because these findings were derived predominantly from two-dimensional cell cultures and rodent models, the magnitude and persistence of these effects within the three-dimensional human bone marrow niche remain uncertain.

Effects of low mechanical stress on osteoclasts. Low mechanical stress may regulate osteoclastogenesis through both cell-autonomous focal-adhesion signaling and coupling factors released by osteocytes. VCL connects integrins to the actin cytoskeleton and transmits mechanical force within focal adhesions (45,46). In vibration-based models, changes in VCL tension and focal-adhesion dynamics have been associated with reductions in the number of multinucleated tartrate-resistant acid phosphatase-positive osteoclasts. However, these findings are model-dependent and do not independently establish a clinically meaningful antiresorptive effect (47).

The TNF superfamily member 11 (RANKL)/osteoprotegerin (OPG) axis represents a second and biologically central mechanism. Low-intensity whole-body vibration has been reviewed as a potential intervention in postmenopausal osteoporosis (48). RANKL binds to RANK on osteoclast precursors and promotes their differentiation, whereas OPG functions as a soluble decoy receptor. Consequently, a reduced RANKL/OPG ratio would be expected to inhibit osteoclastogenesis. Osteocytes are a major source of RANKL in remodeling bone (49). In MLO-Y4 osteocyte-like cells exposed to high-glucose conditions, mechanical vibration increased OPG expression and secretion while reducing RANKL expression and secretion, consistent with attenuation of pro-osteoclastogenic signaling (50). These findings support an osteocyte-mediated mechanism but should be interpreted cautiously because they were obtained using a two-dimensional cellular model under diabetic conditions. Whether a comparable shift in the RANKL/OPG balance occurs across different loading protocols or in human osteoporotic bone remains unresolved.

Effects of low mechanical stress on OBs. Low mechanical stress plays an important role in promoting osteogenesis, as illustrated in Fig. 1. Exposure to low-magnitude mechanical vibration at 35 Hz and 0.25 g has been shown to stimulate OB proliferation by upregulating miR-150-5p and downregulating miR-182-5p and miR-125b-2-3p, thereby activating the MAPK and actin-regulatory signaling pathways (51).

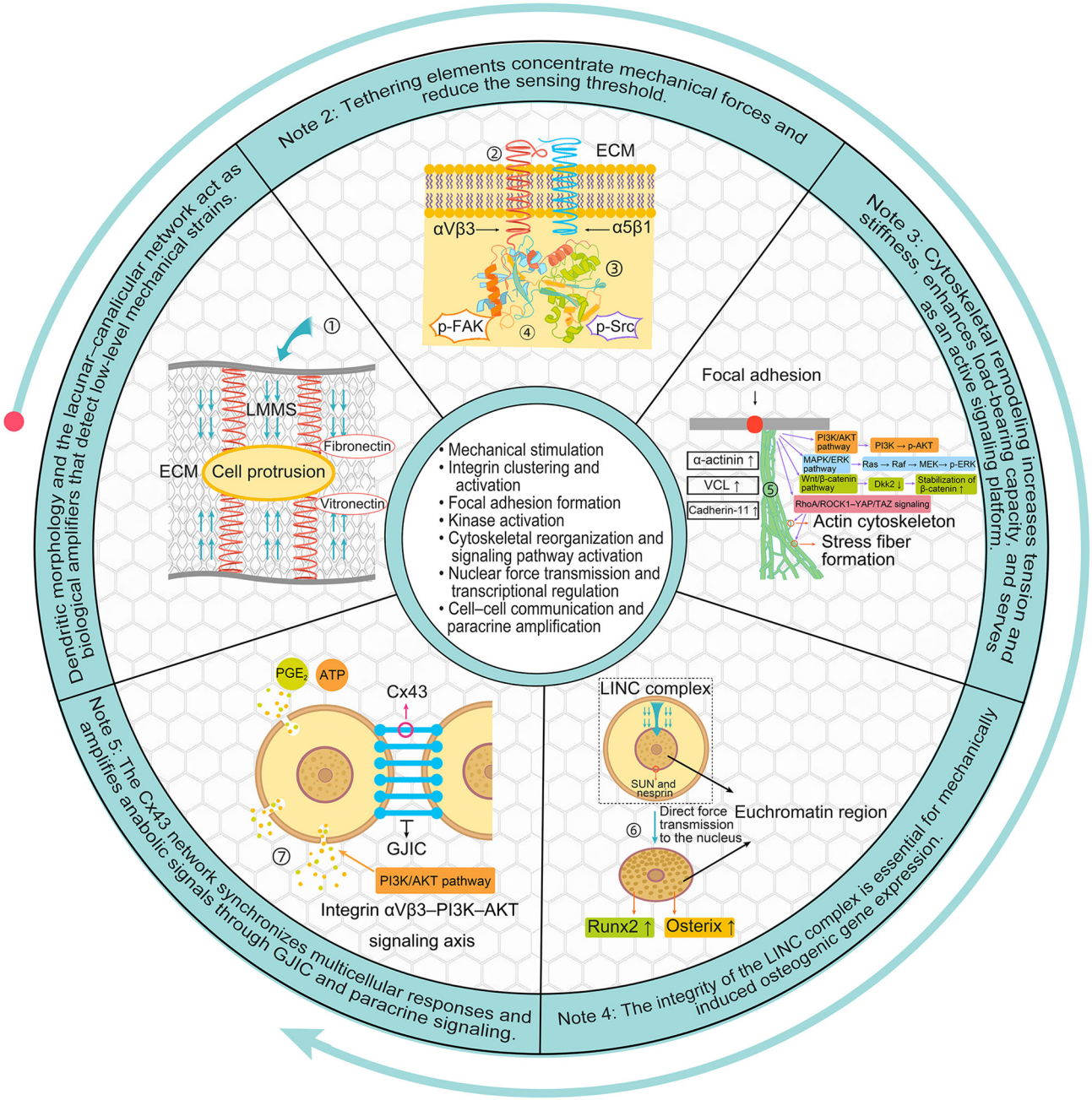

Figure 1. Biological mechanisms of low-magnitude mechanical stress stimulation. LMMS activates integrin/focal-adhesion kinases at the cell-ECM interface, inducing cytoskeletal remodeling and LINC-mediated nuclear force transmission. Cx43 channels coordinate intercellular and paracrine signals. AKT, protein kinase B; ATP, adenosine triphosphate; Cx43, connexin 43; Dkk2, Dickkopf-related protein 2; ECM, extracellular matrix; ERK, extracellular signal-regulated kinase; FAK, focal adhesion kinase; GJIC, gap junctional intercellular communication; LINC, linker of nucleoskeleton and cytoskeleton; LMMS, low-magnitude mechanical stress; MAPK, mitogen-activated protein kinase; PGE_2, prostaglandin E_2; PI3K, phosphoinositide 3-kinase; MEK, MAPK/ERK kinase; nesprin, nuclear envelope spectrin repeat protein; Raf, rapidly accelerated fibrosarcoma kinase; Ras, rat sarcoma virus protein; RhoA, Ras homolog family member A; ROCK1, Rho-associated coiled-coil-containing protein kinase 1; Runx2, RUNX family transcription factor 2; Src, Src family kinase; SUN, Sad1/UNC84 domain protein; TAZ, transcriptional co-activator with PDZ-binding motif; VCL, vinculin; Wnt, wingless-related integration site; YAP, Yes-associated protein; αVβ3, integrin αVβ3; α5β1, integrin α5β1; p-, phosphorylated.

Low mechanical stress also activates Wnt/β-catenin signaling. Following mechanical loading, the expression of pathway-related genes, including β-catenin, COL1, osteocalcin and Runx2, is increased. Immunofluorescence analysis has further demonstrated that low mechanical stress promotes the nuclear translocation of β-catenin in mouse MC3T3-E1 cells, indicating activation of the Wnt/β-catenin pathway. This pathway also contributes positively to the mechanically induced expression of Runx2 (52). In diabetes-induced secondary osteoporosis, low mechanical stress has similarly been shown to promote OB proliferation and differentiation through Wnt/β-catenin signaling. Under high-glucose conditions, the expression of Dickkopf-related protein 2 (Dkk2), an inhibitor of Wnt signaling, is increased, while β-catenin levels decline because of phosphorylation-dependent degradation. These changes reduce the expression of Cyclin D1 and Osterix, thereby suppressing OB proliferation and differentiation. Dkk2 overexpression inhibits MC3T3-E1 cell

proliferation, as reflected by a marked reduction in the proportion of cells in the S and G2/M phases and a corresponding increase in the G0/G1 phase. It also impairs osteogenic differentiation, resulting in reduced alkaline phosphatase activity and fewer mineralized nodules. Low mechanical stress attenuates the high-glucose-induced increase in Dkk2 and restores the expression of β-catenin, cyclin D1 and Osterix. These effects promote OB proliferation and differentiation and partially alleviate the impairment of bone formation caused by a high-glucose environment (53). Low mechanical stress may also exert protective effects in diabetes-induced secondary osteoporosis through the PI3K/AKT pathway. In MC3T3-E1 cells exposed to high-glucose conditions, activation of PI3K/AKT signaling promotes OB proliferation and reduces matrix metalloproteinase 9 (MMP9) expression. Low mechanical stress also modulates the upstream TNF receptor associated factor 6-ERK/p38 MAPK pathway involved in MMP9 regulation, thereby potentially suppressing osteoclast differentiation and maturation, bone resorption and the migration of osteoclast precursor cells (54). The ER is considered a susceptibility-related factor in osteoporosis, and both OBs and osteoclasts express ERs. Estrogen binding to receptors in OBs regulates the production of collagenase, cytokines and growth factors and thereby influences osteogenic differentiation. For example, low-intensity vibration at 45 Hz and 0.9 g significantly enhanced OB activity in ovariectomized osteoporotic rats by increasing ERα expression and altering its subcellular localization, ultimately promoting bone formation (55). In estrogen deficiency-induced secondary osteoporosis, low-frequency mechanical vibration has also been reported to increase bone morphogenetic protein 2 and Runx2 expression, followed by the upregulation of osteocalcin, osteopontin, bone sialoprotein and COL1. These responses are accompanied by activation of the ERK1/2 signaling pathway and enhanced bone anabolism (56). Overall, low mechanical stress promotes osteogenesis by activating major signaling pathways and osteogenic regulatory factors. It may also counteract adverse cellular conditions associated with different forms of secondary osteoporosis. However, much of the available evidence is derived from cell and animal models, and the clinical relevance of these mechanisms requires further validation.

4. Biophysical and mechanical interventions relevant to osteoporosis

The translation of preclinical findings on LMMS into clinical practice has prompted the development and investigation of several non-invasive, physiotherapy-based interventions for osteoporosis prevention and management. These approaches aim to deliver controlled, safe and measurable stimuli to the skeleton through whole-body or targeted regional application. However, not all of these interventions constitute LMMS and their mechanisms and clinical evidence should therefore be considered separately.

Whole-body vibration (WBV) therapy. WBV is the closest clinical analogue of LMMS. Low-magnitude protocols generally use accelerations below 1 g, although the frequency, posture, platform type, cumulative exposure and transmission of vibration to individual skeletal sites vary considerably among studies. Clinical findings remain heterogeneous. The earlier meta-analysis by Slatkovska *et al* (14) and a 2023 meta-analysis of randomized trials (57) reported small improvements in bone mineral density (BMD) that depended on the skeletal site and intervention protocol. Device trials in older adults have also highlighted challenges related to recruitment, adherence and delivery of low-magnitude mechanical stimulation (58). By contrast, a 12-month randomized trial using vibration at 0.3 g and either 30 or 90 Hz found no improvement in BMD or bone microarchitecture (59). An overview of systematic reviews also concluded that most available reviews were of critically low methodological quality (60). WBV may therefore be considered an adjunctive intervention for selected patients, but current evidence does not support its use as an established replacement for pharmacotherapy or exercise programs designed to prevent fractures.

Pulsed electromagnetic fields (PEMF). PEMF therapy is an electromagnetic rather than a mechanical intervention. It is included here only as a related biophysical modality and should not be classified as LMMS. Its proposed effects involve the induction of electrical currents and subsequent modulation of intracellular signaling. Any resulting micromechanical effects are indirect and PEMF has not been demonstrated to be equivalent to mechanical vibration (61). Evidence supporting its use in osteoporosis remains limited and highly dependent on the treatment protocol (62,63). PEMF should therefore be evaluated separately from interventions involving direct mechanical loading.

Therapeutic exercise and physical activity. Therapeutic exercise represents a mixed-magnitude mechanical intervention rather than a pure LMMS exposure. Muscle-bone interactions mediated by insulin-like growth factor I provide an additional biological basis for the skeletal effects of exercise (64). Resistance, weight-bearing, balance and jumping exercises generate heterogeneous skeletal strains that vary according to body mass, movement pattern, loading rate and anatomical site (13,65). Their potential benefits include modest, site-specific improvements in BMD, enhanced muscle strength and physical function, and a reduced risk of falls. These benefits should not, however, be attributed exclusively to low-magnitude mechanical strain. Similarly, Tai Chi is more appropriately characterized as a low-impact, multicomponent form of exercise that improves balance and functional capacity rather than as a form of LMMS (66).

Low-intensity pulsed ultrasound (LIPUS). LIPUS delivers acoustic pressure waves that can generate localized micromechanical strain and fluid-streaming potentials. It is therefore mechanistically closer to a targeted mechanical stimulus than PEMF. Nevertheless, evidence for its use in osteoporosis is derived predominantly from preclinical studies or research on fracture healing (67,68). Direct clinical evidence demonstrating that LIPUS improves BMD or prevents fragility fractures remains insufficient.

Clinical considerations and future directions. Clinical interpretation should distinguish evidence of efficacy from uncertainty regarding implementation. Outcomes vary according to vibration frequency, acceleration, platform type, posture, cumulative exposure, adherence, baseline skeletal

status and anatomical site (57,59,60). Evidence for fracture-risk reduction remains limited and vulnerable patients may require supervision because balance impairment, recent fractures, acute pain, cardiovascular instability, implanted medical devices and other comorbidities may affect the suitability and safety of treatment. These considerations currently preclude the development of a universally applicable LMMS prescription.

Key priorities include adequately powered, preregistered trials that report delivered rather than nominal acceleration, together with adherence, adverse events and site-specific changes in BMD and bone microarchitecture. Falls and fractures should also be included as endpoints whenever feasible. Head-to-head dose-response studies and subgroup analyses based on age, sex, baseline osteoporosis severity, medication use and mechanical transmissibility are required before personalized treatment protocols can be recommended.

Critical appraisal of the evidence. Positive findings in cellular models do not necessarily translate to intact bone. Two-dimensional cultures expose isolated cells to simplified substrates and do not reproduce the three-dimensional confinement, viscoelastic ECM, fluid flow, cell-cell interactions, vascular supply or remodeling history of living bone. Consequently, mechanotransduction in three-dimensional environments may differ qualitatively from that observed on two-dimensional elastic surfaces (69). The anisotropic and multiscale architecture of the bone matrix further influences the transmission and distribution of local strains (70). At the clinical level, null trials and inconsistent site-specific findings from meta-analyses indicate that non-response is common (57,59,60). The field should therefore distinguish mechanistic plausibility from demonstrated antifracture efficacy and avoid extrapolating the effects of a single frequency or acceleration across cellular, animal and human systems.

5. Conclusion and future perspectives

LMMS engages a distributed mechanobiological network involving membrane receptors, cytoskeletal remodeling, nuclear coupling and osteocyte-mediated intercellular communication. Available evidence supports biologically plausible effects on mesenchymal lineage commitment, OB activity and osteoclast-regulatory signaling. However, much of this evidence has been derived from specific two-dimensional cell cultures or rodent models and should not be generalized across different doses, diseases or species.

Clinical translation remains less certain than the preclinical literature might suggest. The effects of WBV on BMD appear to be modest and dependent on the skeletal site and intervention protocol. Evidence based on fracture endpoints remains sparse, while null trials demonstrate considerable variability and non-response. PEMF and therapeutic exercise should therefore be evaluated as distinct interventions rather than being mechanistically grouped with LMMS.

Immediate priorities include standardizing the reporting of delivered acceleration, frequency, posture, cumulative dose, adherence, adverse events and the skeletal sites assessed. Dose-response relationships should be investigated in adequately powered randomized controlled trials, and clinically meaningful outcomes-including falls, fractures and measures of bone quality-should be evaluated alongside BMD. Mechanistic studies should incorporate three-dimensional matrices, osteocyte networks, vascular and immune components, and aged or osteoporotic human cells to more accurately reproduce the *in vivo* bone microenvironment.

Until these evidence gaps are addressed, LMMS should be regarded as an investigational or adjunctive intervention rather than a standalone treatment for osteoporosis. Future studies should identify biological and biomechanical predictors of treatment response and determine whether LMMS provides additional benefits when combined with guideline-recommended exercise and pharmacological therapy.

In conclusion, LMMS provides a valuable framework for investigating how weak mechanical signals influence bone remodeling. However, its mechanistic promise currently exceeds the certainty of the clinical evidence. Further progress will depend on experimental models that more accurately reproduce the three-dimensional bone niche and clinical trials that apply standardized exposure reporting and assess clinically meaningful outcomes.

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Availability of data and materials

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Authors' contributions

ZL and ZS conceived and designed the review. ZL wrote the original draft. ZL, DH and XP conducted the literature search and analyzed the literature. YW contributed to the interpretation of the literature findings. HL and ZS critically revised the manuscript. Data authentication is not applicable. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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