Comparative Effectiveness Research Review Disposition of Comments Report

Research Review Title: *Whole-Body Vibration Therapy for Osteoporosis*

Draft review available for public comment from March 9, 2011 to April 6, 2011.

Research Review Citation: Available at: www.effectivehealthcare.gov/reports/final.cfm.

Comments to Research Review

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Background	In the third paragraph of the introduction, the authors may want to refer to the ample evidence related to the effects of low-magnitude, high frequency mechanical stimuli on bone formation in animal models. These findings led to the development of whole body vibration therapy in human applications.	Technical Briefs are by design short documents with limited scope and length. We understand the role of animal models in leading to whole-body vibration applications in humans. We refer to the role of animal models in the background section, but a more comprehensive description of the historical development of whole-body vibration is outside the scope of this Technical Brief.
Peer Reviewer #1	Background	In the last paragraph of the introduction, it is mentioned that WBV may improve muscle strength and power by increasing neuromuscular activation/muscle circulation, etc. Please refer to some studies on the effect of WBV on muscle activity, such as: Cardinale and Lim, J Strength Cond Res 2003; 17: 621-4. Hazell et al., J Strength Cond Res 2010; 24:1860-5. Roelants et al., J Strength Cond Res 2006; 20: 124-9. Pollock et al. Clin Biomech 2010; 25: 840-6. For the effect of WBV on muscle circulation, please refer to: Kerschan-Schindl et al. Clin Physiol 2001; 21: 377-82.	We have added these references in the discussion of neuromuscular activation and muscle circulation.
Peer Reviewer #2	Background	p. 1 l. 23: I suggest removing "or low bone mass" from that sentence.	We have revised the wording.
Peer Reviewer #2	Background	p. 1 l. 50-51: I think the authors are referring to reference 51 in this sentence not 36.	We have changed this to reflect the correct reference.
Peer Reviewer #3	Background	The background section was comprehensive providing the reader with important statistics regarding the prevalence, complications, and prevention of osteoporosis.	Thank you for your comment.
Peer Reviewer #1	Methods	How many people were involved in literature search and data extraction? If more than one person was involved, were the search and data extraction done independently? What if there was disagreement among raters? Any measures of reliability among raters?	The literature search was conducted by one librarian and peer reviewed by a second librarian. Data extraction was conducted by one investigator, with a quality check by a second senior investigator. Because of the nature of Technical Briefs (which do not synthesize effectiveness outcomes), no rating of studies was done and specific data on effectiveness outcomes were not extracted.
Peer Reviewer #1	Methods	Please provide a flow chart mapping out the number of records identified, included and excluded, and the reasons for exclusions. You can refer to this useful website: http://www.prisma-statement.org/statement.htm	We have included the number of included and excluded studies in the text of the report.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Methods	The inclusion and exclusion criteria are explicitly described in the report, but I think they should be placed in the Methods, rather than the Results section. Moreover, a strong rationale needs to be provided as to why the populations listed under exclusion criteria (patients with cerebral palsy, stroke, PD, spinal cord injury...) were not considered in this report. These people are also at risk for low bone density or osteoporosis, due to related risk factors such as muscle weakness, balance problems, physical inactivity.	While we understand the risk for low bone density in patient populations with specific conditions, we decided a priori to exclude patients with primary diagnoses other than osteoporosis because there was concern that these populations may have different safety concerns than those for individuals at risk for or with osteoporosis but otherwise healthy. The study designs and mechanisms may be different for these patients, so we did not aim to generalize the findings to all of these diverse patient populations. We make this exclusion clearer in the methods section.
Peer Reviewer #1	Methods	The authors may want to incorporate some evaluation of the methodological quality of the selected studies, particularly the RCTs. There are standardized methods to assess the risk of bias, e.g., JADAD, PEDro.	The Technical Brief is intended to provide a brief overview of vibration therapy, including the current understanding of theoretical benefits and harms, contexts in which it is used, and a description of the populations, types of vibration therapies, comparators, and outcomes that have been studied. However, because of the diversity of contexts which are studied, we restrict our review to describing studies that have been done and do not attempt to summarize the outcomes and effectiveness of vibration therapy.
Peer Reviewer #2	Methods	p. 3 l44-46: There is a problem with the appendices. Appendix B is the interview guides (stated as C here). There is no list of key informants included. Also, the page numbers of the appendices are not correct.	Thank you. We have corrected the formatting issues that are noted.
Peer Reviewer #3	Methods	This was a review of literature so patient inclusion and exclusion was not included. The authors did publish their criteria for selecting literature. The authors used excellent search strategies to only include high quality, relevant articles.	Thank you for your comments.

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Public Reviewer Ezenwa	Methods	It is evident that there are two distinct conceptual frameworks in current whole body vibration systems. One framework uses a single displacement level and a single vibration frequency during entire vibration session. This framework also allows for the user to change the displacement level and the vibration frequency before the start of another vibration session. In this single vibration frequency implementation framework all muscle fiber types with fundamental twitch frequencies that differ from the device vibration frequency will not be fully energized resulting in sub-optimal muscle contraction. Use of larger displacement levels would be required to engage muscle groups in optimal muscle contraction. The second conceptual framework uses low vibration displacement levels concurrently with multiple vibration frequencies that encompass all muscle fiber types twitch frequencies during each session. In this method, the low levels of vibration displacements were optimally designed using simulation studies that provided stress on isolated femur equivalent to stress on the femur during walking or stair climbing, see JRRD Vol. 48, number 2, 2011, pages 179-190. Therefore the stress on the bone caused by the vibration displacements is optimal i.e. no more than what a person would encounter from walking or stair climbing. The effective stress on the bone by this method is the combined stress on the bone from low-level vibration input and the stress on the bone by optimal muscle contraction. The benefit of targeting all muscle fibers is that fully energized muscle fibers will optimally recruit innervated muscle contraction and thereby exert optimal contraction stress on the bone. Therefore it does not require using larger vibration displacement levels to achieve more muscle contraction which is important since osteoporosis patients may not be able to tolerate larger vibration displacement levels. The simulation studies in JRRD Vol. 48, number 2, 2011, pages 179-190 agree with single subject study in reference 66. Low level vibration displacements and optimal muscle contraction will prevent damage to the cartilage or brittle bones and would thereby be appropriate for osteoporosis intervention.	We have addressed this point in our discussion of treatment protocols and we have included these theories in the discussion of the intervention.
Peer Reviewer #1	Findings	The evidence tables provide detailed and essential information of the studies.	Thank you for your comment.

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Peer Reviewer #1	Findings	Please include the ratings on methodological quality in one of the evidence tables.	The Technical Brief is not intended to be a systematic review, so this is outside the scope of the report. The purpose of the Technical Brief is to provide a brief overview of vibration therapy, including the current understanding of theoretical benefits and harms, contexts in which it is used, and a description of the populations, types of vibration therapies, comparators, and outcomes that have been studied. We restrict our review to describing studies that have been done and do not attempt to rate the studies or summarize the outcomes or effectiveness of vibration therapy.
Peer Reviewer #1	Findings	You need an evidence table to describe the results of each selected study. For significant results, it may be a good idea to compute the effect size and include this information in the table.	The Technical Brief is not intended to be a systematic review, so this is outside the scope of the report. The purpose of the Technical Brief is to provide a brief overview of vibration therapy, including the current understanding of theoretical benefits and harms, contexts in which it is used, and a description of the populations, types of vibration therapies, comparators, and outcomes that have been studied. We restrict our review to describing studies that have been done and do not attempt to rate the studies or summarize the outcomes or effectiveness of vibration therapy.
Peer Reviewer #1	Findings	In the text, please summarize the findings of the studies in a paragraph or two.	The Technical Brief is not intended to be a systematic review, so this is outside the scope of the report. The purpose of the Technical Brief is to provide a brief overview of vibration therapy, including the current understanding of theoretical benefits and harms, contexts in which it is used, and a description of the populations, types of vibration therapies, comparators, and outcomes that have been studied. We restrict our review to describing studies that have been done and do not attempt to rate the studies or summarize the outcomes or effectiveness of vibration therapy.

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Peer Reviewer #2	Findings	p. 6 l. 3-9 This section on risks of vibration should include information about the effects of damping, and body position on the vibration signal (refer to Ritweger 2010 European Journal of Applied Physiology 108:877-904).	We have provided additional information about these risks.
Peer Reviewer #2	Findings	l. 8 Do the authors mean 50-100 Hz? 5 doesn't seem very high to me.	We have revised this paragraph and removed this statement.
Peer Reviewer #2	Findings	l. 8-10 The authors make a very strong statement here. There is not sufficient evidence provided to support such a strong statement. This comments seems biased toward 1 type of vibration platform device.	We have reworded these lines to better reflect the Technical Brief conclusions.
Peer Reviewer #2	Findings	p. 7 l. 46-50 When stating two studies, list the reference numbers at the end of that sentence, not in the next sentence. There are several places where this should be corrected in the manuscript.	We have corrected the formatting issues noted.
Peer Reviewer #3	Findings	The evidence tables and appendices are extremely descriptive. It appears that the authors have included all relevant studies. The evidence tables were especially helpful in presenting the current evidence.	Thank you for your comments.
Peer Reviewer #4	Findings	In the section, "Describe the Existing Technology," the phrases: "frequency of oscillations per second (Hz/sec)" and "Vibration acceleration is a function of the frequency and amplitude (meter/second*second)" raise concerns about the authors' understanding of the physics of vibration. The first: the SI unit for oscillations per second is Hz, not Hz/sec! The second: this is true only for sinusoidal vibration. Later in the document, it is noted that all studies use sinusoidal vibration. Displacement and acceleration are reported as if they are independent. They are not. Knowledge that vibration is sinusoidal, what the frequency is, and what the displacement is determines the acceleration.	We have changed the wording in the report to make this distinction clearer.
Peer Reviewer #1	Summary and Implications	The authors should include a discussion of the implications of the overall findings of the selected studies. For example, any positive effect on bone outcomes identified? Or are there conflicting findings? Any potential explanations for non-significant results?	The Technical Brief is not intended to be a systematic review, so this is outside the scope of the report. The purpose of the Technical Brief is to provide a brief overview of vibration therapy, including the current understanding of theoretical benefits and harms, contexts in which it is used, and a description of the populations, types of vibration therapies, comparators, and outcomes that have been studied. We restrict our review to describing studies that have been done and do not attempt to rate the studies or summarize the outcomes or effectiveness of vibration therapy.
Peer Reviewer #1	Summary and Implications	Regarding impact of compliance, please refer to the sub-group analysis presented in Rubin et al. 2004.	This reference is included.

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Peer Reviewer #1	Summary and Implications	Regarding potential impact of footwear, please refer to Marin et al. J Strength Cond Res 2009;23:2311-6.	We have noted footwear as an issue to consider in study protocols in the Summary and Implications and Next Steps section.
Peer Reviewer #1	Summary and Implications	Please refer to an important paper by Kiiski et al. J Bone Miner Res 2008; 23: 1318-25, in the discussion of safety issues.	We have added this reference in our discussion of safety issues in the Findings section.
Peer Reviewer #1	Summary and Implications	There is a need to address the limitations explicitly at two levels: 1. Studies reviewed and 2. The systematic review itself.	The Technical Brief is not intended to be a systematic review, so this is outside the scope of the report. The purpose of the Technical Brief is to provide a brief overview of vibration therapy, including the current understanding of theoretical benefits and harms, contexts in which it is used, and a description of the populations, types of vibration therapies, comparators, and outcomes that have been studied. We restrict our review to describing studies that have been done and do not attempt to rate the studies or summarize the outcomes or effectiveness of vibration therapy.
Peer Reviewer #1	Summary and Implications	Throughout the discussion, please provide proper citations when referring to the findings of particular studies included in this review.	We have corrected the formatting issues.
Peer Reviewer #2	Summary and Implications	The authors raise some very important points in this section. For example, p. 11 l. 14-26, the viability of whole-body vibration as a stand-alone or adjunctive therapy is an important consideration.	Thank you for your comments.
Peer Reviewer #2	Summary and Implications	p. 12 l. 19-35 The authors correctly point out that bone density and fracture outcomes do not show fast responses. Some discussion about using pQCT techniques here is merited. There are some advantages to using pQCT to detect bone changes compared to DXA. Also, somewhere in this paper there should be a distinction made between areal BMD and volumetric BMD.	We have added discussion of these points.
Peer Reviewer #3	Summary and Implications	The summary and implications were concise and key points and recommendations were high-lighted. Recommendations are clearly stated in the next steps section.	Thank you for your comments.
Peer Reviewer #1	Next Steps	The future research section is clear and provides some very good ideas for further investigations in this area of research.	Thank you for your comment.
Peer Reviewer #4	Next Steps	Rather weak statement of future research directions. Need to understand the physics of vibration.	A description of the physics of vibration is outside the scope of this report.

Commentator & Affiliation	Section	Comment	Response
Public Reviewer Ezenwa	Next Steps	It is worth noting that it is imperative to conduct studies on the effect of whole body vibration on stages of osteoporosis without mixing the study strategy with forms of other intervention such as exercise and others, and to detail the vibration parameters. Irrespective whole body vibration conceptual framework, this knowledge will be helpful to health decision makers, third party payers, and the consumer.	We have noted that it is important to explore whole-body vibration therapy as both a distinctive and adjunctive therapy and the importance of exploring subgroups of patients with differing risks and severity.
Peer Reviewer #2	Appendix A	p. A-1 The authors need to revise the criteria for the bone density classifications. For example, normal bone density is a T-score greater than or equal to -1.0. Refer to the recommendations of the International Society for Clinical Densitometry by Baim et al., 2008.	We have corrected the error in these classifications.
Peer Reviewer #1	General	The report is clinically meaningful, especially considering the increasing interest in whole body vibration (WBV) therapy in both clinical and research communities. The key questions asked are appropriate and the literature search is comprehensive.	Thank you for your comments.
Peer Reviewer #1	General	Generally, the report is well structured, but more details should be included in the methods section. The main points can be made more explicit. The conclusion is balanced.	Thank you for your comments.
Peer Reviewer #2	General	This manuscript is a technical brief on the use of whole-body vibration as a treatment for osteoporosis. This topic is timely and important as these devices are being made readily available to the public and there are not specific guidelines available for use in persons with low bone mass. Therefore, the report is clinically meaningful for the target population of osteoporosis patients. The report does a good job identifying key questions and describing the evidence for the target population. Some of the sections could be strengthened.	Thank you for your comments.
Peer Reviewer #2	General	This report is well-organized and clearly presents the main points. It serves its purpose as a technical brief.	Thank you for your comment.
Peer Reviewer #3	General	This technical brief is meaning for individuals considering recommending whole body vibration to individuals with osteoporosis. The guiding questions used for this technical brief to guide the data collection where appropriate and thorough.	Thank you for your comments.
Peer Reviewer #3	General	The paper is well structured and organized from the table of content through the appendices. The summary and implications were concise and key points and recommendations were high-lighted. The conclusions could be used to inform practice decisions.	Thank you for your comments.
Peer Reviewer #4	General	Clinically meaningful. Provides good survey or what is known clinically. Weak on the physics of vibration, and does not benefit from the wealth of research information extant on work-related vibration injury, which would shed light the topic.	Thank you for your comments. A description of the physics of vibration is outside the scope of this report.

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Public Reviewer Recker, NOF	General	The draft technical brief states that "claims about whole-body vibration therapy for the prevention and treatment of osteoporosis cannot be made without further research." It may be noted that one of the cited articles, in the draft technical brief, which was a systematic review and meta-analysis of randomized controlled trials about whole-body vibration, concludes that "before recommendations can be made for clinical practice, large-scale long-term studies are needed to determine optimal magnitude, frequency, and duration." NOF agrees that additional research is needed on whole-body vibration therapy.	Thank you for your comments.
Public Reviewer Leismer, VibeTech	General	Passive vibration therapy (PVT) is a modality of vibration therapy that is in the early stages of development by VibeTech, Inc. (http://vibetechglobal.com). This modality changes the form of the technology from one which is best suited for able-bodied individuals, to one that allows access by users regardless of their level of mobility. This unique technology provides targeted, variable loading to the user in a seated or supine position without requiring any physical exertion by the user. In the current form of the PVT technology, static compressive loading is achieved in the lower extremities and is deemed the "preload", while low-intensity vibrations are superimposed to render a therapeutic effect. The technology goes one step further by allowing for full adjustability in vibration frequency and amplitude via a novel variable displacement actuator. Factors that can be adjusted and tightly controlled for with this new technology include: frequency, displacement, preload, and joint angle. The device generates uni-axial vibration at the footplate (equivalent to vertical vibration on a whole-body vibration platform). As of the date of this technical brief, VibeTech has 1 issued patent and 3 pending patent applications that describe this technology. VibeTech has current and pending clinical studies to evaluate the effectiveness of its PVT technology in nursing home and assisted living populations with mobility impairments (both muscle and bone parameters are being analyzed in conjunction with the treatment).	We have mentioned the development of this new technology.
Public Reviewer Leismer, VibeTech	General	Not commonly discussed in the literature is the fact that vibration magnitudes greater than 1-G cause the user to lift off the vibration platform upon each vertical oscillation. Depending on the frequency of the system, the user may not return into contact with the platform within the same oscillation of vibration, thus the input signal to the user can be significantly different than the output produced by the machine. This law of physics provides the grounds for the argument that measured forces at the vibration plate (mean and alternating) are more important than the level of acceleration supplied by the machine.	We have noted this safety concern in our description.