Author's response to reviews

Title: Effect of standing posture during whole body vibration training on muscle morphology and function in older adults: a randomised controlled trial

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Version: 2 Date: 26 July 2010

Author's response to reviews: see over
26 July 2010

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Re: MS: 5333082713385789
Research article
Effect of standing posture during whole body vibration training on muscle morphology and function in older adults: a randomised controlled trial Monica Mikhael, Rhonda Orr, Fleur Amsen, David Greene and Maria A Fiatarone Singh BMC Geriatrics

Dear Editor

Please find attached the authors’ rejoinder to the reviewers’ comments and a revised manuscript. I have placed the rejoinder in blue below each individual question. The emendations made to the manuscript have been made in blue for ease of location. There is however, no indication in the manuscript of deleted text.

Please do not hesitate to contact me if there are queries arising from the revised submissions.

We offer our gratitude for the extension date for the resubmission.

Sincerely,

Rhonda Orr
Reviewer's report

Title: Effect of standing posture during whole body vibration training on muscle morphology and function in older adults: a randomised controlled trial

Version: 1 Date: 23 January 2010

Reviewer: Jun Iwamoto

Reviewer's report:

Mikhael et al. performed a RCT to examine the effects of standing posture during low magnitude WBV training on muscle function and muscle morphology in older adults. They showed that WBV improved muscle strength and contraction velocity in some muscle groups in older adults, but that differential adaptation to standing posture was observed only for upper body contraction velocity. The study is well done, and the paper is well written.

Comments

1. First of all, please clarify the reason why the authors need to report the 3-month effects of WBV training on muscle function (strength, power and velocity), body composition and physical performance, despite the 6-month RCT being designed.

We agree that there may be confusion for the reader. We planned a priori to assess physical performance and muscle outcomes at three months and bone outcomes at six months due to well-known differences in the time course of adaptations in those domains. Therefore we have limited this paper to the completed three month outcomes.

2. Please show scientific reason for choosing 12 Hz in performing WBV training.

We chose 12 Hz to obtain an acceleration of 0.3 g based on ‘the dose recommended by Rubin et al [44] to be beneficial to bone and not destructive to osteoblasts’ (p21).


3. The 3-months effects of WBV could be attributable to hormones and growth factors. Please discuss this point.

There have been suggestions that WBV adaptations may also develop from vibration-induced fluctuations in hormones. An acute bout of WBV increased levels of testosterone and growth hormone and decreased cortisol (Bosco et al., 2000). Enhanced production of growth-stimulating hormones and attenuated production of growth-inhibiting hormones possibly contribute to gains in skeletal tissue observed in other studies (Flieger et al., 1998; Rubin et al., 2001a,b; Oxlund et al., 2003; Christiansen and Silva, 2006; Gilsanz et al., 2006; Xie et al., 2006; Judex et al., 2007). Not all these studies examined the effect of WBV alone on hormones. It is possible that the concomitant exercise may have been responsible for the increases in hormonal levels.
By contrast, other reports indicate that serum concentrations of growth hormone, testosterone, and insulin-like growth factor were unaffected following an acute bout of WBV (Di Loreto et al., 2004, Kvorning et al., 2006, Cardinale et al., 2008). Cardinale et al., 2008 also showed that IGF-1 levels were elevated immediately-, 1 h-, and 2 h-post-WBV plus static squat vs. static squat alone in elderly subjects following 5 min of WBV exercise.

To date, the literature is unclear as to how WBV exercise in isolation affects systemic hormones.

4. Limitation ought to be discussed regarding the sample size.

The limitations due to sample size were discussed on page 21. We identified the study as a pilot and consider this a reason for a type II error.

‘There are several limitations in our study design. The study was underpowered for the secondary outcomes, increasing the likelihood of a type II error.’

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

'I declare that I have no competing interests.'
Reviewer's report

Title: Effect of standing posture during whole body vibration training on muscle morphology and function in older adults: a randomised controlled trial

Version: 1 Date: 18 March 2010

Reviewer: Stephen R Stannard

Reviewer's report:

BMC Geriatrics, MS ID: 5333082713385789

Effect of standing posture during whole body vibration training on muscle morphology and function in older adults: a randomised controlled trial

Monica Mikhael et al.

Summary

This randomized controlled trial was undertaken to compare the effects of three months of vibration platform therapy with bent and straight knee on upper and lower body skeletal muscle function. The results showed that upper body contraction velocity increased with flexed knee exercise and lower body strength increased with locked knee exercise. The (only) novel finding pertaining to the hypothesis was that locked knee vibration exercise improved upper body contraction velocity.

This was a carefully written paper, free from spelling and grammatical errors.

Major Revisions

The experiment is reported as being a 6 month randomized controlled trial, yet only the three month data is included. It is my opinion that if the research team waited and published both 3 and 6 month data the resulting publication would have considerably more impact and represent more robust scientific reporting. There are two reasons for this:

1) When subsequently reporting the 6 month data, you must again report the pre-training data and/or the 3 month data for comparison. Normally it is not acceptable to report the same data set twice within the literature.

2) If you chose not to report the 3 month data when publishing the entire (6 month) study you may miss important difference in training response which occur in the first 3 months compared to the second three months. Indeed it is possible that functional improvements may occur in the first three months, but disappear in the second three month period. If you then only report pre-training and 6 month data, you would miss any improvements all together. If you DID report the 3 month data again when publishing the entire study, you would be presenting the data twice. Furthermore, reporting the entire study would allow body composition data to be included.

Response for 1) and 2)

We agree that there may be confusion for the reader. We planned a priori to assess physical performance and muscle outcomes at three months and bone outcomes at six months due to well-known differences in the time...
course of adaptations in those domains. Therefore we have limited this paper to the completed three month outcomes.

The authors need to clarify what they mean by “lateral acceleration” (pg 19) when describing the vibration platform used. Normally the force (and thus acceleration) would be vertical in nature when applying WBV to a person in a standing or squatting position so that the force being applied at the feed directly opposes that of gravity. If the acceleration produced IS lateral, I can’t understand how the intervention would work!

Agreed, lateral acceleration has been omitted.

It is not clear how you set a pneumatic resistance machine to produce percentages of 1RM; perhaps this is a characteristic of the Keizer machines, but this should be mentioned. Also, power is a product of force and velocity so if you set the resistance, you are measuring velocity and calculating (not measuring) power. Also, if speed of muscle shortening is increased (e.g. upper body) with LK for the same resistance, this means power is increased. However, to increased speed from a stationary position when resistance is the same, means that either acceleration was for a longer period, or force (strength) was also increased.

The Keiser pneumatic resistance machines enable 1 N increases in resistance so precise percentages of 1RM can be set. We consider that power testing is not a novel practice and full description of the test is not necessary. The reference given [49] is our previous paper. Force is set, velocity and distance are measured and power is thus calculated 400 times/sec, and average power produced over the concentric contraction is thus captured. The peak power over a range of %1RM is reported.

The complete description from [49] follows:
Peak muscle power and velocity were assessed once at 20%, 40%, 50%, 55%, 60%, 65%, 70%, 75%, 80% and 85% 1RM on the same five resistance machines used for strength testing. The concentric phase of each repetition was performed as rapidly as possible and the eccentric phase over 3 seconds. All trials were verbally cued ‘1..2..3..Go!’ One trial at each load was given with 30-60 seconds rest between loads. The Keiser A400 software calculated work and power during the concentric phase of the repetition by sampling the system pressure (force) and position at a rate of 400 times per second. Power was calculated as the average power between 5% and 95% of the concentric phase (excluding the first and last stroke to eliminate artefact). The highest mean power produced throughout the loads tested, was recorded as the peak power. Total peak power was calculated by summating the peak power values obtained in the 5 exercises. Velocity was the highest speed in the cylinder between 5% and 95% of the concentric phase.

Given that the novel aim of the study was to compare locked and flexed knee vibration, the result that only upper body contraction velocity was different between these two treatment groups is a little disappointing, but interesting nevertheless.

The lack of result could be due to a type II error as discussed in limitations

Minor revisions

You should include participant numbers in each table description.

This has been done.
I don’t think you need note twice that the study was probably underpowered.

The lack of result could be due to a type II error as discussed in limitations.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interest
Reviewer's report

Title: Effect of standing posture during whole body vibration training on muscle morphology and function in older adults: a randomised controlled trial

Version: 1 Date: 11 March 2010

Reviewer: Tom J Hazell

Reviewer's report:

Major Compulsory Revisions

1. The idea of the study is of interest but why not wait till the end of the 6 month training protocol to present both the mid and end time points? It is confusing to refer to pre-tests that were not measured at 3 months and to 6 months of training when only 3 month measures were completed. If the data is stand alone at the 3 month time point as presented then the mention of it being a 6 month training study is unnecessary. Why not complete the 6 month study and report all the data?

We agree that there may be confusion for the reader. We planned a priori to assess physical performance and muscle outcomes at three months and bone outcomes at six months due to well-known differences in the time course of adaptations in those domains. Therefore we have limited this paper to the completed three month outcomes.

2. The limitation of the lack of familiarization trials is a large one. The lack of familiarization trials means that a learning effect could explain much of the response over time rather than a training effect. It is questionable that the control group would see such increases from just standing with no exposure to WBV and this may suggest the increases are due to performing the measures for the second time.

We agree that the lack of familiarization is a limitation and that was acknowledged: ‘A lack of familiarisation tests prior to baseline assessment, as well as different assessors for baseline and three month testing may have led to results confounded by learning effects and differences due to assessor encouragement and testing experience.’

Although a lack of familiarization may have contributed to changes over time, this learning effect would have affected groups equally and cannot therefore explain significant group differences. Additionally the learning effect would only apply to 1RM testing and chair stand as gait velocity and stair climb were tested twice at baseline. Balance performance is generally only tested once, as even small amounts of ‘practice’ may confer a training effect.

It is possible that the flexed knee position adopted by the control group (same as the flexed knee intervention group) has produced the observed improvements in lower extremity functional performance. These are concordant with the improvements seen in the flexed knees group.

However, the improvements observed in the control group could also be attributed to the effect of socialisation. These participants ‘exercised’ as a group three times a week for 3 months. In a previous study of sham exercise (calisthenics) in patients with type 2 diabetes vs Tai Chi as the active intervention, we observed significant improvements in balance and gait speed in both groups (not significantly different from each other).
3. The placing of subjects into groups poses another problem as it was not based on any of the pre-measures made. Why not match subjects based on key measures, i.e., muscle strength, power, performance, or even muscle mass. The small number of subjects is also problematic as is the unequal number of subjects per group. While this is addressed as a limitation it is a significant methodological problem that undermines the results collected.

The allocation of participants into groups was according to the study design of a double blind randomized control study, stratified by gender, age and use of osteoporotic medications, the most robust of study designs. Such stratified randomization with strata selected on the basis of potential confounders of the primary and secondary outcomes of the trial, would be considered statistically more robust than matching. Although there were uneven numbers due to the pilot nature of the study, the success of randomization is suggested by the lack of clinically or statistically significant differences in baseline characteristics among study groups (see Tables 2 and 3).

4. In Figure 1 it appears that the control group performed a similar position to the LK group then the FK group? Is this true? This is not clear in the methods.

Yes the control group maintained the same knee position as the FK group. This was identified in Table 1. This was designed intentionally so that there would be only one intervention difference between controls and the flexed knee group, which was the active vibration stimulus.

<table>
<thead>
<tr>
<th>Vibration Group</th>
<th>Vibration</th>
<th>Posture on Platform</th>
</tr>
</thead>
<tbody>
<tr>
<td>FK</td>
<td>Active</td>
<td>Flexed Knees (20° flexion)</td>
</tr>
<tr>
<td>LK</td>
<td>Active</td>
<td>Locked knees</td>
</tr>
<tr>
<td>CON</td>
<td>Sham Control</td>
<td>Flexed knees (20° flexion)</td>
</tr>
</tbody>
</table>

5. Why report percent changes instead of actual changes over time? Should Figures 3-5 not present the baseline and 3 month post-training data to demonstrate the results more clearly?

The authors’ view was that presenting percent changes over time actually gave the reader a more meaningful and consistent representation of change (which could be compared to other interventions such as PRT), rather than giving absolute values where some of the units may have been less easily understood eg strength (N), power (W), velocity (cm/s) balance (unit less). However, if the editor prefers, absolute changes can be shown.

While the control group was not significantly increased over the two WBV groups statistically, the strength/power measures are consistently higher in the control group which confounds the use of simple percent changes to report the data.

The authors do not share this view as there was no statistically significant or clinically meaningful difference between the groups, and the reported percent changes were analysed with baseline value or a covariate and
percent change as the dependent variable in an ANCOVA model. However, the sample size may have resulted in a type II error. This is acknowledged as a potential limitation (p21).

6. If the increases in leg muscle CSA are clinically meaningful but not statistically significant then shouldn’t the functional performance tests show an improvement? With the control group simply standing for their training resulting in an increase in 2.2 cm² and the FK and LK groups increasing 2.4 and 3.7 cm² respectively may suggest that the standing position alone caused most of the increase in CSA if these increases are in fact important.

Increases in leg muscle CSA do not necessarily lead to improved functional performance tests. There are factors other than muscle mass and strength that contribute to functional performance. Bhasin et al (1996, 1999, 2001) found that even administered anabolic steroids improved muscle cross sectional area and strength but showed no concomitant improvement in functional performance additionally.

7. The results do not cover all measures made and the tables include pre-data that did not get measured at 3 months which is the end point for this study.

Some measures that did not have 3 month results were presented as a baseline representation of the study population. However, the measures that were not assessed at 3 months by design, have now been omitted for clarity.

8. With the training being overseen by two trained research assistants couldn’t they watch for any subjects performing an isometric contraction? Have you done any EMG work to assess this? Has any data been collected on the potential for performing isometric contractions while being exposed to WBV and its effect on muscle strength and power?

The research assistants closely observed the participants during training and reminded them not to intentionally contract leg muscle groups isometrically, but it can be difficult to establish when a participant unconsciously performs an isometric contraction. Obviously, even quiet standing requires muscle contraction compared to sitting or lying, and therefore all standing WBV exposure standing protocols would include such unconscious postural control contractions necessary to stand quietly for 20 minutes. EMG has not been used for assessments. Other studies have conducted isometric exercise during WBV, but our research wishes to test the efficacy of WBV exercise alone.

9. The co-morbidities differ substantially between groups (control group [18] when compared to the FK [8] and LK [9])? Could this have any effect on the results?

The individual co-morbidities listed were the co-morbidities with larger numbers, other co-morbidities were present. The mean number of co-morbidities did not differ significantly across the groups (control group [2.5±1.1] when compared to the FK [1.3±1.2] and LK [2.6±1.19]). These results were already incorporated into Table 2.

Discretionary Revisions

Abstract

-Pg 3 – The purpose of the study should be clarified (ie. why examine the differences in standing posture?).
The authors were adhering to the word limit policy of the journal. The purpose has been clarified in the background.

-Pg 3- Methods are inaccurate as the current study was on 16 people who completed 3 months of training and not 19 men and women participating in 6 months of training.

19 participants were randomized into the study and participated in training, 2 withdrew and 1 participant’s results were not analysed. The results clarify that n=16 completed 3 months of the study

-Pg 3 - The results are unclear. Why not use a specific format (ie. lower body strength and power followed by upper body strength and power).

The authors agree and will change the order.

Background

-Pg 5 - The explanation of the proposed mechanism by which WBV acts is unclear. Do alpha-motorneurons cause motor units to contract or do the muscle fibres contract? The referencing and explanation of the proposed mechanism of action should be more clear.

This has been clarified to read

**WBV uses high-frequency mechanical stimuli generated by a vibrating platform which are transmitted through the body [25]. The mechanical stimuli produced are thought to use neural pathways, stimulating muscle spindles, the sensory receptors located within the belly of the muscle. The la afferent signals are transmitted monosynaptically to activate alpha-motoneurons, initiating muscle fibre contractions [26, 27, 28]. The vibration stimulus is thought to result in a tonic vibration reflex, or tonic contraction of the muscle [29].**

-Pg 6 - There are a large number of WBV training studies on older adults demonstrating positive adaptations that should be used as the background literature to explain the rationale for this study (see Bogaerts et al. 2007, 2007, 2009; Furness & Maschette 2009; Machado et al. 2009; Raimundo et al. 2009; Rees et al. 2008, 2008; Runge et al. 2000).

The authors have provided 14 references (refs #2, 30-40) to indicate the reported improvements to muscle function, balance and muscle plasticity (p5-6). The salient point made on p6 is that there are few studies that examine the effect of WBV in isolation (ie without the use of concomitant static and dynamic exercise on the platform). Most of the literature suggested above does not solely use WBV as the active intervention, as our systematic review evaluates this (Mikhael M, Orr R and Fiatarone Singh. The effect of whole body vibration exposure on muscle or bone morphology and function in older adults: a systematic review of the literature. Maturitas. 2010; 66(2):150-157).

-Pg 7 – the specific hypothesis should not include bone strength and density as no post-bone measures were completed or presented.

The authors agree and have omitted the bone strength and density measures

-Pg 7 – The rationale for flexed knees increasing muscle activity should be supported with relevant literature examining WBV and muscle activity (see Cardinale & Lim 2003; Roelants et al. 2006; Abercromby et al. 2007; Hazell et al.
Additional references to the literature have been made (p7). The inclusion reads:

The static flexed knee condition during WBV training has been shown to significantly increase activation of leg muscles (Hazell et al, 2009, Roelants et al, 2006)

Methods

-Pg 7 -The current study is 3 months not 6 months. The continual reference to 6 months of training is misleading and inaccurate.

We have omitted the reference to 6 months

-Pg 8 & 12 -Should body composition be reported when post-measures of body comp were not performed?

We have omitted the body composition measures

-Pg 9 -Exclusion criteria includes acute or lower back pain but one of the co-morbidities is chronic lower back pain?

The text has been amended to acute lower back pain

-Pg 9 -Both the frequency and amplitude should be in the methods. Why use 12 Hz and 1 mm? The rationale that it is “beneficial to bone and not destructive to osteoblasts” needs to be further substantiated. There are several WBV studies on older adults showing WBV stimuli of higher frequencies and amplitudes are beneficial to bones (ie. Verscheuren et al. 2004).

The frequency and amplitude are stated in Table 1. 12 Hz and 1 mm amplitude were used to produce an acceleration of 0.3g as determined by Rubin (Rubin C, Turner AS, Mallinckrodt C, Jerome C, McLeod K, Bain S. Mechanical strain, induced noninvasively in the high-frequency domain, is anabolic to cancellous bone, but not cortical bone. Bone. 2002 Mar;30(3):445-52). The authors have used 0.3g as a safe an effective vibration dose in other studies.

-Pg 11 -Did the subjects use their arms to balance while on the platform? The subjects holding on to the bars could potentially have been the reason for the increases seen in upper body strength and velocity. It doesn't appear so from Figure 1 but this should be clarified in the methods.

The participants did not use their arms. They were positioned by their sides during the training sessions. This is described in the methods (p10):

‘All participants stood on the vibration platform with their feet shoulder-width apart, hands by their sides, and wore standardised thick cotton socks to prevent any dampening that might result from footwear [46].’

-Pg 11 -Can you comment on the potential dangers of subjects standing erect on the platform with locked knees? Most WBV platform manufacturers suggest not standing upright on the platform to prevent transmission of the accelerations to the head.
The potential dangers of long-term WBV are not yet elucidated. High amplitude and low frequency combinations have been suggested to be more potentially injurious than low amplitude, high frequency regimes. Rubin et al (ref #44) have suggested that locked knees transmits the low magnitude vibration (<0.4g) signal relatively safely to the hip and spine. Most commercial manufacturers are not able to produce vibration platforms that give accelerations as low as 0.5g, hence their warnings of not standing with locked knees.

-Pg 12 -Why was power tested at 9 different percentages of 1RM? If doing this was required then why are the data not presented at each percentage? Also, it is not clear which power data are presented in the results/tables.

This is a standard procedure Prof Singh has developed for power testing (de Vos NJ, Singh NA, Ross DA, Stavrinos TM, Orr R, and Fiatarone Singh MA. Optimal Load for Increasing Muscle Power during Explosive Resistance Training in Older Adults. The Journals of Gerontology: Series A: Biological Sciences and Medical Sciences. 2005; 60A(5):638-647).

The outcome of interest is peak power. Peak power occurs across a range of percentages of peak strength (usually 50-80%) but can be determined by measuring power through the full range of strength.

Table 3 indicates that the measure is Peak Power. No power data are reported in the Results

-Pg 12 – Suggest that there is a separation of the pQCT and body composition DEXA so it's clear that the DEXA was for body composition and the pQCT was for muscle CSA.

This section has been revised.

-Pg 13 -Are Height and Weight really covariates? Weight should be mass because weight is the force exerted by a given mass and this should be changed throughout the entire manuscript.

The authors agree and this has been changed throughout the manuscript. Height and weight are descriptors and potential confounders which would have been used as covariates if any had differed between groups.

-Pg 14 – Which variables were not normally distributed and which were measured with non-parametric stats?

All measures were normally distributed

-Pg 15 – The use of the month when each subject’s baseline assessment for muscle performance and body composition as a covariate is rationalized by a reference using post menopausal women, is this necessary for men too? This is relevant when you have more men than women in your WBV training groups.

Body composition (muscle, bone and fat) change with the seasons in both men and women, due to the influence of Vitamin D levels and physical activity changes in winter (see ref #53).

Results

-Table 1 is not necessary where 8 of the 11 columns are identical across all three groups. At the very least it could be significantly reduced to avoid the repetition.

This table was simplified as suggested.
-Pg 16 – Compliance was over 13-17 weeks? Wasn’t the study 3 times per week for 3 months/12 weeks? Where does 13-17 come from? This is unclear.

It is rare that participants have 100% attendance and complete their full training requirement in the minimum study duration. We have thus allowed the participants an additional 4 weeks to complete the total number of training sessions required. This was a proof of concept (efficacy) study. We wanted to ensure that the same dose was received if possible by all participants.

-Pg 16 – Is it necessary to report the pre-DEXA data when a post-test was not completed? Should the pre-data for muscle performance not be in a table with the post-data for performance to show the reader the actual pre-values and post-values instead of a percent change? Maybe Tables 3 and 4 could be modified and combined.

As stated in #7, DEXA and muscle performance data were presented as a baseline representation of the study population. We have modified Table 3 as previously indicated but prefer not to combine or modify Tables 3 and 4. We will leave this to the discretion of the editor.

-Pg 17 – The primary outcomes section could be more clearly and thoroughly presented. This particular section omits lower body power results as well as the muscle performance data. Perhaps using a simple format with sub-headings that cover the 4 measures you made: lower body strength and power then upper body strength and power followed by muscle performance tests.

Lower body power results as well as the muscle performance data are presented in Tables 3 and 4. There were no significant changes in these measures and a text version of these findings would have been repetitive. We have added: ‘No significant changes were observed in muscle peak power in any group (Table 3).’

Discussion

-Pg 18 – Would the data collected at 6 months help with the potential Type II errors?

We believe it is possible.

-In general, this section does not adequately discuss the results in terms of how they compare to other literature and what the potential mechanisms by which WBV causes the reported adaptations.

-The idea that contraction velocity and muscle power is extremely important in older adults is a great point but it needs to be supported better with the available literature that also demonstrates WBV may increase power. See the references listed above that have not been referenced.

-While the result of an increase in upper body strength/power is intriguing and surprising there has been some muscle activity work in static postures examining lower and upper body muscles (see Hazell et al. 2007).

This study used concomitant static exercises with WBV and so the results cannot be compared to our study which examines WBV in isolation.
A paper by Machado et al. (2009) looked at the ability of WBV training to increase muscle mass, they used CT scans but its still relevant as it is one of the few WBV papers looking at body composition.

This study used concomitant static exercises with WBV and so the results cannot be compared to our study which examines WBV in isolation.

Do you believe the simple standing protocol to be intense enough to cause significant adaptations? Maybe the discussion should comment on the fact that dynamic exercises may need to be performed with WBV exposure to significantly increase power, performance, and muscle mass in older adults.

The purpose of this study is to clarify the independent effects of WBV on muscle morphology and function. Many published papers have attributed adaptations to WBV when the intervention has in fact been WBV + exercise (isometric or dynamic). We agree that future studies with a factorial design preferably are needed to further substantiate isolated and synergistic effects of WBV and exercise on these outcomes.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare I have no competing interests.