

Author's response to reviews

Title: The feasibility of whole body vibration in institutionalised elderly persons and its influence on muscle performance, balance and mobility: a randomised controlled trial. [ISRCTN62535013]

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Author's response to reviews: see over

RESPONSE TO THE REVIEWERS.

Dear Sir,

We thank you for your contribution to the improvement of our manuscript. We are pleased that the changes we made in the first revision accorded to your expectations. Our response to the second review is listed below in order of appearance. We hope that the answers and the changes we made to the manuscript correspond to your expectations and that the manuscript can be accepted for publication. Nevertheless, feel free to make all necessary supplementary linguistic and editorial changes.

Reviewer Olivier Bruyere

Reviewer's report: *None*

What next?: *Accept without revision.*

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

Quality of written English: *Acceptable.*

Statistical review: *No.*

Reviewer Christophe Delecluse

Reviewer's report: *no further remarks.*

What next?: *Accept without revision.*

Level of interest: *An article of importance in its field.*

Quality of written English: *Acceptable.*

Statistical review: *No.*

Reviewer Vance Berger

Reviewer's report: *I think the revision looks much improved, and I have only one more question, plus one more comment.*

First, the question. Was the randomization simultaneous because all subjects were together at the same time and in the same place, and randomized together at the same time? Or does this mean only that the allocation sequence was prepared all at the same time, but patients were enrolled sequentially? If the former, then this would effectively eliminate the selection bias that would still be a concern in the latter case (in which case it would have to be investigated). Even in the former case, the elimination of selection bias and the reason why should be stated explicitly.

All subjects were indeed randomized simultaneously, together at the same time and thus not enrolled sequentially. This item has been clarified and a reference has been added in the Methods section of the revised manuscript (Randomisation, first sentence, page 4).

Finally, the comment. The exclusions after randomization are still violations of the ITT approach, and data should be imputed for these missing data, probably using the worst rank approach. See Lachin JM, Worst-rank score analysis with informatively missing observations in clinical trials, CONTROL CLIN TRIALS 20 (5): 408-422 OCT 1999 and Lachin JM, Statistical considerations in the intent-to-treat principle, CONTROL CLIN TRIALS 21 (3): 167-189 JUN 2000.

We understand your concern. First we wish to highlight the fact that these participants have started the study, and then were lost for follow-up: one female presented groin pain (without apparent lesions upon physical examination) after the first exercise sessions and one female became afraid to go to the rehabilitation room; both refused further participation; one male developed airway infection during the study (accompanied with severe decline in clinical condition and confined to bed rest making re-assessment impossible). Therefore, we think these participants cannot be considered as “exclusions after randomization”, but were “lost for follow-up”.

Since the occurrence of airway-infection is not in any way related to the study, it can be assumed that the risk over a six-week period is similar for both WBV+ and control groups. Moreover, airway infection does not correspond to one of the indicators of the ‘disease state’ under investigation, i.e. sedentarism and reduced physical ability in institutionalised elderly. Therefore we consider the latter case as missing completely at random (MCAR) [1] and thus ignorable in our analysis [2]. This has been clarified in the revised manuscript and references have been added (page 6, first paragraph of the Results section line 11-17).

Data-analysis was performed considering the end evaluations of the two female subjects (who refused further participation) as missing values as well as by including them using the worst rank score analysis (WRS) and the last observation carried forward approach (LOCF). After their refusal to further participate in the study we tried to convince the two female subjects to pickup again the study protocol and to participate in the end-evaluations (even if they were not compliant to the study intervention [1]). Unfortunately, they refused any further participation in the study, an issue we were ethically obliged to respect. During the several contacts that have taken place with these 2 subjects we observed no visible worsening in their functioning. Therefore, we feel that substitution of their missing end-evaluation values by the worst rank score (a technique used when subjects are lost for follow-up due to absorbing events like death [2]) is not appropriate here. Therefore, we performed an ‘intention-to-treat’ analysis using the ‘last observation carried forward’ approach as an alternative analysis [1]. Since these approaches lead to distortion of the covariance structure of the data and the mean value [1], we did not report new raw data in table 4. We have added the results of the WRS and LOCF analyses to table 4, the results section and the discussion section of the revised manuscript (Results section: first paragraph line 18-22, second paragraph line 8-16, third paragraph line 4-5; Discussion section: second paragraph, fifth paragraph second line) and the abstract (Results line 6-8).

REFERENCES

1. Lachin JM: **Statistical considerations in the intent-to-treat principle.** *Control Clin Trials* 2000, **21**:167-189.
2. Lachin JM: **Worst-rank score analysis with informatively missing observations in clinical trials.** *Control Clin Trials* 1999, **20**:408-422.