Author’s response to reviews

Title: Web-based exercise versus supervised exercise for decreasing visceral adipose tissue in older adults with central obesity: a randomized controlled trial

Authors:
Marcel Ballin (marcel.ballin@umu.se)
Andreas Hult (andreas.hult@umu.se)
Sabine Björk (sabine.bjork@umu.se)
Emmy Lundberg (emmy95a@hotmail.com)
Peter Nordström (peter.nordstrom@umu.se)
Anna Nordström (anna.h.nordstrom@umu.se)

Version: 2 Date: 17 Mar 2020

Author’s response to reviews:

Authors’ responses to comments by the Editor and reviewers

To the editor: We are most grateful for the opportunity to submit a revised manuscript. The comments and feedback given on the manuscript were insightful, and we have addressed these accordingly in order to improve the manuscript. We hope that you can now reconsider and accept our paper for publication in BMC Geriatrics. Please see our point-by-point responses to the comments by the reviewers below.

REVIEWER #1

I have only minor comment:
1. As author mentioned, some of the results in the current study published previously (JAGS 67:1625-1631), however, participants characteristics differ slightly among intervention group (N=38) in the previous study and SE (n=38) in age, PA levels etc. Please double check data.

   a. Authors’ response: Thank you noting this. We have now double checked and corrected the errors.

2. Authors described the design of the study in both text and figure, however, it was still very difficult to understand the design of the study. Based on my understanding, control group in JAGS 67:1625-1631 later introduced to WE. Were there any seasonal difference between two intervention. Usually, PA decrease during winter season and this may influence the finding of the study.

   a. Authors’ response: The reviewer is correct in that it was the group who served as control group in JAGS 67:1625-1631 which was introduced to WE in the present paper. We now see and agree that
the study design was not sufficiently clearly described in the previous version of the manuscript, and have therefore revised and hopefully improved this considerably for increased transparency and understanding.

Figure 1 has been revised and improved and on P 5, lines 95-108, we have revised the description of the study design:

“This study was a two-armed randomized controlled trial conducted in Umeå, Sweden, during January 2018 – November 2018. Participants were randomized 1:1 to an intervention group or a wait-list control group (ClinicalTrials.gov registration no. NCT03450655). An overview and timeline of the study, follow-up assessments and delivery of interventions is presented in Figure 1. Following randomization and baseline assessment, the intervention group received SE for 10 weeks at a university hospital research clinic, while the wait-list control group lived as usual. After this initial 10-week phase, both groups underwent follow-up assessment at the research clinic. The 10-week results of the trial have been published previously (27, 28). Next, the wait-list control group underwent a 10-week wash-out period, after which they returned to the research clinic for another reassessment, which served as baseline in the wait-list control group’s intervention. The wait-list control group’s intervention was 10 weeks of WE, after which they returned for a final follow-up assessment. To compare the effects of the two interventions, changes in the outcome variables during weeks 0-10 in the SE group were compared to changes in the outcome variables during weeks 20-30 in the WE group.”

In terms of potential seasonal difference, we have now added to the manuscript on P 6 line 117-118 that the participants were recruited during January 2018 – February 2018. It is an insightful comment by the reviewer that PA levels differs depending on the season, especially during winter when participants may be less likely to be physically active outdoors. However, this is not likely to be an important factor in the present study for the following reasons. First, none of the interventions were prescribed during winter season. The SE intervention was conducted in Spring 2018, and as previously reported in JAGS 67:1625-1631, the adherence to the intervention was very high. The WE intervention was delivered in Autumn 2018, and as described in our manuscript, had a similar adherence. However perhaps most important to the comment, the WE intervention was remotely delivered. This means that the participants were able access the intervention at home, at any time that best suited them, regardless of potential seasonal barriers. We are however unable to determine to which extent participants changed their habitual PA outside of the exercise given that PA was only measured objectively during 1 week of registration prior to the start of the present study, as part of the Healthy Aging Initiative protocol.

3. Furthermore, when participants are randomized. Participants who immediately randomized to exercise were more highly motivated compared to participants who were delayed in the intervention. Please discuss this issue if appropriate.

a. Authors’ response: This is an excellent point by the reviewer, for which we are very thankful. We have now revised and extended a paragraph in the discussion section, and included discussion of motivational issues. Please see P 14, lines 315-330:

“To our knowledge, this was the first study to evaluate the effects of vigorous WE on VAT in older adults. We argue that the lack of effect may partly be explained by an insufficient intervention duration characterized by lack of high intensity. This has some support from previous research where longer interventions seem preferable for improving body composition (36) and higher intensities could potentially be more favorable for decreasing VAT (37). While the duration of the intervention was identical in both groups, the larger decrease in VAT in the SE group could partly be explained by the presence of supervisors facilitating for them to quickly learn how to exert a high intensity, as opposed to the WE group which was unsupervised and most likely had an extended learning period. Furthermore, the lack of effect on VAT within the WE group as related to intensity could also be related
to discrepancies in motivation between the groups, given that SE was prescribed immediately after randomization in contrast to the WE which was prescribed at a much later stage. As a result, this would imply that effects of WE may have been slightly underestimated. In order to gain a more detailed and valid understanding of the effects of WE on VAT, and how it compares to SE also in the long-term, parallel randomized-controlled trials with a longer intervention period and additional long-term follow-up assessments are needed.”

REVIEWER #2

1. There are important data missing from the manuscript that may add to the discussion of whether there is value in WE for this population, despite no change in VAT. To increase the impact of this manuscript, it is recommended that the following data be included in a revised manuscript. The inclusion of this data will help determine a more holistic benefit of a WE program. Change in Lipid levels following interventions, Change in fasting glucose levels following interventions, Changes in SBP and DBP, Food logs to determine whether either exercise program changed eating habits

a. Authors’ response: Thank you for this comment. We agree that adding data may be valuable. Specifically, we have chosen to add data on blood lipids and blood glucose. A description of how these outcome measures were assessed has been added to the methods section on P 10-11, lines 223-235:

“Total cholesterol (TC, mmol/l), high-density lipoprotein cholesterol (HDL, mmol/l), low-density lipoprotein cholesterol (LD, mmol/l), triglycerides (TG, mmol/l) were collected by venipuncture by the research nurses and subsequently sent for analysis at the accredited laboratory at the Department of Clinical Chemistry, Umeå University Hospital. Fasting blood glucose (FBG, mmol/l) was measured using the HemoCue 201 RT system (Radiometer Medical ApS, Denmark)

In terms of the effects of the intervention on these outcome measures, please see Table 2. As demonstrated, there were neither significantly different changes in lipids or glucose between WE and SE, nor were there any effects within the WE group. Consequently, we have added a discussion of these findings on P 15-16, lines 352-361:

“Looking at the cardiometabolic blood markers, WE had no effect on lipids and FBG. This is in contrast to a previous study which demonstrated positive effects of WE on FBG and TC(44). However, the participants were adults with type 2 diabetes, which would explain the beneficial effects of the interventions given that exercise is more effective for improving metabolic outcomes in those with initially higher values (45). In the study on older adults by Wijsman and colleagues, there were small, albeit significant, effects of their WE intervention on FBG and lipids, possibly due to the greater weight-loss in their study compared to ours(26). Given the inconsistent results, additional randomized controlled trials including older adults with hyperglycemia and dyslipidemia are required in order to establish the effectiveness of WE on cardiometabolic risk markers in older adults.”

In terms of blood pressure, our data are unfortunately very problematic and we do not think that these are suitable for inclusion in the present manuscript. As demonstrated in our previous paper (PMID: 31564841), the wait-list control group significantly reduced their blood pressure during the first 10 weeks of the study. By the time they were re-assessed prior to starting WE, they had reduced their blood pressure even further, resulting in large and statistically significant differences between the groups in blood pressure (p < 0.001, please see Table 1). When then analyzing changes in blood pressure within the WE group (data not shown in previous version of manuscript), there was actually a slight increase in blood pressure following the WE intervention (around +3 mmHg in SBP and 1 mmHg in DBP). This is most likely due to the fact that these participants were not presenting
diagnostic values of blood pressure, compared to SE group (128 mmHg vs 143 mmHg at baseline, p < 0.001 for difference). It is well-established that exercise has more pronounced effects in individuals with higher BP than in those with lower BP (PMID: 23608661), and even though we adjust for baseline values in the ANCOVA-analysis, this analysis does not take into account the issue mentioned above in terms of the effect of exercise on blood pressure being dependent on diagnostic values. Thus, it is not surprising that there was a reduction in the SE group (-7 mmHg, PMID: 31564841) but no effect/slight increase in the WE group. Another dilemma with the blood pressure data is that during the follow-up assessment of the WE intervention, there were participants who reported that they had gone off their antihypertensive medications, which severely confounds the data and distorts the true effects of the intervention. Based on these facts and arguments, we believe that including data on change in blood pressure after WE would not improve the manuscript or increase its impact. Instead, it would potentially be misleading, and could increase the risk that the potential benefits of WE on blood pressure are dismissed incorrectly. In order to evaluate the effects of WE, or any exercise intervention for that matter, on change in blood pressure, it is critical to include participants with diagnostic values, or at least compare groups that are equal, and not with such a considerable difference (15 mmHg) prior to the initiation of the intervention, especially since positive effects have been reported in a similar study on older adults, where the baseline value in blood pressure was considerably higher (146/86, PMID: 24195965) than in the present WE group (128/80).

Finally, while we definitely agree that food logs would have been of great interest and value to determine whether dietary habits were altered during the intervention, food logs were unfortunately not used in the present study.

1. Also, the authors should more clearly explain whether the sample was split into 2 groups or if it was the same group used following a washout period. The text implies same group and washout, but he figure show two separate groups.

a. Authors’ response: We agree that the study design was not sufficiently clearly described, and the figure was a bit confusing. There were 2 groups in the present study – intervention group and wait-list control group. Intervention group performed SE. Wait-list control initially served as a control group in the first phase of the study but were offered WE at a later stage in the study (after the wash-out). To increase transparency and improve understanding, we have revised Figure 1 as well as the text at P 5, lines 94-108:

“This study was a two-armed randomized controlled trial conducted in Umeå, Sweden, during January 2018 – November 2018. Participants were randomized 1:1 to an intervention group or a wait-list control group (ClinicalTrials.gov registration no. NCT03450655). An overview and timeline of the study, follow-up assessments and delivery of interventions is presented in Figure 1. Following randomization and baseline assessment, the intervention group received SE for 10 weeks at a university hospital research clinic, while the wait-list control group lived as usual. After this initial 10-week phase, both groups underwent follow-up assessment at the research clinic. The 10-week results of the trial have been published previously (27, 28). Next, the wait-list control group underwent a 10-week wash-out period, after which they returned to the research clinic for another reassessment, which served as baseline in the wait-list control group’s intervention. The wait-list control group’s intervention was 10 weeks of WE, after which they returned for a final follow-up assessment. To compare the effects of the two interventions, changes in the outcome variables during weeks 0-10 in the SE group were compared to changes in the outcome variables during weeks 20-30 in the WE group.”