Author's response to reviews

Title: The minimal clinically important difference of six-minute walk in Asian older adults

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Response to reviewers’ comments

The minimal clinically important difference of six-minute walk in Asian older adults

Boon Chong Kwok
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The manuscript has been revised and the replies to the comments made by the reviewers are reported in this document.
Response to 1st reviewer’s comments: Torunn Askim

Thank you for the advice to enhance our manuscript. Below are the point-to-point responses to the queries about the manuscript. We hope that the responses have adequately addressed your concerns about our manuscript.

Major revision:

1. The research question is not very original in itself as several studies have assessed the MCID of 6MWD earlier. The authors give reference to two of these previous studies but have not mentioned a third study by Gremeaux et al, published in Archives of Rehabilitation Medicine in April 2011. This study should also be added as a reference to the Introduction. However, the MCID in a frail old Asian population is not investigated earlier and could be of interest to its field.

**Response:** The authors are grateful on your sharing of an important literature. We have revised the introduction and included it in the 3rd and 4th paragraphs of the Introduction section.

2. The aim is to ‘determine the MCID for 6MWD from a modified 6-minute walk test protocol in moderately frail older adults with a fear of falling.’ The phrase ‘modified 6-minte walk test’ is a bit confusing. If the only modification is the 10 versus 15 metres walking distance it would be better to not mention the modification in the aim but describe the test protocol in detail in the methods section. If you have done other modifications, please explain and revise the text accordingly. The aim should also include ‘Asian older adults’ as this is the specific population under investigation.

**Response:** The only difference in conduct of our 6MWD is the distance and we have revised the phrase to prevent confusion to the readers. The term ‘modified’ has been removed from the 6MWD. The revised aim can be found in the last sentence (last paragraph) of the Introduction section and quoted below.

“Therefore this study was undertaken to determine the MCID for 6MWD in moderately frail Asian older adults with a fear of falling.”

3. The definition of 6 minute walk distance (6MWD) is rather unclear. How does the 6MWD differ from the 6 minute walk test? And, how is the modified 6-minute walk test protocol defined? This issue need to be clarified. It is also unclear to me how and when the GROC was administered. I assume that you assessed the patients on a range of different outcome measures in the RCT. Was the GROC administered in close relation to the 6MWD or not? How did you ensure that the included patient gave their answer in relation to their change in walking distance and not for example in relation to their change in quality of life?

**Response:** Our 6MWD differed only in distance and we have overlooked this confusion, thus it should not be considered modified. Quoted below is an additional sentence added to paragraph one of Methods – Outcome measure section.
“We decided that this minor change would not drastically impact our study findings because a study found no statistical significant difference between using two different walkway lengths, 20m vs 50m.”

With regard to the GROC, the participants reported their change with respect to their overall health change from baseline. Administration of the GROC was not biased to any particular outcome measure. As the 6MWD is representative of health, we chose to use the term ‘overall health’ in the question. This was described in paragraph two of Methods – Outcome measure section.

“The outcome assessor questioned each participant during the follow-up by asking, “Overall (health), how much change do you perceive after the intervention compared to baseline?” which was in relation to the overall benefits experienced from the intervention.”

4. Another weakness is the poor report of change in outcome measures from before to after the intervention period. Did a real change occur or not? What is the actual distance walked at baseline and at follow up? These results should be reported either in a separate figure or in a table to help interpretation of the results.

Response: As per advice, a new Table 2 was added to address the concerns of 6MWD data representation. Specifically, we found that the changes in 6MWD were 9.3 and 37.3 m when comparing between the 2 groups.

5. A mean change of 35 metres is reported. Was this a statistical significant difference? Did the change exceed the measurement error for the 6MWD in this population? It is recommended that calculation of MCID is based on both an anchor-based and distribution based method. It will strengthen this paper significantly if the authors add a distribution-based method, such as SEM or effect size to their analyses.

Response: We have now improved the representation of 6MWD, including the 35 m change and statistical significant in Table 2. A distribution-based method using SEM was added to the study and this 35 m has exceeded the 12.9 m (SEM). This can be found in the Results section and quoted below.

“The SEM was calculated from an intraclass correlation coefficient of 0.981 and baseline SD of 93.9 m. These values translated to a SEM of 12.9 m for the 6MWD.”

6. The MCID results need to be discussed against the measurement error reported for 6MWD in other studies. The results also need to be discussed against the actual distance walked. It is likely that MCID will change along the scale of 6MWD. Hence, the MCID will be different in patients/populations with a walking distance of 300 metres compared to patients with a walking distance of 600 metres.

Response: We have included in the discussion our difference in baseline 6MWD against another study. Quoted below is from paragraph 2 of the Discussion section.
“Evidently, the baseline mean of 6MWD in our study was about 300 m as compared to Holland et al’s 400 m, which could account for our smaller MCID value.”

7. The MCID found in the present study is the smallest MCID reported in any population so far. The reliability and validity of this result should be more thoroughly discussed. Assumable, the Asian people have a lower body height compared to western populations and consequently a shorter walking distance, which again could be a possible explanation of the small MCID. BMI, which includes height, is reported so it should be easy to add body height to the patient characteristics to help interpretation of the results.

Response: The body height demographic has been added to Table 1. We have also included this recommendation into our discussion, which is quoted below.

“Furthermore, the participant’s shorter height may be a factor of reduced 6MWD performance [21]. Hence, our MCID estimate would be proportionately smaller as compared to taller non-Asian population.”

8. This study was conducted in relation to a randomised controlled trial and not primarily designed to answer the present research question. This issue should also be listed as a limitation of the study and suggestions for an even more optimal study design should be proposed.

Response: We have included this recommended point into our limitation as quoted below.

“Another limitation was the small number of participants without a GROC change, which might have affected the accuracy of estimating the specificity for the cut-off value. Also, the study was derived from a randomized controlled trial that was not primarily designed to estimate the MCID of 6MWD.”

9. Please also add a reference to the statement; ‘...other definitions of frailty exist’ in the last paragraph on page 8.


10. The relationship to the randomised controlled trial is rather unclear. Are the results from the RCT already published? The authors only give reference to the protocol. It is not sound to publish the results from one of the outcome measures (6MWD) before the main results from the trial are published. It is also unclear whether you included patients randomised to one or both groups. More details about the intervention should also be added to the Methods section. These issues need further clarification.

Response: Our manuscript on the RCT is concurrently under review, and we should mention that the 6MWD is not the primary outcome of the RCT. Falls and falls prevention are the primary outcome
measures of the RCT. Data from both groups are analysed in the study and we have referenced the interventions, which had been reported in detail earlier.

Minor revision:

11. In the title the term ‘6 minute walk’ is used. Please be uniform and use the same term as in the rest of the manuscript (6 minute walk distance or 6 minute walk test).

Response: The term is now standardized to 6-minute walk distance.

12. In the Methods of the abstract, it is stated that ‘Patients who completed the trial rated the intervention efficacy on the GROC’. This is not in line with information given in the full text. Please also see my previous comment on the administration of GROC.

Response: We have corrected this discrepancy and rectified the abstract according to the main manuscript. The change to the Methods of Abstract section is quoted below.

“Participants who completed the trial rated their perceived change of overall health on the Global Rating of Change (GROC) scale.”
Response to 2nd reviewer’s comments: Subashan Perera

Thank you for the advice and opportunity to enhance our manuscript. Below are the point-to-point responses to your queries. We hope that the changes are substantial and have adequately addressed your concerns.

(1) Abstract Results: The descriptive statistics of 6MWD by itself is irrelevant to the main message of the paper. The MCID estimate, sensitivity, specificity, area under ROC curve are all important and relevant results.

Response: We have corrected the Abstract Results based on your recommendation and is quoted below.

“From the anchor-based method, the MCID value for the 6MWD was 17.8 m (sensitivity 56.7% and specificity 83.3%) while distribution-based method estimated 12.9 m.”

(2) Method, Participants: The descriptive statistics on participants are more appropriate for the beginning of the results section.

Response: We have shifted the descriptive statistics to the start of the results section.

(3) Statistical Analysis: last paragraph. "...analysis will be carried out..." should be changed to "...analysis was performed..."

Response: We have corrected the identified phrasing according to your advice in the main manuscript. It now reads:

“Spearman correlation analysis was performed to evaluate the association between changes in fear of falling and changes in 6MWD.”

(4) Statistical Analysis: Why did the authors choose to completely ignore the distribution-based method for determining MCID? Those estimates are functions of SD and reliability, and could be easily computed with the available data and would strengthen the manuscript substantially.

Response: We accept the reviewer’s critique and we have now included a distribution-based method using SEM to strengthen the manuscript. The relevant sentences in the revised manuscript read as follows:

Introduction – “In addition, a second method (distribution-based method) to derive the MCID value was recommended [13,14]. One distribution-based method is to derive the standard error of measurement (SEM), which may be representative of the MCID value [14,15].”

Statistical analyses – “In order to derive the MCID with the distribution-based method, we used the SEM of the 6MWD. The baseline standard deviation, SD, and test-retest reliability, intraclass
correlation coefficient [ICC(3,1)], of the 6MWD among participants who did not perceive change were used to calculate the SEM [12]. The formula for deriving SEM was \( SD \times \sqrt{1 - ICC} \).

Results – “The SEM was calculated from an intraclass correlation coefficient of 0.981 and baseline SD of 93.9 m. These values translated to a SEM of 12.9 m for the 6MWD.”

(5) Table 2: Numbers of participants without a GROC change is too small for estimating specificity with any reasonable level of precision.

Response: We have replaced Table 2 with a more informative Table for better data representation to the readers. We have taken your advice to include the SEM, which would help improve the strength of the estimated MCID.

(6) ROC curve: Change axes to range from 0 to 1 only.

Response: We have replaced the Figure 2 ROC curve with minimal gap at the front and end.

(7) ROC curve: It is not clear why the ROC curve would dip below diagonal.

Response: The ROC curve crossed the line of identity because 16 participants deteriorated in 6MWD performance. These values, when treated as threshold points, were associated with 0% specificity but a high level of sensitivity (detecting all participants who perceived no change in their function).

(8) ROC curve: It is not clear why the ROC curve has only 5 steps. One gets a pair of sensitivity and specificity for each potential cutpoint for 6MWD, and there are most certainly more than 5-6 potential cut points in 73 participants with a SD of 45.2 m.

Response: We have consulted the statistician for our study and the reason for the 5 steps was due to the statistical software scale set up. From the SEM method, 12.9 m was estimated for MCID and we identified 2 cut-off of clinical significance – 14 m and 17.8 m. This can be found in the results section of the manuscript and quoted below.

“There were 2 cut-offs identified from the ROC analysis in Figure 2, AUC 0.70, 95%-CI 0.54 to 0.84, 14.0 m (sensitivity 64.2% and specificity 66.7%) and 17.8 m (sensitivity 56.7% and specificity 83.3%).”