Author's response to reviews

Title: A randomized controlled trial of tai chi for long-term low back pain (TAI CHI): Study rationale, design, and methods.

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Author's response to reviews: see over
Dear Dr. Hoffman,

Re: MS: 1080787280248627

Title: A randomized controlled trial of tai chi for long-term low back pain (TAI CHI): Study rationale, design, and methods.

Thank you for your recent decision letter and inclusion of reviewer’s comments regarding our manuscript. The reviewer’s comments were extremely helpful in improving the overall quality of this manuscript. The comments have been addressed in point form below. The outlined changes have been made to the revised manuscript as per the Editor’s requirements.

Sincerely,

Amanda Hall
Response to Reviewer, Rainer Ludtke’s Comments:

Reviewer's General remarks
All statistical aspects (randomisation, sample size calculation, statistical analysis) are valid, so from my point of view no major compulsory revisions need to be made.

I have, however, some suggestions of minor relevance.

1. Randomisation: Please clarify, whether or not any stratified randomisation is planned (I suppose not).
   ▪ You are correct, stratification is not planned

2. Sample Size calculation:
   o In the first sentence of the respective paragraph you mention that the study was designed to detect a difference of 1.5 pts on the bothersomeness scale, the standard deviation SD being 2.4 pts. This makes a standardised effect of 1.5/2.4=0.625 SD. How does this match to the following sentence, where you assume to detect an effect of 0.5SD?
     ▪ Thank you for picking up on this, we had omitted one of our outcomes; the Pain Numerical Rating Scale detecting a difference of 1pt, scale has SD=2. We have now included this in the text (p.12 last line).

   o As this is not standard procedure, please give a reference to the formula you used to incorporate the correlation of the baseline and change measures. According to my sample size software a two sided t-test will need n=128 patients to detect an effect of 0.5 SD with a power of 80%, but you mention n=154. Did you make any adjustments for non-normality?
     ▪ We agree with your calculation n=128 without any adjustments. However, we did adjust our sample based on findings of previous trials of similar design to allow for loss to follow up as stated in the methods and also for correlation. The reference to incorporate correlation can be found in “An
3. Please clarify, what kind of interaction effects you want to detect (interaction of baseline characteristics with treatment group?).
   - Yes, that is correct.

4. Statistical Methods: I would be pleased if you could add a sentence how you plan to deal with missing values (multiple imputations? Last observation carried forward?…)
   - Although we had originally planned an analysis using linear regression, we have reconsidered and feel it is better to use a linear mixed models approach which can better deal with drop-outs. We have adjusted the text to reflect this decision (p.16 lines 4-7).

5. It is not completely clear whether you want to fit 5 distinct univariate ANCOVAs (referring to the 5 post-randomisation time-points) or a multivariate repeated measurement ANCOVA. Please clarify!
   - We don’t follow this statement as there is only one follow-up time point.

6. In the light of potentially missing values I would suggest to use GEE (generalised estimating equation) estimators, hereby not imputing any missing value and assuming that missing values were at random. But this is not a must!
   - Thank you, we agree and have changed the text to included analysis by linear mixed models (as above p16, lines 4-7).

7. It is not completely clear to me on what basis you want to select potential predictors of outcome. What does it mean that you want to select variables on the base of ease of assessment and psychometric properties? I understood that you tried to beware of muticollinearity of factors but not how you selection procedure goes on, once you found it.
A secondary aim of our study is to potentially develop a Clinical Prediction Rule that can be used by clinicians to determine if tai chi will be beneficial for their patient. Thus, we want to select variables that could be easily assessed in the clinic with measures that have established psychometric properties.

8. It is rather unusual to set $p=0.05$ as a threshold for including or eliminating factors from a regression model. Usually criteria like AIC (Aikaike information criterium) or penalised criteria are adopted. Please comment.
   
   - The threshold for a variable to enter the model would $p<0.25$. $P=0.05$ is for statistical significance for the variable to be retained in the multivariate model.

9. Do you only want to include interaction effects without including main effects?
   
   - No. Our understanding is that you have to enter main effects when examining interaction effects.

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 interests