Reviewer’s report

Title: Sample size estimation for Randomised Controlled Trials with repeated assessment of patient reported outcomes: what correlation between baseline and follow up outcomes should we assume?

Version: 0 Date: 20 Jun 2019

Reviewer: Liz Turner

Reviewer's report:

Overall this manuscript is a valuable contribution to the literature, which would benefit from some careful proof-reading and elaboration on some results.

Here I offer some comments that should help with clarity:

Pg. 4, lines 15-17. It is stated: "an essential step is the calculation of sample sizes that will allow a reasonable chance (power) of detecting a predetermined difference (effect size) in the outcome variable, at a given level of significance." Please could you qualify with a more complete statement to show that power is a conditional statement e.g. something like "when the treatment is actually effective".

Pg. 5, line 3: suggest to amend to something like "assuming equal sample sizes and equal standard deviation per group" so that the SD assumption is stated up front and not only in the description of the parameters.

Pg. 5, line 21: the delta term here is for difference in mean change and not difference in post means as it was in the previous two formulae. Similarly, the common standard deviation for the two groups is for the SD of change. It would help the reader if the notation indicated this e.g. by using something like delta with a sub-script of "change" or something like that for both the delta term and the sigma term - or at least explicitly stating this fact about the SD as well as the mean.

Pg. 6, line 1: "When ρ and σ are known, the test statistic follows a Normal distribution." Stating "the test statistic" sounds like it is referring to something that has already been described but no test statistic has been explicitly introduced at this stage. Please carefully lay out what "the test statistic" is.

Pg. 6, lines 5-7: "a target difference of 0.50 and a standard deviation of 1.0." It could help the reader to be reminded that this is for change in the case of the change analysis.
Pg. 6, lines 5-7. It would be helpful to comment on what is shown in Figure 1 rather than just stating what it is.

Pg. 8, line 4: what is ScHARR? Please spell out the first time it is used.

Pg. 8, line 9: "the correlation between baseline and post-randomisation outcomes were calculated...." Should be edited to "…was calculated…".

Pg. 8, lines 15-16: "a sample mean with allowance for clustering by trial derived from a multilevel mixed-effects linear model with a random effect for the trial". Since there are only 20 trials, it is important to use REML. Please clarify/confirm.

Pg. 8-9: Given that there are 464 pre-post correlations from 20 trials, it would be really helpful for the reader to see the distribution of number of outcomes per trial to help answer questions like: do some trials have basically just a few outcomes and others have a huge number? Or is it because there are lots of time points in some trials. To do this, could the authors add a column to Table 1 that has the number of outcomes in the trial and a second with the number of time points. I know that the reader can infer this from the list of outcomes and from the list of time points, respectively, but those two numbers for each trial could really help the reader to more quickly see where the number "No. of correlations" comes from in Table 1. Note that I realize that the number may not be directly obtained from the product of "no. of outcomes" and "no. of time points" since not all outcomes may be measured at all time points but a footnote could be added to state this.

Could the authors summarize some addition characteristics in the manuscript text including summary stats on number of outcomes per trial and on number of time points. It is really important to note that the 464 correlations are mostly due to there being many time points in a trial than there being many outcomes measured per trial.

Table 1:

- For trial 1, there are 8 time points listed and 2 outcomes so why are there 18 correlations?

- Also, the time points are listed strangely with 3,12 then 12 repeated in the next line and other intermediate time points shown in the next line.

- It would be helpful to know the scale of each measurement. Could that be added to the list of abbreviations, as well as a reference to the validated measures i.e. so that the reader could go and find out more about the measures. It seems incomplete to exclude such information as part of the
degree of correlation is due to the basic measurement properties of the measures e.g. if they are consistent etc.

- For the trial population, please add more details including age range and other important inclusion criteria.

Pg. 12, line 15: "Table 2 shows the baseline to post-randomisation follow-up aggregated by trial." Please summarize what the table shows with a sentence or two in the text.

Pg. 12, line 18: "had less than had less than…” needs to be edited.

Table 2:

- The ordering appears to be alphabetical and is different to Table 1. Why? This is confusing for the reader.

- What is in the "total" row? The mean of the 20 numbers above? No, it looks to be the summary measure again applied to the 20 numbers e.g. for the column labeled max 0.91 is the max of all the max. So what is 0.5 for all 20 numbers in the mean column? Does it mean it is the mean of all 484 correlations? Please label "total" very clearly.

Figure 3:

- Likewise, the ordering is like Table 2 but different to Table 1. Please use the same ordering of trials in all tables and figures.

- It would be helpful if the total number of correlations per trial was also noted e.g. by a number above each box and whisker.

Figure 4

- The regression line is stated as y=0.51-0.04. This is misleading since that is the estimated line for the expected value of y and not y itself. Please edit
**Level of interest**
Please indicate how interesting you found the manuscript:

An article of importance in its field

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

**Quality of figures**

All images and figures within the manuscript should be genuine i.e. without evidence of manipulation. No specific feature within an image may be enhanced, obscured, moved, removed, or introduced. If you have concerns about the veracity of the figures you should choose the first option below.

**Statistical review**

Is it essential that this manuscript is seen by an expert statistician? If so, please give your reasons in your report.

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal

Were you mentored through this peer review?

No