Reviewer's report

Title: A randomised trial of adaptive pacing therapy, cognitive behaviour therapy, graded exercise, and specialist medical care for chronic fatigue syndrome (PACE): Statistical analysis plan

Version: 1 Date: 4 May 2013

Reviewer: Jinhui Ma

Reviewer's report:

This paper reported in detail the statistical analysis plan for the principal papers of the PACE (pacing, graded activity, and cognitive behavior therapy; a randomized evaluation) trial. It also tried to illustrate how the complex intervention, which allowing for the impact of clustering by care providers and multiple care-providers are presented for each patient, was taken into account in the analysis plan.

Major Compulsory Revisions

1. My major concern with this kind of articles is about their length. Their values may fade away when readers find it is difficult to catch the essential message quickly, and consequently lose their interests of reading them in further detail. Apparently there are no strict guidelines on how to report a statistical analysis plan. But based on my experience as a biostatistician for years, I found when variables (primary outcomes, secondary outcomes, explanatory variables, adverse events. etc.) were summarized in a table with variable name, how it is measured, when it is measured and type of the variables (continuous or categorical) etc., both statisticians and clinicians found it was easier to get the key information quickly and clearly. Same thing for the statistical analysis, a table can be built with several columns indicating variable name to be analyzed, statistical method used for analyzing this variable, confounding variables to be adjusted for in the analysis, methods used for model assumption check, methods used for goodness of fit test, etc. Another advantage of providing these tables is that it may be helpful on shortening the main text since the tables speak for itself.

2. My another general suggestion is that a statistical analysis plan for a trial/study, if intent to publish, should be beneficial to other researchers in their future studies, rather than just simply reporting the statistical analysis plan for the present trial/study.

3. In ABSTRACT on page 2, I am expecting some summary of the results, such as what are reported etc., rather than simply saying “The SAP is given in full as approved by the Trial Steering Committee”.

4. In ABSTRACT on page 2, The ‘Conclusion’ section should state what you can conclude from the results (for example the advantage of publishing the SAP etc),
rather than “Online journals offer the greatest potential for publishing….”, which cannot be supported by the results presented in this manuscript.

5. In Section 2.1 Secondary Objectives on page 11, it is not clear what the first objective really means by “As for the primary objectives with outcome as the participants’ self-rated clinical global impression change rating”.

6. In Section 6.4 Method for Handling Dropouts and Missing Data at the first and second line on page 24, the authors stated “There is specific guidance for missing baseline scale data and this will be followed [48]”. This specific guidance should be summarized here rather than just providing a reference.

7. This manuscript provided a statistical analysis plan for the principal papers of the PACE trial. Since a statistical analysis section must be provided in each principal paper when publishing it, the present manuscript should emphasize that the present manuscript is not just the sum of all the statistical analysis sections of the principle papers. Why is publishing this present manuscript important or necessary?

Minor Essential Revisions

1. In Section 2.3 Trial Design regarding “sample size calculations taken from the protocol”, I did not see how the sample size calculation matched with the primary statistical analysis method (mixed-effects linear regressions including participant as a random intercept and investigating adding a random slope on time, as you presented on page 29). How is the clustering effect taken into account?

2. Following my previous question, the sample size calculation was based on the primary outcome/analysis. I am thinking whether it is helpful to provide what statistical power can be achieved for analyzing the secondary outcomes and economic outcomes based on this sample size.

3. On page 39, the title of Table 1 is too short to provide enough information to understand this table. For example, what does the ‘X’ mean when presented in the column “Discontinuation of Follow-up” and row “SF-36PF”? In addition, many abbreviations were used in this table, and detail information regarding what they stand for should be listed at end of the table.

Discretionary Revisions

1. Why do the figures in this manuscript use different arrow symbols? Personally I believe the arrow symbol used in Figure 1 makes the figure look better.

Level of interest: An article of limited interest

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