

July 27, 2009

Thank you for reviewing and accepting manuscript titled "Methodological Issues in Trials of Complementary and Alternative Medicine Interventions" (NRES-D-08-00274R1). We have addressed the comments and suggestions, and the itemized point-by-point response is provided below. The changes in the revised manuscript are bolded.

Reviewer #1:

1. Introduction, page 6: The paragraph describing the purpose of the paper and the selection of the CONSORT standards should be expanded briefly to describe the rationale for selecting CONSORT, and to describe what it is, and why it is important in RCTs. As presently written, the manuscript presumes familiarity with CONSORT by readers, and this may not be the case. A solid concise description will help incorporate CONSORT throughout subsequent sections of the manuscript. For instance, each of the sections could begin with a comment about what the CONSORT guidelines recommend regarding the key point, and then the discussion and exemplar(s) could follow. This would enhance the "teaching" value of the manuscript for other researchers, both expert and novice.

We have expanded the paragraph as reviewer suggested on page 6, lines 8-12, and 16-19. We have also made changes throughout the manuscript to begin each section with a link to the CONSORT.

2. Methods, page 7: While the authors list the 8 key points of the CONSORT checklist, the subsequent discussion does not do justice to all of them, most specifically Objectives on page 10 (see below). Perhaps most, but not all, of the key points, could be discussed, with a statement indicating which key point(s) were not included and why.

We have revised the discussion of other points of the CONSORT checklist as described below. We believe the revisions of the subsequent sections of the manuscript address this comment. We also added a sentence summarizing which points are addressed on page 8, lines 1-2.

3. Intervention, subheading Distinguishing therapeutic and placebo effects, page 10: the last sentence of the paragraph is somewhat awkwardly written and therefore confusing; could it be rewritten more clearly?

This sentence has been revised, page 11, lines 13-18.

4. Intervention, subheading Distinguishing therapeutic and placebo effects, page 10: it would be helpful to note that making sure that the identified potential confounding factors are also measured or assessed in some way is essential in being able to analyze their effects on outcomes.

This has been done, page 12, lines 7-10.

5. Intervention, subheading Treatment fidelity, page 11: Inclusion of a definition of this concept, with a key reference, would enhance this section.

We have included a definition of treatment fidelity and a key reference on page 12, lines 13-17.

6. Objectives, page 12: this section simply lists the CAM study objectives, without any linkage to CONSORT, or substantive discussion. Please include hypotheses and objectives.

We have revised this section to describe why the hypotheses and objectives need to be stated, and linked the discussion to the CONSORT. Both hypotheses and objectives are included. The revisions are on page 13, lines 13-22.

7. Outcomes, page 12: this key topic needs to be linked to CONSORT (see first comment above, Introduction, page 4). Within this section, several sub-topics (e.g., repeated measures outcomes, secondary outcomes, are under-developed and/or not clearly linked to CONSORT.

We provided the links to CONSORT in this section on page 14, lines 12-15, page 16, lines 10-14 and 18-20.

8. Randomization procedure, pages 16 and 17. References would be helpful in the first paragraph of this section. On page 15, the paragraph beginning with "In the reflexology study, prognostic factors." could be strengthened with a reference or two on variables that may be predictive of outcomes, and by reordering the last several sentences to match the order of topics in the first sentence of the paragraph.

We have added a reference in the first paragraph as requested by the reviewer on page 19, line 7. We have reorganized the order of sentences, and added key references on page 20, lines 10-15 and lines 19-21.

9. Blinding, page 18: this key topic needs to be linked to CONSORT (as above).

This has been done on page 21, line 6, and lines 18-19.

10. Statistical Methods, page 18: this key topic needs to be linked to CONSORT (as above).

The "issue" is not clear because of this lack of linkage.

We have revised this section. The changes have been made to provide linkage to the CONSORT on page 22, lines 4-6, 16-18.

11. In considering the repetitive comments above related to key topics not being clearly linked to CONSORT, perhaps the authors would want to consider a succinct table showing the key topics and the important considerations/qualities for each one that should be part of a good RCT. This would provide a very nice way to more fully implement CONSORT into the manuscript, educate the reader, and address this critique.

We followed reviewer's specific comments and made changes throughout the manuscript. We believe that with these changes, a table may be redundant.

12. Results, pages 19-20: as presently written, this section is more of a summary and somewhat redundant with introductory text on the CONSORT guidelines. Delete it and move to the Discussion section.

We have deleted this section. Appropriate edits have been made in the abstract to reflect this change.

13. Discussion, page 20: this section would be enhanced with an introductory few sentences that explain more clearly HOW the CONSORT served as a guide, and how it was helpful. If the lack of linkage to CONSORT described in several areas above were dealt with, then this section could be a more effective and conclusive "tying up" of the manuscript. As noted in Strengths (above), the comment on what CONSORT does NOT include are quite important, and the final paragraph provides a nice close to the manuscript.

We have written a new opening paragraph in the discussion section describing how the CONSORT may be used to guide trial design. These edits are on page 23, lines 7-18.