Reviewer's report

**Title:** Design paper: randomized, phase III two-armed, parallel-group, clinical trial of Anma-massage therapy (Japanese massage therapy) versus no Anma-massage therapy for gynecological cancer survivors

**Version:** 1 **Date:** 11 May 2013

**Reviewer:** Antony J. Porcino

**Reviewer's report:**

This manuscript describes the design of a randomized phase III two-arm trial of Japanese anma massage for managing quality of life issues in gynecological cancer patients. Both single session and multiple use effects are explored. The control group is usual care, with a single session available at the end of the waiting period. This trial addresses a useful intervention for psychosocial needs of gynecological cancer survivors, and adds useful information to the field. The question/hypothesis is clear enough, but broad.

The trial protocol and manuscript do not have any serious flaws. While I do not perceive any major compulsory or minor essential revisions, I would suggest the authors consider the following discretionary revisions.

1) This trial protocol is a mix of pragmatic and explanatory design choices on the pragmatic-explanatory continuum (for example of what this may look like, see PRECIS by Thorpe et al., 2009). The approach to many of those choices seem pragmatic in that they either address real-world issues or allow for comparison with other studies even if they are more explanatory (the cortisol measurements are a good example). The odd mix did, however, require time to reflect on how, what, and why the trial design was meant to accomplish, and I think additional information from the authors through a lens like PRECIS could help readers, interpreters/users of the results, and further trials on this subject.

2) One particular concern regards the choice of a single practitioner to provide all treatment, without description of how that practitioner’s treatment process, training, or experience compares with other providers. While this ensures (as the authors comment) very high internal validity, given the pragmatic nature of other protocol features, this particular design choice needs to be better explained in the context of the trial as a whole.

3) It is noted that a trial inclusion criteria is “Desire to receive Anma-massage therapy”. The effects on the outcome of previous experience with Anma massage, expectations regarding Anma massage, and desire for the treatment have not been addressed in this protocol. I leave this as a “discretionary” revision only because in many research trials these issues are often not fully addressed or are considered to be addressed by the control group. However, it needs to be considered that they may constitute a significant component of the placebo or contextual component of the result. I do not consider this a wrong choice—it will
help both with trial recruitment, and likely reflects real-world uptake of Anma massage should the results prove positive—but would indicate that the results will not reflect purely or only the effects of Anma massage. This issue is common in complementary and alternative medicine research, and may be helpful to the authors in placing their trial design and results in context (see, for example, Boulanger et al. 2012, The Development and Validation of the Client Expectations of Massage Scale)

4) New outcome tools have been added relative to the previous work these authors have done in the field, without clearly identifying the value of the outcome to the testing of the hypothesis, particularly as they relate to the (normal) use of these in massage trials.

Specific questions to address:
1) Will the study design adequately test the hypothesis?
Yes, as stated. However, linkage of the outcome tools to the hypothesis would help, and consideration of the selection bias of people wanting Anma massage on the strength of the potential conclusions to be drawn is needed—the current expectations outlined in the second paragraph of the discussion may not be valid.

2) Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing?
Reference 19 is really the primary methods reference and readers should be directed to that paper as the description in this manuscript and other references is minimal. As well, while the practitioner can “focus on the specific locations where the patients want to improve physical symptoms” (a very pragmatic type of approach), the procedure as described in reference 19 (the procedure description here is not adequate) does not indicate what or how such focus variation is managed nor how it may relate to normal practice thus failing both a pragmatic or an explicit type of protocol delineation. Given the lack of other trials in Anma massage, comparison with other Anma trials is not feasible; sufficient discussion is provided in other manuscripts by the author to allow better comparison with western massage trials (perhaps more direct references would help). Not enough information is given were it to be useful to compare Anma massage trials with Chinese massage (Tuina or Do-in/Ankyo) trials (part of the historical origins of Anma, as per reference 19).

3. Is the planned statistical analysis appropriate?
(a) The sample size calculation as explained is not clear as to the reasoning, given the expected effect sizes from the pilot studies. Additionally, while intention-to-treat analysis is proposed, the authors do not describe whether the sample size was adjusted to accommodate possible data loss or dropouts.

(b) “Pearson’s Chi-squared test … will be used to test differences in categorical variables.” Given the use of t-tests for the parametric data, the Mann Whitney test or another non-parametric test (depends on which categorical variables) may be more appropriate to test differences rather than just discern that a difference
exists.

4. Is the writing acceptable? 
Yes.

**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.