Author's response to reviews

Title: A yoga intervention for diabetes risk reduction: A pilot randomized controlled trial

Authors:

Kelly A McDermott (mcdermottk@ocim.ucsf.edu)
M. Raghavendra Rao (raghav.hcgrf@gmail.com)
Raghuram Nagarathna (rnagaratna@gmail.com)
Elizabeth J Murphy (emurphy@medsfgh.ucsf.edu)
Adam Burke (aburke@sfsu.edu)
R. Hongasandra Nagendra (hrn@vyasa.org)
Fredrick M Hecht (rhecht@php.ucsf.edu)

Version: 5
Date: 17 March 2014

Author's response to reviews: see over
March 17, 2014

RE: Further revisions on MS: 7186885311091630 -- *A yoga intervention for diabetes risk reduction: A pilot randomized controlled trial*

Dear BMC CAM Editors:

In the following table, please find our responses to each of the reviewer comments included in the latest request for revisions. Please let us know if further revisions are necessary.

Sincerely,

Kelly McDermott, PhD
Osher Center for Integrative Medicine
University of California, San Francisco

<table>
<thead>
<tr>
<th>Reviewer</th>
<th>Comment</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assoc Editor</td>
<td>Please address the following queries by the reviewers. Most importantly, please make clear why the 6 patients were excluded in per protocol analysis and why they are deemed to not being important for the research question. Please also ensure that your revised manuscript conforms to the journal style (<a href="http://www.biomedcentral.com/info/ifora/medicine_journals">http://www.biomedcentral.com/info/ifora/medicine_journals</a> ). It is important that your files are correctly formatted.</td>
<td>Language was added to the methods section to make clear that the 6 patients who did not meet inclusion criteria were mistakenly enrolled and randomized and this is why they are included in the ITT and not the per protocol. The manuscript conforms to the journal style.</td>
</tr>
<tr>
<td>Rev. 0528 Minor Essen</td>
<td>What was the motivation for control group to invest time and effort? In fact this study did not have a wait-listed control group and the control condition in this study was not controlled for non-specific effects of the treatment including expectation, belief and the effects of participation in the study (Hawthorne effect).</td>
<td>All participants were given the day-long class about lifestyle changes, which may have been a motivation for participation. As a pilot aimed at feasibility and preliminary efficacy in the early stages of development, a basic walking control group was determined to be an appropriate comparator. In future iterations of this study powered to detect smaller effects, a more tightly controlled comparator will be more appropriate.</td>
</tr>
<tr>
<td>Rev. 0528 Minor Essen</td>
<td>Also these subjects were from India; hence the results might have been influenced by cultural belief on yoga. It is highly recommended for authors should be acknowledged more cohesively and more explicitly given that this is the most serious weakness of the study under discussion section.</td>
<td>This potential bias has been addressed in the limitation section.</td>
</tr>
</tbody>
</table>

continued next page
| Rev. 0528 Minor Essen | In Discussion, the authors mentioned under study limitations, the duration of the yoga intervention may not have been long enough to see the full potential impact on diabetes risk factors. Authors also cited Alexander et al study about an 8-week study of yoga for postmenopausal women. But the present study was on Diabetes and some earlier studies with 8-week yoga training did show significant improvements in diabetes risk profile. | We removed study duration as a potential limitation. |
| Rev. 0528 Minor Essen | It is highly recommended for authors to discuss about selection of yoga practices whether or not appropriate for achieving equivocal results with the previous studies. | Text and citations have been included in the description of the intervention to justify the selection of poses and breathing exercises. |
| Rev. 0528 Discretion. | Since this study was approved by research ethics committees at SVYASA and UCSF and the study was actually conducted and involved subjects from India, whether or not authors registered this trial under Clinical Trials Registry – India (http://ctri.nic.in/Clinicaltrials/login.php)? | The study was not registered under Clinical Trials Registry India. |
| Rev. 0434 Maj. Comp | In the method section, the authors describe that they have conducted an ITT analysis as suggested by the reviewers. However, they did not – because 3 participants who dropped out were excluded from analysis. But follow-up data of the 3 drop-outs have to be imputed and included in the final analysis. Method of imputation (last observation carried forward, multiple imputation methods, etc.) has to be described, too. Please calculate new statistics and add to the abstract that ITT analysis was used. | We included a LOCF analysis in addition to the complete case analysis for the ITT. The LOCF provides a more conservative estimate of within and between group effects. Descriptive text has been added to the data analysis section and assumptions are made explicit. LOCF was added to the results and ITT was added to the abstract. |
It remains ambiguous why the authors want to analyze data per-protocol by excluding the 6 borderline FBG participants! It reads as if these 6 participants were eligible at baseline (had FBG of >5.6 mmol/L) and “were later deemed ineligible based on borderline FBG”.

In the case where their FBG changed during the intervention period a per-protocol analysis is not appropriate and should be omitted. In the case of including participants wrongly with not meeting the inclusion criteria already at baseline, the per-protocol analysis is meaningful. Please give more detailed/definite information about these 6 participants in the result section and rewrite the discussion passage: “Second, 6 participants who were enrolled and randomized were later deemed ineligible based on borderline FBG. The inclusion of these participants in the ITT analysis does not address our original research question about reducing diabetes risk among participants with FBG #5.6mmol/L, however we also included analysis from a per protocol analysis where these participants were excluded.”

Table 2: Please add whether the numbers following the means are SDs (standard deviations) or SEs (standard errors).

The title of table 2 describes results as mean ± SD.