Author’s response to reviews

Title: Acupuncture for postprandial distress syndrome (APDS): study protocol for a randomized controlled trial

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Author’s response to reviews:

Dear Dr. Scherer

Thank you for your letter and for the Reviewer’s comments concerning our manuscript. Those comments are very helpful for revising and improving our paper. We are resubmitting the revised manuscript. We have detailed our responses to Reviewer’s concerns and comments. Following are point-by-point responses to the Reviewers’ comments and suggestions.
Reviewer reports:

The authors of this manuscript describe a protocol for a randomized trial of verum versus minimal acupuncture for postprandial distress syndrome. Generally, the trial is well designed as a pilot study and is adequately described. However, some components of the SPIRIT guideline have not been addressed. Also, the attached document with the page numbers for each item do not correspond to the page numbers of the manuscript in many cases. Specifically, the following items are either missing or not described completely and should be addressed in the protocol. Please include this information and re-do the SPIRIT guideline checklist.

Response: We thank the Reviewer for the question. The missing or not clear items had been described point-by-point. The page numbers of each item in additional file 1 had been corrected.

Lastly, please review the abstract – I think you mean pilot instead of polit in a couple of places.

Response: We are sorry for the wrong typing. We had revised "polit" into "pilot" in the abstract (highlighted in red).

SPIRIT items are as follows:

2b – no additional file listing the WHO trial data set is available.

Response: We thank the Reviewer for the suggestion. The trial had been registered at the ISRCTN registry which is a primary clinical trial registry recognised by WHO. The registry number is ISRCTN18135146. The registry file had been enclosed as additional file 2.

3 – no date or version number for this protocol is provided. Assuming it is version 1, the date should be the date the protocol was submitted.

Response: We are sorry for this missing. The protocol version is 1 and the date is January 18, 2016. We had added it on page 5 (highlighted in red).

5 c – role of funders on trial design not provided
Response: We thank the Reviewer for the question. This work was supported by Beijing Municipal Science & Technology Commission (No. Z16110000516007). It just provides financial support and does not affect trial design.

5d – only the role of the biostatistician is described. What about form development, database development and data management. Also are there any committees?

Response: We thank the Reviewer for the question. The data will be entered into Excel spreadsheets by two separate data entry clerks, following which the data manager will compare the accuracy of the two datasets. If any differences are noted, corrections will be made according to the original CRFs. In addition, we have an independent Data and Safety Monitoring Board (DSMB) to review and interpret data generated from the study.

7 – Reason for choosing minimal acupuncture (comparator) instead of no treatment or some other comparator should be provided

Response: We thank the Reviewer for the question. This trial aims to determine the feasibility and efficacy of verum acupuncture. Therefore, we choose minimal acupuncture to eliminate placebo effect on patients. In addition, “De qi”, literally meaning “arrival of energy”, is referred to a sensation of numbness or distension and may be one indication that acupuncture is exerting its beneficial effects. De qi is related to the depth of needle insertion. Therefore, minimal acupuncture is a proper comparator. Lots of high quality researches chose this comparator [1-2].


12 – Although the instruments used for measuring quality of life are described well, some components of the primary outcome are missing. The primary outcome should be comprised of 5 elements: domain, method of measurement, metric, methods of aggregation, and time point. In the description of the primary outcome, the method of aggregation (e.g., mean, median, etc.) and the metric (e.g., change from baseline, value at baseline, etc.) are missing.

Response: We are sorry about the confusion that has been made for the readers, and we thank the Reviewer for the suggestion. In this trial, the primary outcome is the responder rate based on the
overall treatment effect (OTE) at end-of-treatment (4 weeks after randomization). The patient
will be asked to decide whether symptoms have changed compared with pre-treatment using a
Likert scale. The seven-point Likert scale is ranged from ‘extremely improved’, ‘improved’,
‘extremely improved’ or ‘improved’ will be considered responder. We have added this part in
manuscript (page 8, highlighted in red).

19 and 23 – no description of the data collection, data entry, database, data management, data
security, etc are provided nor any information about auditing the data for quality.

Response: We thank the Reviewer for the suggestion. All researchers including therapists, data
collector, data entry clerks, data manager, statistician, and outcome assessors will receive
training regarding the data management. Upon conclusion of the treatment period, all participant
data will be completed and recorded on the original CRFs. The data will be entered into Excel
spreadsheets by two separate data entry clerks, following which the data manager will compare
the accuracy of the two datasets. If any differences are noted, corrections will be made according
to the original CRFs. We have added this part in manuscript (page 10, highlighted in red).

21a – no description of any plan for safety monitoring are provided

Response: We thank the Reviewer for the suggestion. We will establish an independent Data
and Safety Monitoring Board (DSMB) to review and interpret data generated from the study.
Its primary objectives are to ensure the integrity of the research data. The DSMB will
review the progress of the trial and decide on any premature closure of the study. We have added
this part in manuscript (page 10, highlighted in red). Here are the members of DSMB (additional
file 3)

<table>
<thead>
<tr>
<th>Name</th>
<th>Affiliation</th>
<th>Email address</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jian-De Chen</td>
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</tr>
</tbody>
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26a – although it is indicated that informed consent will be collected, it is not clear who will
obtain informed consent. Also, it is not clear who will actually enroll the study participants and
request randomization
Response: We thank the Reviewer for the question. The Clinical Research Coordinators (CRC) usually being the investigator’s master/PhD students will be responsible for enrolling participants, obtaining informed consent and requesting randomization. We have made it clearly (page 7, highlight in red)

29, 31c – although there may not be plans to provide access to the final data beyond the investigators, this should be stated in the protocol

Response: We thank the Reviewer for the suggestion. All research documents, including both the paper files and electronic documents, will be preserved for at least 5 years after publication. If readers have any questions regarding our published data, they will be permitted to contact our first author or corresponding author to ask for the original data. The private information of patients includes name, age, telephone number, will be critically protected and will never be allowed to disclose (page 10, highlight in red).

31a, 31b – a dissemination plan should be provided, or if there are no plans to publish the results or present them at a conference, this should be stated

Response: We thank the Reviewer for the suggestion. When the trial finish, we will publish the results.