Author's response to reviews

Title: Clinical Research Evidence of Cupping Therapy in China: A Systematic Literature Review

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Author's response to reviews: see over
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Dear Editor,

Thank you very much for sending us the comments, based on which we did revisions and corrections. Please find the revised version with track change and version without track change so you can see the changes and edition. We try our best to improve language and we hope now it is better for both understanding and reading. The detailed responses on the author query and peer reviewers’ comments were followed below.

Looking forward to your further advice.

Best regards,

Huijuan Cao and author team

1. Responses to the Author Query

Reviewer 1 (Karen Sherman):

AU1: the number of studies has increased over the course of 5 decades overall. The first RCTs began in the 1990’s and over half of them were reported between 2006 and 2008. [I am not sure all the detail is needed and I think that the critical parts of Figure 2 and 3 could be combined into one figure].

Reply: We agree with the comments and therefore shorten the description of the n studies as suggested, and the Figure 2 and 3 have been combined into one figure.

AU2: summarizing the data on the types of cupping therapy provided and the medical conditions studied. For example, you could have another table with 2 panels. Those should be summarized by organ system. I am a little confused by the distinction between “pain condition” and lumbar sprain, cervical spondylosis, sciatica, arthritis, etc.-many of those are likely being seen for pain as well – so you might describe what the “pain” actually means. If this change were made, some of the material in the discussion section could be moved here.

Reply: We moved several paragraph of the discussion section to results of “Distribution of diseases/conditions” part, and the “pain condition” we defined the pain as musculoskeletal pain, such as low back pain, skelalgia, fibromyalgia, so to
differentiate with other pain conditions as mentioned. As in some of the studies, authors didn’t report the specific diseases, but only symptoms of pain, we think it may be better to describe the number of these studies and others which focused on the specific diseases (such as herpes zoster, arthritis, etc) separately in different tables.

AU3: the section on methodological quality of RCT is fine, but you also need to add some data describing the results of the trials, if only a count by condition of “positive results” or something like that – it would clearly depend on the nature of the results available to you. Also some data on the size of the studies should be presented if only means/medians and ranges to buttress the discussion point that the studies are small. I don’t like authors should present any new data in the discussion section so you must present those data here.

Reply: We moved the description of estimate effect of cupping therapy for herpes zoster and fibromyalgia from the discussion to results part (see revised manuscript).

AU4: I also think the discussion section should be shorten and focused substantially on the main points of the study. I suggest deleting the material on how cupping might improve various medical conditions according to TCM theory as I think it detracts from the main point of this paper.

Reply: We revised the discussion section as your suggestion and also deleted some text about the effect theory of cupping therapy.

AU5: Finally, there are a lot of errors throughout the manuscript in tenses and in some cases, difficulty in clear expression. The authors would benefit from finding an editor who is a native English speaker to review the manuscript and assist in resolving these technical issues.

Reply: We have worked heavily on the language issues to reduce the errors and wording throughout the text, and hope this version becomes better.

AU6: in first paragraph of Background- 200 years ago is not “ancient times” so the reference to Zhao Xueming should be reworded appropriately.

Reply: We revised the sentence as “Some therapeutic cupping methods and case records of treatment were also described in early Chinese books”.

AU7: in second paragraph the description of cupping is a bit confusing. For example, is fire part of all cupping or only retained cupping?

Reply: Most of cupping methods used fire to make the cups suction on relevant acupoints, only few of cupping methods don’t use fire, such as medicinal cupping and water cupping. We revised this paragraph to clarify these.
AU8: in third paragraph, “Because cupping is widely used in Chinese folklore culture” should be reworded “Because cupping was widely used in Chinese folk culture”.

Reply: This has been corrected.

AU9: in the 4th paragraph “According the modern research” is confusing because I am unclear what the discussion about substances and fluids refers to.

Reply: We deleted this paragraph because it seems not relevant to this paper, and this theory was not proved by sufficient evidence of research.

AU10: Figures and Tables –please make sure to provide legends for the abbreviations.

Reply: We added the legends for “RCT”, “CCT”, “CS” and “CR”.

Reviewer 2 (Rainer Stange)

AU11: Page6 please give only one decimal digit for percentages

Reply: We revised it.

AU12: please explain Bi syndrome shortly

Reply: Wind, cold and dampness invading the body, which is caused by changeable climate and alternate cold and heat, or dwelling in damp places, or wading, or being caught in the rain, and linger in channels and joints resulting in Bi syndrome as the result of stagnation of qi and blood.

AU13: page 3 identifying.

Reply: We revised it.

AU14: page 5 which were published between…

Reply: We revised it.

AU15: page 6/7 I am a clinician not a methodologist, but to me it does not seem to make much sense to do statistical tests on series of publications. Your figures 2 and 3 make a good impression of what is going on. I would skip the tests.

Reply: We revised this section and delete the statistical test.
The majority

Reply: We revised it.

67 with efficacy standards, 51 composite (all with the same descriptions as given? It would be very amazing!) What happened to 16=67-51? Did they use established parameters of evaluation? Are there clusters of parameters?

Reply: I’m sorry to say that not all the composite outcome measurement standards gave the same descriptions, they described the improvement of the symptom of relevant diseases as the main outcome measurement. For example, some authors of the included trial may described cure for fibromyalgia as “symptoms disappeared, no tender points exist”, markedly effective would be “symptoms improved more than 50%”, effective/improve would be “symptoms improved between 25% and 50%”, and ineffective would be “symptoms improved less than 25%”, other authors who also focused on fibromyalgia may changed the figure 50% as 55% or 60% in their trials. The remaining 16 trials used single outcome measure for therapeutic effect, such as VAS score for fibromyalgia.

Please do not use didn’t in a scientific text

Reply: We revised it as “did not”, is that OK?

Please use ICD classification either constantly or omit it

Reply: We delete all ICD stuff.

Fig 4 and 5 please add n=??? for 100%. I am missing the Bi syndrome studies. Did you only want to include western diagnosis for these figures?

Reply: We added the number of n, and we did include Bi syndrome studies in these figures. In Fig 5, the number of Bi syndrome studies is 1.89%.

To me as a non-Chinese researcher in the field, it is very interesting to learn about these amazing number of 525 trials, we are not able to read in their original publication. Thus I am amazed that apparently only few trials had a symptom complex of the Traditional Chinese Medicine as study population (how many with Bi syndrome?) page 9 you state that “wet cupping therapy was hardly used in deficiency. Of course you know about deficiency, but maybe you can explicitly state which of the clinical conditions you consider to be deficient. Do any trials make any remarks on outcome by Chinese syndrome criteria, even if western diagnostic criteria were used for inclusion, maybe by subgroup analysis? This would be very interesting to lean.
Reply: Thanks for your interested in TCM theory and research! First of all, in the 73 included RCTs, over half of them mentioned that the researchers followed the principle of syndrome differentiation according to TCM theory to choose the acupoint, but only 2 of them described the outcome measure of each type of syndrome, respectively. One is wet cupping therapy for cervical spondylosis, another one is moving cupping for diabetic peripheral neuropathy. As the difference between the participants, interventions and outcome measures, it is difficult for us to do relevant synthesis or subgroup analysis due data unavailable from these trials. Unfortunately, the majority of the trials did not make remarks on outcome by Chinese syndrome criteria. Then for the “deficiency syndrome”, for example, we may diagnosed headache as syndrome of blood stasis if the main symptom is lasting headache with fixed aching spot as pain as being drilled, purplish tongue or with ecchymosis; we may also diagnosed headache as syndrome of blood deficiency if the main symptom is headache with dizziness, pale complexion, palpitation, pale tongue and weak pulse. For syndrome of blood stasis, we may selected points from the hand-Yangming, foot-Taiyang and foot-Jueyin meridians as main points, pricking to cause bleeding is applicable when necessary, but for syndrome of deficiency of blood, we may selected points on the foot-Yangming meridian and back Shu points as main points, the reinforcing method is applied, moxibustion is applicable at the same time.

AU22: of course you shouldn’t go into all these trials again, but did you make any notice at all, how many cups were used in the interventions, resp. whether cupping was done repeatedly, in what intervals? This would be very interesting. The Iran study (quotation see below) allowed for replication depending on outcome, which seems to be a common practice in routine care.

Reply: Unfortunately, we did not count the number of cups used in the trials, but based on our reading of the studies, the number of cups used depending on how many acupoints used in the interventions and it might change during the treatment course. In general, the cupping was used once daily (for acute disease) or once every two or three days (for chronic disease) during the treatment, and the duration of the treatment may last half to two or three month according to the diseases.

AU23: You should state explicitly why it apparently dose not makes sense to do a meta-analysis to calculate overall effect size at least for a subset of your trials. Basically this would seem possible, if so many trials “used composite outcome measure which categorized the effect of the treatment into four grades according to the change of the symptoms”.

Reply: Actually we did meta-analysis for two diseases, herpes zoster and fibromyalgia. We concluded the main finding (overall meta-analysis) in the discussion section at first, and we moved some of this part to result section now. These results were published as two systematic reviews (one is in press) as we mentioned in the text. Although many studies adopted the composite outcome
measure for evaluation the improvement of symptoms, most of the trials did not test
the same disease/condition, so we were not able to conduct the meta-analysis for all
the trials.

AU24: Beside therapy, one trial you quote[88] added to the understanding of a topical
representation of disturbances of the soft tissue to regional disorders of
non-dermatological structures as a rational for an efficacy of cupping. This additional,
med-line listed publication is in German however. Did any of the Chinese
publications put similar questions?

**Reply:** We revised the reference as your suggestion. We could not find a similar
research in Chinese in our searches.

AU25: You correctly state that your systematic research ended Dec 2008. You may
mention that meanwhile, two more RCT have been performed and published outside
China apparently with good methodological quality to illustrate the international
importance of the method.

**Reply:** We added these two RCTs in the discussion section.

2. Responses to Editor Query

ED1: Format your abstract according to the following guidelines: The abstract of the
manuscript should not exceed 350 words and must be structured into separate sections:
Background, the context and purpose of the study; Methods, how the study was
performed and statistical tests used; Results, the main findings; Conclusions, brief
summary and potential implications. Please minimize the use of abbreviations and do
not cite references in the abstract

**Reply:** We revised the abstract following your suggestions.

ED2: Remove the abstract from the title page of your manuscript and place this on the
following page.

**Reply:** We revised it.

ED3: Include the email addresses of all authors within your title page.

**Reply:** We revised it.

ED4: Revise your Competing Interests statement so that it is entitled Competing
Interests. If there are none to declare, please write 'The authors declare that they have
no competing interests'
ED5: Include an Authors' contributions section before the Acknowledgements and Reference list. For the Authors' contributions we suggest the following kind of format (please use initials to refer to each author's contribution): AB carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript. JY carried out the immunoassays. MT participated in the sequence alignment. ES participated in the design of the study and performed the statistical analysis. FG conceived of the study, and participated in its design and coordination. All authors read and approved the final manuscript.

Reply: We added the Authors’ contributions section.

ED6: Adhere to the PRISMA guidelines for reporting systematic reviews found at http://www.prisma-statement.org/

Reply: We revised the manuscript follow the PRISMA guidelines.

3. Other changes we made to the original manuscript

Revision1: According to the change of text, we revised the list of reference.

Revision2: As we combined the fig2 and 3, we changed the other figures’ number and added the number and legends of all the tables and figures on the last page.