Author's response to reviews

Title: Moxibustion for Cancer Care: A Systematic Review and meta-analysis

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

RE: Moxibustion for Cancer Care: A Systematic Review
(MS:6851658233224344)

We appreciate the comments for improving the above mentioned manuscript. According to the comments my colleagues and I made the several changes. We also re-searched the databases again and updated the review according to new search results. All of changed points were highlighted with yellow mark.

Reviewers’ comments:
Reviewer 1

Comment 1) For future discussion, I, as a reviewer, would like to recommend the authors discuss the pros and cons of systematically reviewing and drawing a conclusion from the published studies while it is more likely that the number of included studies would be limited. Having said that, I value this effort on the ground that a systematic review on a subject field where there is no such work before will provide a good starting point.

Revised> We have now added some discussion of the pros and cons of systematic reviews (page 12, 2nd paragraph)

Reviewer 2

Comment 1) In my opinion this is not a unique review for Moxibustion and Cancer.

Revised> Several reviews have been published but the most of them are not systematic reviews and open to bias. Even if one of them seemingly employed the method of a systematic review, that overview also lacked of comprehensive searches and open to selection bias. Furthermore, the inclusion criteria were wrong. Currently this review is the only one which adopted systematic and transparent methods with comprehensive searches. We have now added these points to the introduction (page 4, lines 1- 8 from the bottoms).

Comment 2) Your review focus on 2-3 papers about chemotherapy side effects and Moxibustion.

Answer> In the methods section and aims of this review, we explain that we focused on the evaluation of evidence in moxibustion for cancer care.
Comment 3) You did not discuss about the scientific mechanisms for Moxibustion in the Discussion. The brainstem structures influenced by the Moxibustion applications and this scientific mechanism must have been indicated in the discussion.

Revised> We are not aware of such a mechanism. Instead of this we discussed the more plausible mechanism of modulation of immune systems (page 11, 3rd paragraph and page 12, 1st paragraph).

Comment 4) Further, the Heat Shock proteins which are the significant focus for cancer therapy are influenced by moxibustion too. This item also has not been discussed.

Revised> We have now added this possible mechanism in the discussion (page 11, 3rd paragraph and page 12, 1st paragraph).

Comment 5) The readers who will read your review about Moxibustion effects on cancer can not have a inspiration for further researches and knowledge. The review simplifies the effects of Moxibustion. For respect to Moxibustion therapy, I am on the behalf of the readers to read 2-3 original articles about Moxibustion and Cancer.

Answer> We thank you for your comments regarding the concern with our review as not giving much information to the readers. Would you please read the methods section carefully? We consider this section as the core of our protocol.

Let me introduce you briefly to the method of a systematic review. Systematic reviews and meta-analyses are a key element of evidence-based healthcare (Khan KS et al. Five steps to conducting a systematic review. J Royal Soc Med. 2003; 96: 118-121 or Cochrane Handbook for Systematic Review: http://www.cochrane-handbook.org/). It is the explicit and systematic approach that distinguishes systematic reviews from traditional reviews and commentaries. Systematic reviews generally consist of the following five steps: (1) framing the question; (2) identifying relevant work; (3) assessing the quality
of studies; (4) summarizing the evidence; (5) interpreting the findings.

During the review, it is required to exhaustively search the available databases (with commercial ones), which often looks like a simple internet search, but it is definitely not. Systematic review is one type of research. Anyone can do this type of work, however they should follow the proper protocol and detailed method of systematic review with an understanding of the procedure.

Although we only included five randomized clinical trials, we followed the pre-defined protocol and employed quality assessment according to the Cochrane criteria. For further information, please visit the Cochrane DBs or simply google the term ‘systematic review.’ You can find the rigorous methods, which the authors follow here, for systematic review. Systematic reviews often show the limitations of previous research and suggest possible future trials. This can often be confused with narrative or overview. However, the authors of systematic review input a lot of time and effort in finding the eligible studies. Then the results are analyzed objectively to find any evidence.

I think you might question the usefulness of systematic reviews and meta-analyses with only a small number of trials. We have also addressed this fact concerning the eligibility in the discussion section.

We have now also add the pros and cons of systematic review in the discussion (page 12, 2nd paragraph)

Editorial requests:

Comment 1) Please ensure that your manuscript adheres to the guidelines of PRISMA: http://www.prisma-statement.org/statement.htm

Revised> We have checked the categories in PRISMA.

Comment 2) Competing interests. Please include a 'Competing interests' section between the Conclusions and Authors' contributions. If there are none to declare, please write 'The authors declare that they have no competing interests'.
We have now added the competing interests and authors' contributions.

**Comment 3** Authors' contributions. Please 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.

We have followed the guideline.

**Comment 4** Please include a separate Conclusions section in your manuscript. Manuscript sections should include (in the following order): Abstract; Background; Methods; Results; Discussion; Conclusions; Abbreviations (if any); Competing interests; Authors' contributions; Acknowledgements; References; Figure legends (if any); Tables (if any); Description of Additional files (if any).

We have followed the guideline.