Author’s response to reviews

Title: Comparative efficacy of Chinese medicine injections for treating acute cerebral infarction: A network meta-analysis of randomized controlled trials

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Author’s response to reviews:

Responses to Reviewer 3:
BCAM-D-17-01353

Manuscript title “Comparative efficacy of Chinese medicine injections for treating acute cerebral infarction: A network meta-analysis of randomized controlled trials”

Shi Liu, Jia-Rui Wu, Dan Zhang, Kai-Huan Wang, Bing Zhang, Xiao-Meng Zhang, Di Tan, Xiao-Jiao Duan, Ying-Ying Cui, Xin-Kui Liu

Dear Reviewer 3:

We appreciated your critical comments on our manuscript (BCAM-D-17-01353). We also wish to take this opportunity to thank the reviewer for his constructive comments and valuable
recommendations. Based on your and other reviews’ suggestions, we carefully revised the manuscript. We are now sending the revised article for your reconsideration to publish in BMC Complementary and Alternative Medicine. The point to point responses to all comments are blow, and the corresponding revisions are in the body of manuscript. We look forward to hearing from you soon for a favorable decision. Thank you again for your time and consideration.

Sincerely,

Jiarui Wu

exogamy@163.com

A point to point response was answered below.

1. The reviewer’s comment:

Redundancy of Background and discussion.

The Methods and Results sections are well-written, but other two parts contain many redundants.

Therefore, I recommend authors to revise structure and logic, especially of Background, with neurologists specializing acute cerebral infarction if you can. This is not a review of acute cerebral infarction, but a review of Chinese herbal injection. I believe previous reviewer 1 pointed out almost the same point, and this is not a problem of English correctness of each sentence, but a problem of big picture of this article. The previous reviewer 1 also pointed out the references in conclusion, and I agree with reviewer 1 and believe that authors should remove these references. Conclusion is YOUR conclusion and does not need any references after presenting your results.

First paragraph of background introduce too much and less-related information about detailed number of mortality and disability rate.

In second paragraph of background, authors stated that "there is no routine, effective, generally accepted, specific treatment for ACI", but afterwards, authors also mentioned that "Grade-I recommendation in the Guidance of diagnosis and treatment of acute ischemic stroke in China 2010". I believe such Grade-I recommended conventional medications are "routine, effective, generally accepted, specific treatment for ACI" all over the world.

In third paragraph of background, authors stated that "the pathogenesis of ACI is due to the stagnation of Qi and blood. Therefore, promoting blood flow is of primary importance" and it sounds like TCM doctors treat patients with close concept with conventional neurologists. However, authors also stated that "the overall treatment concept is different from that in Western medicine". I can understand the meaning of both sentences because I am a Western physician.
specializing traditional medicine, but your logic might be confusing for usual physicians. This is what I mean that you need to revise your logic with neurologists.

The second and third paragraph of discussion contains too much repeated results. You can remove majority of information in these paragraphs, and leave only the last sentences in each paragraph and combine with the first paragraph.

The authors’ answer:

Thanks the reviewer for the comments. We have already revised our manuscript carefully. In Background section, we did some modifications and revised structure and logic, deleted redundancy. In Conclusions section, we removed these references. As for Discussion section, we have simplified its contents and deleted redundancy. We hope our revised manuscript would meet your criteria.

2. The reviewer’s comment:

Structure of Results.

Authors mixed outcomes in the section "pairwise meta-analysis" and "Bayesian network meta-analysis", and separated the markedly effective rate and improvement of neurological impairment in further analysis. Authors can separate these two outcomes from the initial pairwise meta-analysis, and I believe that this re-structuring of results might be easy to read for many readers.

The authors’ answer:

Thanks the reviewer for the comments. Your advice is significant for me. We have already revised the Results section, and separated the pairwise meta-analysis results of difference outcomes (Results section, line 307, page 14; line 320, page 15; line 346, page 16; line 352, page 16).

3. The reviewer’s comment:

Limitation

I am not sure about the difference in background of included patients. For example, if the severity of participants included in the SXN trial was mild, and that in other CHI trial was worse, then you might have the beneficial result for SXN. How did you evaluate and normalize participants' background in you analysis? If not, it might be one of limitations of your analysis.
The authors' answer:

Thanks the reviewer for the comments. Your comment was crucial for us. The acute phase of ACI generally refers to 2 weeks after the onset of disease. Thus, this network meta-analysis enrolled patients with the course of disease within 2 weeks. Though acute phases were limited, the severities of patient were various. Therefore, we add this point in Discussion section (Discussion section, line 515-516, page 24).

4. The reviewer’s comment:

Minor revision required.

Title

The words "Chinese medicine injections" appears only in title, and authors use the words "Chinese herbal injections (CHIs)" in the rest of parts. It should be consistent.

Page 6, line 122

The words "RCTs at home and abroad" does not make sence; especially "at home". Do you mean "inside of China" like domestic, or "outpatient treatment at patients' home"?

Page 7, like 145

I believe just MRI is an usual term, and "nuclear" is not needed.

Page 9, like 187

There are no full spelling of ADRs/ADEs in main text.

Page 19, like 413

There are no full spelling of NMA in any part of this article.

Page 22, like 470

What is "gray literature"?

The authors' answer:
Thanks the reviewer for the comments. We have amended these mistakes in corresponding section. Gray literature refers to the ongoing literature. If researchers registered trials, we can search its content in website of clinical drug trials. In this network meta-analysis, we have searched the China clinical drug trials, but there were no related trials. Thus, this point may cause a selection bias for our network meta-analysis.

Responses to Reviewer 4:

BCAM-D-17-01353

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Sincerely,

Jiarui Wu

exogamy@163.com

A point to point response was answered below.

1. The reviewer’s comment:

I have gone through the manuscript. I also have checked the answers given by the authors for earlier reviewer's comments. The manuscript can be accepted now provided the authors upload the file without track changes.
The authors’ answer:

Thank you for your recognition of our manuscript. After modification, we have uploaded a manuscript without track changes.