Author's response to reviews

Title: Meta-analysis of acupuncture for relieving non-organic dyspeptic symptoms suggestive of diabetic gastroparesis

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Author's response to reviews: see over
Dear Editor and Reviewers:

We thank the Reviewers for your careful and constructive reviews and thank the Editor for considering our manuscript and for your careful attention. We thank for the opportunity allowing us to provide point by point response to the questions, suggestions, and criticisms posed by the Reviewers and the Editor in regard to the first submission. We re-analyzed original data and re-wrote manuscript as suggested. We believe that the revised manuscript has been improved considerably by responding to the criticisms of the reviewers by incorporating their suggestions.
Here we present our response to the comments raised by the reviewers step by step in the following pages. Thank you again for giving us the opportunity to revise our manuscript.
We look forward to hearing of your decision on it.

Sincerely yours,

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**Reviewer: HYANGSOOK LEE**

Q1. Although the authors assessed the risk of bias using the Cochrane ROB assessment tool, they combined 8 RCTs without considering the ROB of each study. As shown in the funnel plot, we suspect that the studies reporting negative or neutral outcomes are missing or it is highly likely that the high risk of bias in the included trials exaggerated the effect estimate of acupuncture. Then, the authors should have dealt with this issue e.g., using sensitivity analysis, to determine whether this finding is robust.

Only 8 out of 14 RCTs reported how they randomised participants and only one sham-controlled trial (Wang 2008) which was given low risk of bias for randomisation and allocation concealment, apparently did not report how they adequately concealed group assignment. Randomisation by lot is one thing and adequate allocation concealment method is another. Given that inadequate random sequence generation and allocation concealment result in overestimation of treatment effects, the authors should re-analyse the data considering the high risk of bias of the included studies.

the outcome assessors in most studies seem to be participants who were not blinded. The outcome measures are mostly patient-reported ones, then risk of bias for outcome blinding would better be given high in medication-controlled trials of acupuncture.

Reply: Thank you for your suggestions. Sensitivity analysis of response rate to acupuncture limited to studies with low risk of selection bias was added and manuscript was rewrote accordingly, see P8, L158-161; P11-P12, L239-247; P15, L316-319. We replaced “unclear risk of bias” with “high risk of bias” associated with blinding outcome assessment, see Figure 2; P9, L194-196.

Q2. In the Discussion section, it would be better for the readers to suggest clinical and research implications of this review’s findings.

Reply: Clinical and research implications were added in revised manuscript, see P15, L329-331; P16, P17

Q3. There are a number of grammatical errors and misspellings in the text, figures and tables. The manuscript should be shown to a native English speaker to receive language editing service.

Reply: Many thanks. We checked and corrected grammatical errors and misspellings throughout the manuscript including figures and tables, and we also have had our manuscript edited as you kindly suggested.

Q4. Regarding inclusion criteria, studies testing a combination of acupuncture and Chinese herbal medicine were excluded. If so, the authors should give a clear reason why Shen 2010 and Wang 2010 were included. The term ‘acupoint application’ needs additional explanation.
Reply: The cause why Shen 2010 and Wang 2010 were included was given in study description section, see P6, L116-119; P9, L178-182. Explanation of term ‘acupoint application’ was added at the foot of Table 1, see P27.

Q5. In statistical analysis, the authors should state pre-specified classification for pooling studies, e.g. according to the control type or outcome measures.

Reply: we added the description of pre-specified classification for subgroup analysis and sensitivity analysis to statistical analysis section, see P8, L158-161.

Q6. The whole ‘risk of bias’ in the results section should be revised as mentioned above.

Reply: ‘Risk of bias’ in the results section has been revised according to your suggestion, see P9, L191-196.

Q7. Regarding response rate, did the all studies report the outcome on a 3-point Likert-type scale? I wonder whether there were any studies reporting response rate on a 4-point Likert-type scale. If so, it should be reported how these were dichotomised and analysed.

Reply: Many thanks for this suggestion. Indeed, one trial reported the acupuncture effect on 4 point level scale, “clinical cure” (effect index ≥95%), “significant improvement”, “improvement”, “no improvement”. We think that it may be acceptable to combine “clinical cure” into “effective.” See P10, L215-217.

Q8. Page 15, lines 322-3: twice daily acupuncture does not seem to be an easily acceptable practice outside China. A more generalisable suggestion would be reasonable. Moreover, it is controversial how long acupuncture’s effect lasts although the authors state 4-6 hours. It would be necessary to provide evidence for this.

Reply: Twice daily acupuncture is suitable for in-patients. Here, we deleted the suggestion of acupuncture two times one day. The references claimed that acupuncture’s effect lasted for 4-6 hours was provided in revised manuscript. See P17, L359-362.

Q9. Page 15, line 317: HAD scale – is it a quality of life measure?

Reply: Many thanks for your careful consideration. Hospital Anxiety and Depression Scale (HAD) is a widely used scale to assess symptoms of depression and anxiety and it might not be suitable to measure the quality of life for DGP here. So, we deleted it from the manuscript and added another scale for quality of life, see P17, L357.

Q10. Table 1: For reporting acupoints, I suggest WHO standard nomenclature for
acupoint be used for the readers. (E.g. RN12 should be CV12)

Reply: Thank you for your suggestion. The names of acupoint were revised according WHO standard nomenclature for acupoints, see P26-27, Table 1.

9. Table 1: For control groups, dosage and regimen of pharmacological medication should be provided (e.g. bid, mg, etc.)

Reply: Details about dosage and regimen of pharmacological medication for control groups was added in Table 1 in P26-27.
Reviewer: Huijuan Cao
Q1. The manuscript is seriously hampered by the quality of English used - the meaning of multiple sentences could not be deciphered. Authors may want to consult or get these reviewed by qualified persons.

Reply: Thank you for your suggestion. We have had the manuscript edited.

Q2. Methods for the systematic review should be more precise. First of all, method of data synthesis should be appropriate regarding to the clinical and statistical heterogeneity. Only the data from trials with same participants, outcomes, intervention and control could be pooled together in a meta-analysis. Authors synthesized the trials with different comparisons into one meta-analysis, it is inappropriate even the subgroups were introduced. Furthermore, quantitative synthesis should not be employed when there was significant statistical heterogeneity (I^2>75%), plenty of meta-analysis in this review should be re-wrote as qualitative description.

Reply: We highly appreciate your suggestions above. We re-analyzed data and re-wrote manuscript. When there was significant heterogeneity (I^2>75%), we used qualitative description to present the effect of acupuncture in revised manuscript. We agreed that methods used for systematic review should be more precise and it would be best to combine some trials with same participants, outcomes, intervention and control because these precise results can give a guide for practice. But in some cases, it may not answer some questions, such as which therapy is more effective, acupuncture or gastroprokinetic agents? Therefore, if there was no significant heterogeneity, we would like to pool studies and give an overall effect to answer such a question.

Q3. Searching strategy may also need to be revised. Searching the defined items as Keyword may leave out some of the relevant studies. Appendix of searching details in at least one database (such as PubMed) should be provided.

Reply: Search terms for PubMed were provided in revised manuscript, see P5, L98-101. Search terms for Chinese databases were used, in fact, as “主题” not as “关键词”.

Q4. Some necessary references are needed in the text. For example, in the 'Risk of bias', references should be added to indicate which trial described randomization procedures, and etc.

Reply: Thank you for your carefulness. We checked our manuscript carefully and added the references.

Q5. In Table 1, details of intervention (such as frequency or treating duration of acupuncture) should be provided, also the dosage of the western drugs should be addressed, too.

Reply: Details of acupuncture and control groups about frequency, treating duration and dosage were provided in this revised Table 1, see P26 and P27.
Q6. Since the GRADEpro was used to evaluate the grade of evidence, summary of finding table could be added in the review.

Reply: Summary of finding table was added as supplementary Table 1.

Q7. There were 14 included trials in this review, but in “adverse events”, authors mentioned “Four out of the 16 trials…,” please make sure no other such kinds of mistakes in the review.

Reply: Thank you for your suggestion. We checked our manuscript carefully and there may be not, we think, such kinds of mistakes.