PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	The effectiveness and safety of manual acupuncture therapy in patients with post-stroke depression: protocol for a systematic review and meta-analysis
AUTHORS	Liu, Wei; Rao, Chang; Zhao, Qi; Du, Yuzheng; Nan, Xi; Li, Zefang; Yin, Chunsheng

VERSION 1 – REVIEW

REVIEWER	Li, Sheng GZHUCM, Department of Acupuncture and Moxibustion
REVIEW RETURNED	17-Mar-2021

GENERAL COMMENTS	Thank you for allowing me to read this article. I am sure this is an interesting topic which will prove the evidence for manual acupuncture clinical effect on PSD. But the protocol is too simple. My suggestions are: 1."we have extracted more detailed information on the treatment schedule of acupuncture (acupoints selection, twist technique, retention time, frequency, etc) in order to study the effectiveness of manual acupuncture therapy from multiple angles" The purpose of this trial is to compare the clinical effect between the manual acupuncture and the non-acupuncture. Thus, it is premature to study the effectiveness of manual acupuncture therapy from multiple angles. 2. The analysis is too simple, for example: primary outcomes: Depression severity: evaluated mainly by Hamilton Depression Rating Scale 119 (HAMD), Montgomery-Asberg Depression Rating Scale(MADRS), Beck 120 Depression Inventory (BDI) and Zung Self-Rating Depression Scale(SDS). How to compare the depression severity between two groups, If the primary outcomes is different in the two groups. 3. The types of interventions is very complicated, thus the subgroup analysis is very important, need detail illustrational.

REVIEWER	Li, Lin-Yan Wujing Community Health Center, Affiliated to Shanghai University of Traditional Chinese Medicine, Tradtional Chinese Medicine
REVIEW RETURNED	03-Apr-2021

GENERAL COMMENTS	This protocol covers the review question, inclusion criteria, search strategy, study selection, data extraction, quality assessment, data synthesis and plans for dissemination. The rationale and the objectives of the study is clearly stated, the outcomes are clearly defined, the English language is sufficient quality, the reference list

	cover the relevant literature adequately. Therefore, this manuscript is suitable for publication.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

1. Comment: "we have extracted more detailed information on the treatment schedule of acupuncture (acupoints selection, twist technique, retention time, frequency, etc) in order to study the effectiveness of manual acupuncture therapy from multiple angles" The purpose of this trial is to compare the clinical effect between the manual acupuncture and the non-acupuncture. Thus, it is premature to study the effectiveness of manual acupuncture therapy from multiple angles.

Response: Thank you very much for pointing out this problem. We have explained in more detail in this revision. The purpose of extracting more detailed information on the treatment schedule of acupuncture should be to provides more analytical basis for subgroup analysis and sensitivity analysis.

Therefore, in Page2 Line 40-43, we changed the formulation from "Compared with previous studies, we have extracted more detailed information on the treatment schedule of acupuncture (acupoints selection, twist technique, retention time, frequency, etc) in order to study the effectiveness of manual acupuncture therapy from multiple angles" into "Compared with previous studies, we will extract more detailed information on the treatment schedule of acupuncture (acupoints selection, twist technique, retention time, frequency, etc) in order to provides more analytical basis for subgroup analysis and sensitivity analysis."

2. Comment: The analysis is too simple, for example: primary outcomes: Depression severity: evaluated mainly by Hamilton Depression Rating Scale 119 (HAMD), Montgomery-Asberg Depression Rating Scale(MADRS), Beck 120 Depression Inventory (BDI) and Zung Self-Rating Depression Scale(SDS). How to compare the depression severity between two groups, If the primary outcomes is different in the two groups.

Response: It's mentioned in the Cochrane Handbook for Systematic Reviews of Interventions that "the standardized mean difference (SMD) is used as a summary statistic in meta-analysis when the studies all assess the same outcome, but measure it in a variety of ways (for example, all studies measure depression but they use different psychometric scales).
(https://training.cochrane.org/handbook/current/chapter-06#section-6-5-1-2) Therefore, if different scales are used to measure continuous outcomes, like depression severity and QOL in our article, SMD will be used as a measure of effect size in efficacy outcome. It's calculated as the difference in mean outcome between groups divided by the standard deviation of outcome among participants.

The problem you pointed out let us realize that there are deficiencies in the analysis part of the article. Therefore, we added the "Data synthesis" in Page 8 as following:

"Continuous outcomes will be calculated as mean differences (MDs) or standardized mean differences (SMDs). If different scales are used to measure continuous outcomes, like depression severity and QOL, SMD will be used as a measure of effect size in efficacy outcome. It's calculated as the difference in mean outcome between groups divided by the standard deviation of outcome among participants. If the same scale is used in the included literature, mean difference (MD) will be used. In addition, safety outcome will be the number of participants who dropped out due to adverse effects and the number of participants who reported at least one adverse event or effect. For these dichotomous outcomes, the odds ratio (OR) will be calculated as the effect estimate."

What's more, we also added some details for the analysis of primary outcomes in Page 5 Line 123-125 as following: "If the included studies used two or more of above scales, we will give preference to clinician-rated scales. Following hierarchy will be applied: (1) HAMD; (2) MADRS; (3) BDI; (4) SDS and (5) all other depression scales. "

3. Comment: The types of interventions is very complicated, thus the subgroup analysis is very important, need detail illustrational.

Response: Thank you so much for this comment, subgroup analysis is truly important. Therefore, we added this part in Page 7-8 Line 176-183 as following:

"Meanwhile, subgroup analysis will also be conducted to explore the main sources of heterogeneity. Compared with previous studies, we will extract more detailed information on the treatment schedule of acupuncture which could provide us more analytical basis for subgroup analysis. If the necessary information is available, subgroup analyses will be carried out according to certain factors (acupoints selection, twist technique, retention time, frequency, period of treatment and different types of control group). After grouping, two or more groups of studies will be analyzed and compared in order to explore the causes of high heterogeneity."

Reviewer 2

1. Comments: This protocol covers the review question, inclusion criteria, search strategy, study selection, data extraction, quality assessment, data synthesis and plans for dissemination. The rationale and the objectives of the study is clearly stated, the outcomes are clearly defined, the English language is sufficient quality, the reference list cover the relevant literature adequately. Therefore, this manuscript is suitable for publication.

Response: Thank you very much for your recognition of this article.

We tried our best to improved our manuscript and made some changes in it which have been marked in yellow in the "Main Document - marked copy" . In addition, Qi zhao was very helpful in revising this article, so we added her as one of the authors. We appreciate earnestly for your warm work, and hope our correction will meet with approval.