

Peer Review File

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Reviewer A

I would like to acknowledge the opportunity to review this interesting systematic review protocol entitled “Assessment of metabolic risks for non-communicable diseases using Sasang constitution: A protocol for a systematic review and meta-analysis” It deals with an interesting theme and I believe it will be of utter importance in assessing the evidence behind this approach. I have some comments in order to improve the quality of the protocol:

Abstract:

- I believe dates should be updated, as the authors should not search until December 2020, but actually December 2021.

Reply: Thank you for your attentive review. Accordingly, we have revised the search period to December 2021 (See Page 3, line 9 and Page 6, line 5).

- It is quite beautiful to spell out the entire name of the main databases, such as “Medical Literature Analysis and Retrieval System Online”, but I believe it would be helpful if the authors also spelled out the acronym in parenthesis for MEDLINE and EMBASE.

Reply: We have added the acronym for main databases (See Page 1, “List of abbreviations” and Page 7, “2.4.1. Data sources and search strategy”).

- Authors refer to a “qualitative evaluation of clinical evidence”. It would be interesting the authors described exactly what tool they are planning to use. Is it GRADE?

Reply: The GRADE or GRADE-CERQual developed by the GRADE Working Group will be applied. We have added related content (See Page 3, lines 18-20 and Page 9, “2.4.6. Qualitative evaluation of clinical evidence”).

- Ideally, the decision to choose between fixed-effects or random-effects should be taken previously to the data synthesis. There are many materials online that say that authors could define the type of effects based on the heterogeneity and other stuff, but this is just wrong. Please see (<https://www.meta-analysis-workshops.com/download/common-mistakes2.pdf>).

Reply: We read the attached document carefully, and have modified our texts as advised (See Page 3, line 17 and Page 8, “2.4.5. Data synthesis”).

- Authors state the following in the discussion section of the abstract: “This study will contribute to helping clinicians and health authorities efficiently detect any relevant metabolic risks that patients may have and design effective strategies to treat and manage them, based on systematic clinical evidence.” I guess it is not what the study will do. This study will only “help clinicians detect metabolic risks” if it proves to be true that SCM is associated with NCD risk factors. Therefore, this is what the study

will do for clinicians and health authorities. The study will show if the SCM is or is not associated with NCD risk factors. Only if it is associated, is that the study may help clinicians.

Reply: We have modified our texts as advised (See Page 3, “Discussion” and Page 9, “3. DISCUSSION”).

INTRODUCTION

- Authors could spend more lines explaining the basics of each SCM type. For the non-acquainted reader, it is difficult to follow the rationale of each SCM type (lines 81-85).

Reply: We have added some explanatory text as advised (See Page 5, Paragraph 2).

- I would not use the expression “till date”, as it is not regular English (line 89).

Reply: We have modified our text as advised (See Page 5, line 27).

RESEARCH QUESTIONS

- In my opinion, two research questions are redundant. I believe the question regarding “association” is enough. If there is an association, it indicates that levels are different between SCM.

Reply: We deleted the second question as advised (See Page 6, “2.2. Research question”).

- Furthermore, authors must clearly state if they are seeking an association between SCM and “metabolic risks” or “metabolic risks factors”. It is a subtle difference, but if they are assessing cholesterol, triglycerides, etc. they are actually seeking “metabolic risk factors”.

Reply: We have modified our text as advised (See Page 6, “2.2. Research question”, “2.3.1. Study design”, and Page 7, “2.3.4. Outcomes”).

Eligibility criteria

- Line 118: It is wrong to state that the subjects of “our study” will be the individuals. A metaanalysis includes studies, not individuals, so the subject of your study will be the studies that have included individuals with “reasonable diagnostic criteria”.

Reply: We have modified our text as advised (See Page 6, “2.3.2. Subjects”).

- Authors should be more specific about the diagnostic criteria. For example, they could cite what are the “certified questionnaires”, pointing to an adequate reference for it. In addition, one could argue if the medical diagnosis (without the use of validated questionnaires) is a good diagnostic criterion.

Reply: We have added more details on the diagnostic criteria as advised (See Page 6, “2.3.2. Subjects”).

-The search strategy presented in Table 1, specifically the #8 strategy is inadequate to retrieve observational studies. Please refer to Li et al 2019 “Search strategies to identify observational studies in MEDLINE and Embase”

(<https://pubmed.ncbi.nlm.nih.gov/30860595/>).

Reply: We have revised the search strategy as advised (See Page 7, line 25 and Page 15, Table 1).

-Please confirm if databases will be searched until December 2020 or 2021.

Reply: We have revised the search period to December 2021 (See Page 3, line 9 and Page 6, line 5).

- The points I mentioned in the abstract regarding the data synthesis (fixed vs random effects) and the discussion also apply to the main text.

Reply: We have modified our texts as advised (See Page 3, line 17 and Page 8, “2.4.5. Data synthesis”).

Reviewer B

The protocol idea is very interesting that they are going to do a risk assessment of NCDs based on SCM. I think that it is a meaningful research protocol for evaluating traditional medicine. It was also clear to understand the reviewing methodology as it was described in the literature.

On the other hand, I think that the classification of SCM constitution needs to be described in more detail because it is a key part of this protocol. Also, who diagnoses SCM constitution and how, and how many people are diagnosed with Sasang constitution as of now? How many people are diagnosed with SCM method constitution and how much validity is recognized outside the field of NCD? What are the characteristics of the SCM recipients themselves? These characteristics can lead to research bias. There is a little explanation from Line 81, however it is shortage. I would recommend to add these above explanations with literatures for publication as a protocol paper.

Reply: Thank you for your attentive review. We have added a description of the diagnostic expert and questionnaire as an accredited diagnostic method of the Sasang constitution (See Page 6, “2.3.2. Subjects”). Statistics on the number of SCM diagnoses so far cannot be confirmed. However, since Sasang type is considered an innate factor for everyone, in principle, a specific Sasang type of every individual can be diagnosed. We have added some explanations on categorization of Sasang types (See Page 5, Paragraph 2).