**Dear Editors,**

Thank you for the review of our manuscript, entitled “Subclinical hypothyroidism and the metabolic syndrome -- a meta-analysis of cross-sectional studies” that was submitted to *World journal of meta-analysis*. We appreciate the constructive comments and have revised the manuscript in accordance with the reviewer’s comments. The reviewer’s comments are listed below in italics, each followed by our response indicating how the manuscript was changed. Also, we have our MS edited by the *SPI* language editing company before our first submission.

**REVIEWER #1**

*Ye et al. performed a meta-analysis of subclinical hypothyroidism and metabolic syndrome using MEDLINE, EMBASE, Cochrane database, and manual search of literature using references of original manuscripts, reviews, and meta-analyses. This is an interesting study and addressing an important area. Major comments: Although the authors showed that there was no heterogeneity between results from different studies (in terms of χ2 and I2), it is well acknowledged that the study design, confounding factors included, as well as the definitions of subclinical hypothyroidism and metabolic syndrome vary greatly between studies, for example: - literatures may use TSH alone, TSH + T4, or other possible definitions to define subclinical hypothyroidism; - a number of pharmacological agents are known to affect thyroid hormone metabolism, but not all studies excluded subjects taking medications that affect thyroid function; - In additional to subclinical hypothyroidism, nonthyroidal illness may also have altered thyroid hormone profile but without evidence of thyroid dysfunction, suggesting that the observed association might be confounded by nonthyroidal illness. - Model adjustments are different Therefore, I would suggest the authors to present the above information in Table 1 and discuss how these issues might affect the findings and interpretation of the current study.*

**Response:** Thank you for your comments. We have added inclusion/exclusion criteria and the definition of SCH in each study in table 1. Also we have discussed the potential confounding effects of these issues as limitations of the studies.

*P.10, “SCH has been proven to be associated with increased risk of cardiovascular disease and mortality…” the paragraph is too strong. Up-to-date, we are still not sure whether subclinical hypothyroidism is associated with cardiovascular disease and mortality. Since it has been reported that subclinical hypothyroidism is associated with components of metabolic syndrome (as well as suggested by the current study), the association with cardiovascular disease might be mediated by the effect of these risk factors. It is still not sure whether the association is independent or dependent on other risk factors. The authors should perform a more comprehensive review and discussion on this conflicting issue.*

**Response:** We have modified our statement accordingly and discussed this issue in paragraph 1 in Discussion Section.

*Minor comments: 1. The authors used “trial” to describe the included studies is incorrect, no trial is included in the current study. It should be “study” instead of “trial”.*

**Response:** we have corrected it accordingly.

*2. Under the section of “Data sources and searches”, usually Cochrane database is included in the initial search, not sure why authors use it “finally” after searching in MEDLINE and EMBASE.*

**Response:** we have mortified it accordingly.

*3. Page 7, line 2: WMD should be first defined here instead of in page 8. [weight mean difference (WMD)]*

**Response:** we have corrected it accordingly.

*4. Page 8, you have defined body mass index as BMI in page 6 (same apply to other component of metablic syndrome), so you don't need to spell out the full name here.*

**Response:** we have corrected it accordingly.

*5. Throughout the manuscript, please change euthyroidism population/group to euthyroid population/ group.*

**Response:** we have corrected it accordingly.

*6. It is of interest to discuss the association between overt hypothyroidism and the components of metabolic syndrome, as subclinical hypothyroidism is regarded as an initial stage of overt hypothyroidism.*

**Response:** we have added it accordingly.

*7. English needs improvement.*

**Response:** we have mortified it accordingly.

**REVIWER #2**

*The authors performed a meta-analysis about the correlation of subclinical hypothyroidism and meyabolic syndrome. The article is interesting and the statistical analysis well performed. I recommend minor revisions, and in particular revision of english language*

**Response:** Thank you for your comments. We have it revised.

**REVIWER #3**

*This meta-analysis is needed and valuable. However, the manuscript requires some clarifications regarding the following： 1. Authors only mentioned “Six cross-sectional studies “ in the abstract. They were not mentioned in the text, what are they? And why only cross-sectional studies? So what are their inclusion criteria?*

**Response:** Thank you very much for your comments. We have specified the study identification and characteristics of included studies in the ***Results section*** and Table 1, as well as inclusion criteria in ***Methods section.***

*2. The authors described in the last paragraph of result, “No significant publication bias was found after assessment using the Begg’s funnel plot (p=0.573)”. However, in the 6 included studies, the participants in 3 Chinese population occupy more than half of the total participants(13978/19546, 71%). There may be race heterogeneity. If so, the results should be carefully explaied. Therefore, further statistical analysis should be carried out after the three studies from China are excluded.*

Response: It is true that race heterogeneity may affect the final conclusion, thus we perform an additional subgroup analysis to calculate the OR for MS in Chinese studies and non-Chinese studies and we found that race difference did not significantly affect the final conclusion. (OR for MS in Chinese studies: 1.256, 95%CI 1.063- 1.484; OR for MS in non Chinese studies: 1.130, 95%CI 0.938- 1.360, p for interaction= 0.404)

**REVIWER #4**

*Doctor Zhang and colleagues report the results of a meta-analysis of observational studies evaluating the association between subclinical hypothyroidism and metabolic syndrome and its individual components. Overall methodology and spelling is correct, and the results are very interesting. Comments: 1- Abstract: in line 34 authors state that they used random or fixed models as appropriate, but there is no reference to which method was used.*

**Response:** Thank you for your comments. We have revised it.

*2-Methods: in line 66, authors state that they follow QUOROM statement, please update to PRISMA guidelines.*

**Response:** we have updated it.

*3-Data synthesis: in line 114 and 115, authors state that they computed pooled OR and WMD. In this section it should be mentioned if they used for this purpose the numbers reported in the studies or adjusted OR (estimate more reliable of effect size at study level in observational studies, and should be used).*

**Response:** we use unadjusted OR to compute the pooled OR, we have specified it in the revised MS. It is true that adjusted OR is more reliable in the observational studies; however, most of the included study did not report the adjusted OR directly, which make it impossible to use adjusted OR as effect size in our meta-analysis. We have also discussed this issue in the limitation section.

*4-Data synthesis: in line 114 and 115, authors mention that they used fixed- or random-effect models as appropriate, but there is no indication in the text or figures of which method was used. I suggest to change this sentence, and replace it by one stating the method used and an explanation of the reason for the choice.*

We have revised it as *“The pooled ORs and WMD for the outcomes were calculated using fixed effects models since there may be potential heterogeneity among the studies.”*

*5-Data synthesis: line 115 to 118. X2 (or Cochran Q test) and I2, measure two different (although related) concepts. The first measures the heterogeneity and the second the inconsistence, please clarify these concepts. Also, note that the power of the heterogeneity test have low power when the number of included studies is small (as is the case) so the p value considered as significant should be greater than the reported by the authors.*

**Response:** we have it revised.

*6-Data synthesis: line 121, the Egger's test is also a low power test when the number of studies is small, for this reason the p value commonly accepted as significant is <0.1.*

**Response:** we have it revised.

*7-Overall: article could gain in clarity improving the english.*

**Response:** we have it modified.

**REVIWER #5**

*This reviewer has put his comments directly in the pdf file of our MS.*

Thank you very much for your comments.

We have revised the MS and add necessary data as required.

Besides, the reason why we did not calculate the total cholesterol or LDL-C level in our meta-analysis is that TC and LDL-C are not the components of diagnostic criteria for the MS, even though TC and LDL-C may be associated with the MS.