Author’s response to reviews

Title: Maternal body mass index and risk of neonatal adverse outcomes in China: a systematic review and meta-analysis

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Author’s response to reviews:

Reply to the Reviewers

Thank you very much for your interest in our manuscript entitled “Maternal body mass index and risk of neonatal adverse outcomes in China: a systematic review and meta-analysis.” To aid in the re-review of this manuscript, we have included a point-by-point response to each comment. The reviewers’ comments are italicized and placed in square brackets. In addition, within the revised manuscript, we have used underlined text to highlight changes in response to the reviewers’ comments.

We appreciate the suggestions and comments by the reviewers. As a consequence of the valuable suggestions, we believe that our manuscript has been much improved.

Merry Christmas!

[Editor Comments]

[1. The reviewers have requested a few additional clarifications and language corrections. While the manuscript file includes the legend for the PRISMA flow chart (Figure 1), the figure itself does not seem to be included in the manuscript. When re-submitting, please carefully review the...]
manuscript to ensure that all supplemental files, tables and figures referenced in the manuscript or PRISMA guidelines are included in the revision.]

Thank you for your careful work. We have amended sentence structures and grammatical issues throughout the manuscript using Nature Research Editing Service (NO. TXY39S9H). And, we did miss the figure 1 when uploading revised manuscript. Sorry about that! We have checked carefully to ensure that all supplemental files are included in the newly uploaded manuscript. (PRISMA guidelines in Additional file 1).

[Dazhi Fan, Pd.D (Reviewer 2)Comments: Comments for the Authors...]

The article is ready for publication. I have no question.

[Angela Vinturache, Pd.D (Reviewer 3)Comments: Comments for the Authors...]

Thank you for the opportunity to review this manuscript. This is a revised version of the initial submission. Most of the issues have been addressed in this version following the concerns raised by the previous reviewers.

Specific Comments

< Abstract>

[1. Pooled statistics were derived from Stata/SE, ver. 12.0 - This is an ambiguous statement. Pooled statistics were used for what? STATA software was used for the analysis.]

Thank you for your careful work and instructive advices. Accordingly, we have added the ABSTRACT section as follows:

“The dichotomous data on maternal BMI and harmful neonatal outcomes were extracted. Pooled statistics (odds ratios, ORs) were derived from Stata/SE, ver. 12.0.”

(ABSTRACT, page 2, line 12)
[2. The conclusion does not align with the aim of the study. I believe the conclusion is that raised pre-pregnancy BMI is associated with adverse neonatal outcomes. The analysis from this manuscript did not look at the management of obesity. There are two issues with the statement "Reasonable treatment for maternal weight to avoid maternal underweight, overweight or obesity" : 1) it is incorrect in the sense that there is no treatment to my knowledge for weight; at the most there is some management guidelines that refer to adjustments of lifestyle and diet; 2) the statement is unclear, general, and confusing: what is reasonable?]

We appreciate this question. According to your advice, we have re-wrote the conclusion based on the findings of the study as follows:

“Raised pre-pregnancy BMI is associated with adverse neonatal outcomes. Management of weight during pregnancy might help reduce their adverse neonatal outcomes in future intervention studies or programmes.”

(ABSTRACT, page 2, line 35)

< Body of the manuscript >

[1. There is still a challenge along this manuscript, from title to the Discussion section, in defining the outcomes of this study: maternal vs obstetrical vs neonatal. The authors should check the manuscript and make the necessary changes.]

We appreciate this question. We have checked the manuscript from the title to the conclusion, and found many mistakes and revised them as follows:

“Management of weight during pregnancy might help reduce their adverse neonatal outcomes in future intervention studies or programmes.”

(ABSTRACT, page 2, line 33)

“Neonatal outcomes”

(KEYWORDS, page 2, line 41)
“This systematic review and meta-analysis of over 1.6 million Chinese mothers examined the quantitative effect of maternal BMI on adverse neonatal outcomes.”

(DISCUSSION, page 11, line 8)

[2. Page 5: is row data or raw data? There are several grammar errors along the manuscript. I trust the authors will attend to those.]

Thank you for your careful reading of our manuscript. We are sorry for such negligence. We have already made modifications in the newly uploaded manuscript.

[3. Page 5: In the sentence "Odds ratios and the 95% confidence interval were synthesized for the dichotomous outcomes from of each study" the verb synthesized does not seem the best choice. Please find a better word to define what the action was in this sentence.]

Thank you for your instructive suggestions. Accordingly, we have modified this verb to “pooled”, as follows:

“Odds ratios and the 95% confidence interval were pooled for the dichotomous outcomes of each study.”

(Statistical analysis, page 6, line 9)

[4. In the narrative review of papers not included in the metaanalysis the authors mention a large study of the association between maternal BMI and the risk of PTB. Whereas the authors offer an explanation on why those studies were not included one cannot wonder what would have been the impact of those numbers on the results of the present study. I maintain the opinion of the reviewer who challenged the authors selection criteria to consider eligible only the studies with sample sizes higher than 1000.]

Thanks you for your comments. We appreciate your concern about the 1000 selection criteria we used. Ninety-one studies were excluded using this criteria, most of which had a sample size of
around 100 and were published on Chinese journals. During the second stage of study selection, we found the quality of these studies were low based on the Newcastle-Ottawa Quality Assessment Scale for cohort studies. As we focused on well-designed and large prospective or retrospective cohorts of pregnant women, a selection criteria was therefore made. In addition, we also compared several other criteria like 500, 1500 with 1000 and finally selected the 1000 which could best excluded the low-quality studies without influencing the inclusion of moderate quality studies. Consistent with the present study, previous meta-analyses studies also used the 1000 sample size as selection criteria. [Drug Alcohol Depend. 2018; 1 (191):234-258] [Int J Cardiol Heart Vasc. 2018; 19 :90-97] [Exp Ther Med. 2018; 15 (4):3952-3966]. Considering all of the above points, we therefore used 1000 sample size as a selection criteria in the present study.

[5. Overall, the Discussion section is very thin, findings little discussed in the context of the literature. Even more so when compared with the amount of results presented. The first paragraph of the Discussion should be moved down in the section, which should start a summary of the findings before moving on to stress the significant or novel ones. ]

Thank you for your instructive suggestions. Accordingly, we have modified and added the DISCUSSION section as follows:

“This systematic review and meta-analysis of over 1.6 million Chinese mothers examined the quantitative effect of maternal BMI on adverse obstetric and neonatal outcomes. In summary, being overweight or obesity obese was associated with an increased risk of macrosomia, LGA, PTB and neonatal asphyxia, while being underweight increased the risk of LBW and SGA.”

(DISCUSSION, page 11, line 6)

Neonatal asphyxia is defined as the state producing a combination of systemic hypoxemia, hypercapnia, and metabolic acidosis that may occur before and during birth, and during neonatal period [69]. The present study is the first attempt to assess the pooled risk of neonatal respiratory diseases attributable to maternal BMI. Our research indicated that the incidence of neonatal asphyxia in infants whose mothers were overweight or obese was generally higher than that of the comparison group. This is consistent with the results of a population based study [70]. However, asphyxia in newborn infants causes cerebrovascular disease and neonatal brain injury and may lead to lifelong neurodevelopmental disabilities [71].”
[6. The "Elective and medical PTB" describe the same term, iatrogenic PTB.]

Thanks you for your correction. We have already made modifications in the newly uploaded manuscript (DISCUSSION, page 11, line 54).

[7. On page 11, the statement about the caesarean sections is among the discussion about maternal BMI and PTB, distracting the reader from the problem at hand. C section rates should be included in a separate section. However, the paper was focusing on neonatal outcomes. ]

Thanks you for your comments. According to your advice, We have deleted the statement about the cesarean sections in the newly uploaded manuscript.

[8. The Conclusion contains some general statements that require a re-write based on the findings of the study.]

We appreciate this question. According to your advice, we have re-wrote the conclusion based on the findings of the study as follows:

“An analysis of the current evidence in the literature suggests that maternal weight status is critically important to neonatal health during the perinatal period. In summary, being overweight or obese was associated with an increased risk of macrosomia, LGA, PTB and neonatal asphyxia, while being underweight increased the risk of LBW and SGA. Management of weight during pregnancy might help reduce their adverse neonatal outcomes in future intervention studies or programmes. In the meantime, we recommend intervention developers and behavior change agents in the field to developing tailored interventions within women of childbearing age.”
The majority of the previous reviewer’s queries have been answered, however there are a couple outstanding. There remain some language errors and errors in the references that need to be corrected.

Summary - a revision of a manuscript with significant changes: "Maternal body mass index and risk of neonatal adverse outcomes in China: a systematic review and meta-analysis"

References: errors of formatting remain - capital letters of journal names.

PRISMA checklist has been completed as requested

Tables have been updated according to reviewer suggestions (number of studies)

< Abstract >

[1. Results: comparing BMI with weight. Should be consistently comparing weight or BMI for clarity. Conclusion: focus is on neonatal not obstetric outcome]

Thank you for your instructive suggestions. According to your suggestion, we have already made modifications in the newly uploaded manuscript. (ABSTRACT, page 2, line 18, 35)

< Introduction >

[1. could include in introduction that antenatal care is standardized across China, as per previous reviewer query.]

Thank you for your instructive suggestions. To clarify this point, we have added the BACKGROUND section as follows:
“China has made impressive achievements in improving maternal and child health (MCH) over the past few decades [14]. In China, pregnant women are registered at the primary hospitals, and in the 32nd gestational week, they are referred to a secondary hospital or a tertiary hospital for management till delivery. And, children are given the health examinations in the newborns, postnatal period, infancy, and at preschool [15]. These efforts established a strong foundation for the development of MCH in the 21st century, which covers both urban and rural areas [14].”

(BACKGROUND, page 3, line 38)

[2. Page 2, Line 36 - replace "receiving the greatest attention among..problems" with "a global health problem".]

Thank you for your careful reading of our manuscript. We have already made modifications in the newly uploaded manuscript. (BACKGROUD, page 2, line 48)

[3. Page 2, Line 45 - "Consequently"]

Thank you for your careful work. We have already made modifications in the newly uploaded manuscript. (BACKGROUD, page 2, line 52)

[4. Page 2, Line 53 - increasing health burden]

Thank you for your careful work. We have already made modifications in the newly uploaded manuscript. (BACKGROUD, page 2, line 60)

[5. Page 2, Line 59 - increasing rate]

Thanks you for your comments. We have already made modifications in the newly uploaded manuscript.
“In 2015, China's one-child policy was replaced by a universal two-child policy increasing the rate of second pregnancies [7].”

(BACKGROUND, page 3, line 3)

[6. Page 3, line 17 - more consistent to continue to refer to body mass index]

Thank you for your careful work. We have already made modifications in the newly uploaded manuscript. (BACKGROUD, page 3, line 24).

[7. Page 4 line 4 - "frome" should be "from"]

Thank you for your correction. We're very sorry that it was a mistake in our writing. We have already made modifications in the newly uploaded manuscript. (Page 4, line 20)

[8. Page 4 line 17 - consistent with previous reviewer's questions - should include here the handling of papers with data from overlapping populations. The question was answered but not attended to in the text.]

Thank you for your instructive suggestions. To clarify this point, we have added the MATERIALS AND METHODS section as follows:

“If articles assessed the same participants, we only selected the study with a greater number of participants, the best methodological qualities and that report the most information to avoid attributing more weight to these studies in the meta-analysis.”
We followed the standards, which were used across all regions of China, including the World Health Organization (WHO; underweight: <18.5 kg/m², normal weight: 18.5-24.9 kg/m², overweight: 25.0-29.9 kg/m² and obese: >30 kg/m²), the Asia-Pacific standard (APS; underweight: <18.5 kg/m², normal weight: 18.5-22.9 kg/m², overweight: 23.0-24.9 kg/m² and obese: >25.0 kg/m²) and the standard for Chinese adults proposed by the Working Group on Obesity in China (WGOC; underweight: <18.5 kg/m², normal weight: 18.5-23.9 kg/m², overweight: 24.0-27.9 kg/m² and obese: >28.0 kg/m²).”

We followed the standards, which were used across all regions of China, including the World Health Organization (WHO; underweight: <18.5 kg/m², normal weight: 18.5-24.9 kg/m², overweight: 25-29.9 kg/m² and obese: >30 kg/m²), the Asia-Pacific standard (APS; underweight: <18.5 kg/m², normal weight: 18.5-22.9 kg/m², overweight: 23.0-24.9 kg/m² and obese: >25.0 kg/m²) and the standard for Chinese adults proposed by the Working Group on Obesity in China (WGOC; underweight: <18.5 kg/m², normal weight: 18.5-23.9 kg/m², overweight: 24.0-27.9 kg/m² and obese: >28.0 kg/m²).”

“fetal distress (defined as signs indicative of fetal hypoxia, which included fetal bradycardia, severe variable decelerations and persistent late decelerations), and neonatal asphyxia (defined as Apgar score <7 at 1 minute).”
We appreciate the suggestion. According to your advice, we have added the related references in this section. (Reference 17)

We appreciate this question. We confirmed that all the women included in all the studies are Chinese. In the process of study selection, only Chinese population was included. (Study selection, Page 4, line 49)

Thank you for your correction. We have already made modifications in the newly uploaded manuscript. (Page 11, line 24)

Thank you for your correction. We have already made modifications in the newly uploaded manuscript. (Page 11, line 45)
Thank you for your correction. We have already made modifications in the newly uploaded manuscript. (Page 11, line 51)

Thank you for your comments. We have already made modifications in the newly uploaded manuscript.

“Furthermore, we followed the checklist of the PRISMA, which includes a comprehensive search strategy, assessment of publication bias, and heterogeneity testing with a stratified analysis to explore the impact of maternal BMI measured or obtained before or during the first trimester on birth outcomes.”

(DISCUSSION, page 12, line 24)

Thank you for your correction. We have already made modifications in the newly uploaded manuscript. (Page 12, line 53)