Author’s response to reviews

Title: Maternal and birth cohort studies in the Gulf Cooperation Council countries: a systematic review and meta-analysis

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Maternal and birth cohort studies in the Gulf Cooperation Council countries: a systematic review and meta-analysis

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REPLY TO EDITOR’S and REVIEWERS’ COMMENTS

Reply to the Editor

Editor: Thank you for submitting the revised version of your manuscript. I have now received a second round review from one peer reviewer, and I agree with the comments and suggestions when I read through the manuscript myself. In your response, please address each of the comments individually and make note of where and how the manuscript has been changed. If no changes are made in relation to an individual comment, please explain why.

Response: we would like to thank the editor and the reviewer for reviewing the second revision of our manuscript and for their valuable feedback and suggestions. We feel the second revision of the manuscript has been further improved as a result of the review process. Please find below a point-by-point reply addressing each of the editor’s and reviewer’s comments.
Reply to Reviewer #2:

Dear authors: Thank you for considering my previous comments. Your manuscript has improved a lot. I still have some concerns.

Response: Thank you for re-reviewing our manuscript and providing us with additional comments and suggestions. Please find below a point-by-point reply addressing each of the raised comments or suggestions.

Major comments

Comment: Please consider revising your title. As it is right now, I believe is not reflecting what is your manuscript about.

Response: We thank the reviewer for their comment. All study authors are in agreement that the current title accurately reflects the scope of the systematic review. Specifically, we feel that the title clearly indicates the following:

- Study design: a systematic review and meta-analysis
- Setting: Gulf Cooperation Council countries
- Study subjects: pregnant women and their offspring from maternal and birth cohort studies

Also, the title reflects clearly the study objectives that are stated in the abstract and main text. All study authors are satisfied with the current title but would greatly appreciate suggested improvements from the reviewer.

Comment: Please revise your background to include information about what is affecting pregnant women/children in GCC. Make sure you include epidemiology on your selected outcomes (maternal obesity, CS, fetal macrosomia). The difference or the importance of maternal/child care for this region/compared to other regions. When you do this, do not forget to keep it short and sharp. Right now you're providing more than enough information about what can affect maternal and infant health, without giving the readers any information about the situation of maternal/child mortality/morbidity in the region.

Response: We thank the reviewer for their comment. Authors would like to highlight that the presented systematic review and meta-analysis is not about discussing single or couple of maternal and/or child outcomes in the GCC countries. Our manuscript presents and discusses maternal and birth cohort studies in GCC countries to highlight exposures and outcomes being studied to identify gaps-in-evidence as well as to provide pooled estimate on common exposure-outcome pairs. Nevertheless, lines 81-88 in the clean copy provide information on the growing concern on maternal and prenatal exposures in the GCC countries.

Comment: Please note that your objectives (general and specific) are not clear enough. They sound repetitive. I would suggest you to revise them carefully. "systematically review and to chronicle exposures and outcomes.... specific objectives include 1) to chronicle the exposures and outcomes". You could say The objective of this systematic review is to describe the different prenatal exposures that can affect pregnant women and/or their child and estimate their association with three selected outcomes 1) maternal obesity, 2) caesarean section and 3) fetal macrosomia.
Response: We thank the reviewer for the comment. In line with the reviewer’s suggestion, we have revised the wording of the stated objectives to avoid repetition and improve comprehension (Lines 101-105 in the clean copy). Please note that these objectives were set a priori and aligned with the original objectives in the published protocol.

Comment: Please justify the selection/importance of the selected outcomes.

Response: We thank the reviewer for their feedback. In the qualitative synthesis of evidence, the outcomes reported in the original studies were summarized under two outcome categories (maternal and birth) as stated in the manuscript. With regard to the quantitative synthesis of evidence, the second objective stated in our published protocol was to “summarizes the strength of association between maternal exposures during pregnancy (ie, body mass index) and different maternal and birth health-related outcomes (ie, birth weight and mode of birth delivery).” In order to perform meta-analysis, at least three adjusted effect estimates were required for each specific exposure and outcome pair. This was stated in the published protocol and the current manuscript (Lines # 192-193 in the clean copy). Maternal obesity (exposure) and (i) Caesarean section (outcome); and (ii) macrosomia were the only exposure-outcome pairs that had three or more adjusted effect estimates available.

Comment: Please revise your inclusion/exclusion criteria: are you including only cohorts? Justify the exclusion of solid study designs such as RCTs, cross-sectional and case control.

Response: We thank the reviewer for the comment. The inclusion and exclusion criteria in this manuscript are aligned with those stated in our peer-reviewed and published protocol manuscript. As long as our criteria were very clear and conducting the review followed our published and registered protocol, the authors believe that there is no need to justify why other study designs were excluded. We agree with the reviewer that other solid study design such as RCTs could be more informative to look at the association between outcome-exposure pair; however, RCTs do not exist for the majority of maternal and child health exposure and outcome pairs, such as maternal obesity and macrosomia. As such, cohort study designs provide the best available evidence.

Comment: Note you’re also excluding conference abstracts and grey literature (also make sure you include this in your limitations). Any exclusion on publication language. Please make sure to specify how many titles you found in GCC languages and include in your limitations that you did not search in regional/national databases.

Response: We thank the reviewer for their comment. We have now added one more point to the limitation sections addressing the raised comment (Lines 452-456 in the clean copy).

Comment: Please specify how many people where involved in resolution of conflicts from selection criteria and data extraction.

Response: We thank the reviewer for their comment. We have now inserted the number and initials of the researchers involved in resolution of conflicts from selection criteria (line # 127 in the clean copy) and data extraction (Lines # 152-155 in the clean copy).

Comment: Please justify the decision of the six exposure domains, and consider including an additional category of "mixed". I believe some are overlapping (medical/medical service, maternal/reproductive and perinatal, maternal or infant and socio-demographic), as you mention in the next sentence "a study could incorporate more than one exposure...". I would also suggest for you to define each exposure...
domains, in the same section and not separate (for example: we categorized measured exposures into: 1. xxxx). To evaluate associations you should be able to have a clearly defined category, otherwise how you can exclude mixed associations? Regarding the measured outcomes please note these are overlapping as well, what is the difference between birth and maternal, perhaps it should be pregnancy, maternal and neonatal outcomes.

Response: We thank the reviewer for their feedback. We would like to highlight that individual studies reported several shared and different exposures. As stated in our published protocol, we anticipated some degree of study heterogeneity with regard to exposures and outcomes. In order to maximize the reader’s understanding of the measured exposures, we categorized the exposures reported in individual studies into six exposure domains based on the nature and source of the exposure, as stated in the manuscript (Lines 166-169 in the clean copy). For example, it is widely known in the literature that BMI are anthropometric measures. This is also applicable to categorization of outcomes into two domains. It is worthy to note that some studies, as summarized in table 1, might measure several exposures and several outcomes on the same study subjects. In such cases, each measured exposure, according to the defined six exposure domains, fell under only one of the six domains, as well as each measured outcome fell only under one of the outcomes domains, but not under both of them at the same time. Exposures and outcomes were assigned to the most appropriate single category.

As for the suggestion of considering adding a “mixed” category, we would like to highlight that there is no need to add the suggested “mixed” category. According to our categorization scheme of exposures, based on the nature and source, into six domains, each of the measured exposures should fall under only one category. In the manuscript, lines # 171–181 in the clean copy, we clearly defined which exposures were categorized under each of the six-exposure domains. As suggested, we now have defined each exposure domain, in the same section and not separately.

Comment: Again the results appear more as a summary of the individual studies than results from a systematic review, when describing your results make sure you're describing any particularities identified in a certain country and differences by age, educational level, etc. (i.e. x country reported higher rate of CS, a study in x, reported xx% of women had fetal macrosomy

Response: We thank the reviewer for the raised comment. Apart from the meta-analysis, we agree with the reviewer that the results appear more as a summary of the individual studies. Indeed, the first objective stated in our published protocol and the current manuscript was to “summarize and characterize the exposures and outcomes that have been examined and discussed in the maternal and birth cohort studies in the six GCC countries (qualitative synthesis)”. Authors would like to highlight that this is a systematic review and its objective is not to provide any comparisons between countries on the burden of the measured outcomes and exposures. Describing any particularities identified in a certain country and differences by age, educational level, as recommended by the reviewer would be out of the scope and objectives of our review.

Comment: Revise your discussion, according to my previous comments. Revise your limitations, some are missing, while others are not as relevant.

Response: We thank the reviewer for their suggestion. We included one additional limitation in the Discussion section. Previous comments from the reviewers on earlier versions of the manuscript did not highlight any discrepancies in our Discussion of the review findings. In view of the journal’s word limit and suggestion to reduce the manuscript length, the authors are satisfied with the depth and breadth of the current discussion and no further changes will be made to this section.
Minor comments

Comment: To make the manuscript easy to read, I would suggest you to reduce it's length by removing duplicate or unnecessary information, for example possible categorization of ROB (yes, no, can't determine...) just mention what tool you used, what aspects the tool was evaluating and how many people did the ROB assessment.

Response: We thank the reviewer for their feedback. We agree with the reviewer that the earlier version of the manuscript would benefit from a reduction in length. Accordingly, we have revised the manuscript and reduced the word count from 5,677 words to 5359 words.

Comment: Make sure to describe in data extraction, information needed for the meta-analysis.

Response: We thank the reviewer for their comment. We feel that the data extraction process and information required for quantitative synthesis is accurately and concisely described in the manuscript (please refer to lines # 193-203 in the clean copy).

Comment: Suggest to revise your conclusion, to make a stronger and shorter statement.

Response: We thank the reviewer for their feedback. In view of this comment, we have reduced the length of the conclusion. We feel that the final version of this section of the manuscript succinctly concludes the main findings and implications of this review.

Comment: Revise your references, there are some typos or some do not follow journal style. There are also two references, not clear to me which one was the most recent version.

Response: We thank the reviewer for identifying our typographical errors. We have now reviewed the cited references, corrected typos, and made sure they are following the journal's style. We addressed the issue of duplication between reference # 30 and # 133. Authors have now removed reference #133 and provided the correct citation for reference # 30. We would like to highlight that references # 14 and 128 are not duplicates, the latter is an update.

Comment: Suggest to revise your tables. For example Table 1 is very long, when you have a high number of articles you can present a summary of findings table, where instead of including each article you mention the number of articles reporting your outcome and include the reference. Suggest you to search for examples in other reviews with >50 articles.

Response: We thank the reviewer for their feedback. We agree with the reviewer that table 1 is long to the extent it might be difficult to be published in the main text. We now have considered the reviewer’s suggestion of including the number of articles reporting exposure and outcomes domains with the citing the references (Please refer to Table 1). We feel that the supplementary tables contain rich and informative data about the reviewed cohort studies that would be of interest to researchers in this field. As such, we prefer not to reduce the size or format of these supplementary tables as this would require us to delete important extracted data.