Author's response to reviews

Title: Early pregnancy body mass index and spontaneous preterm birth in Northwest Russia: a registry-based study

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Author's response to reviews: see over
Dear Editor

Thank you for the opportunity to improve our paper. We thank the reviewers for their comments. We are happy to say that most of their comments have been addressed in the re-submitted version of the manuscript. Our answers on their comments and criticisms are summarized below. Location of the changes in the manuscript (page(s) and line(s) numbers) is specified in this summary for each comment. We hope that the revised version of the manuscript is of sufficient quality for publication in the Journal.

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Sincerely yours,

Ekaterina Sharashova
Answers to the Reviewer 1 comments

1. Methods, second paragraph: Have the MCBR data been validated? How accurate or reliable is this registry. Please comment.

- The MCBR was established in cooperation with the University of Tromsø (UiTø), Norway using the Norwegian Medical Birth Registry, Bergen, Norway (MFR) as a model. Several quality control exercises have been carried out, and the quality and completeness of the MCBR was found to be acceptable. Details on the quality of the data and data collection routines are presented elsewhere (Quality Assurance/Quality Control [QA/QC]) – ref.19 in the article.

- Addressed on pages 5-6, lines 110-119.

Furthermore, you state that the data is recorded by a midwife or physician from medical records and interviews with the mothers. Did the physician/midwife receive appropriate training? If so, add ‘by a “trained” physician or midwife’. Who enters the data into the registry database –again is this quality controlled?

- The personnel was trained (3 workshops and one-on-one training with each midwife/doctor responsible for filling out the forms in each of the hospitals; detailed user manuals were provided as well – ref.19 in the paper). After all the information was collected and recorded on the registry form by the trained physicians and midwives, the forms were sent by courier to the Registry Office in Murmansk, where the data where entered into an Access database by 2 trained persons (double entry). Details on data collection and data entry are presented in ref. 19.

- Addressed: pages 5-6, lines 114-119 with the ref. 19 for more information; page 6, lines 126-127.

2. Methods, sixth paragraph: You state “Mother’s education was classified as basic or less……”. However, in Table 1 you write ‘basic or none’. Please be consistent and use one or the other.
3. Methods, sixth paragraph: You write ‘Alcohol use’, but have ‘alcohol abuse’ in Table 1. Which is it? Please clarify again whether this is before pregnancy, during pregnancy or both.

- It is “alcohol abuse during pregnancy”: page 7, lines 156-157 and table 1.


- Excessive weight gain is a diagnosis that is stated by a doctor (O26.0 according to ICD 10). It is based on a combination of pre-pregnancy BMI, total weight gain during pregnancy and/or rates of weight gain 2nd and 3rd trimesters (average range/week). This information was obtained from obstetric journals.

- Addressed: page 7, line 159.

5. Results, paragraph two: Maternal background characteristics. This is a very lengthy paragraph. I suggest shortening significantly and refer the reader to Table 1.

- Shortened: page 8, lines 179-182.

6. Limitations, paragraph three: Regarding the reporting of gestational age using date of the last menstrual period (LMP) –and the biases associated with LMP compared to ultrasound recording of gestational age, please add a reference to support this. For example, Dietz et al. Paediatr Perinat Epidemiol. 2007 Sep;21 Suppl 2:62-71.

- Added: page 13, lines 290 (ref. 24).

7. Limitations, paragraph five: Please add in lack of data on history of preterm delivery, or pregnancy loss as well as use of fertility treatments as further limitations.


Furthermore, what about reporting and measurement bias? Particularly for smoking and alcohol use – these were self-reported and therefore sensitive items such as these are more likely to be underestimated or not reported at all. Please comment on the validity of the data also.
- Addressed: page 14, lines 308-310.

- There is no self-reporting involved in relation to alcohol. Doctors have diagnosed women with an alcohol problem: page 6, line 125.

8. Table 1: The cells for age at delivery are not aligned properly. For example there are no values in the cells for maternal age >35 as these are opposite maternal age 30-34. Please fix.
   - Addressed: page 21, table 1.

9. Table 1: Please add details of pregnancy complications (diabetes, hyperemesis, preeclampsia, etc.)
   - Added: pages 21-22, table 1 (last 4 rows).

10. Table 1: You have ‘smoking before pregnancy’. Was this only smoking before pregnancy or also during? You state during pregnancy in the methods but before in Table 1. Please clarify accordingly.
    - It is “Smoking before pregnancy”: page 7, line 156 and page 21, table 1.

11. Table 1: You write ‘Alcohol abuse’, but have ‘alcohol use’ in your methods section. Which is it? Please clarify again whether this is before pregnancy, during pregnancy or both.
    - It is “alcohol abuse during pregnancy”: page 7, lines 156-157 and page 21, table 1.

   Also, why do you have a symbol representing ‘statistical significance’ for age at delivery only and not the other significance variables?
    - It is taken out as irrelevant: page 21, table 1.

12. Table 2, footnote. Again, alcohol ‘use’ or ‘abuse’ and pre- or during pregnancy, or both? Define excessive weight gain.
    - Addressed: page 23, lines 460, 463.

13. Figure 1: First text box – add an ‘s’ to ‘birth’.
14. Figure 1: Fourth text box – add an ‘s’ to ‘week’

- Added: figure 1.

15. Figure 1: Last text box - Delete ‘data of’ and add ‘the’ between ‘in’ and ‘analysis’

- Deleted: figure 1.

16. References: generally relevant and up to date. Numbers 2 and 18 need formatting however.

- Formatted according to the journal’s recommendations (http://www.biomedcentral.com/bmcpregnancychildbirth/authors/instructions/researcharticle#formatting-references): page 16, lines 352-354 and page 18, lines 402-403.

Discretionary Revisions

17. Introduction, third paragraph: Sentence beginning “The findings did reach ….sample size”. This needs re-structuring. For example “Although the findings of this study were statistically significant, the results should be interpreted with caution due to the relatively small sample size”.

- Restructured as suggested by the reviewer: page 5, lines 95-96.

18. Introduction, third paragraph: Please add the following: “Inconsistent results on the associations between maternal BMI and PTB warrant further large-scale studies from different countries”.

- Added: page 5, lines 96-98.

19. Introduction, third paragraph: Please add “as well as further afield” to the end of the sentence “implications for local health care practices”.

- Added: page 5, line 101.
Answers to the Reviewer 2 comments

Background

Minor Essential Revisions:

1. The data (and references) on prevalence of pre-obesity and obesity among reproductive age women in Russia do not seem to be the most representative or the most recent available. The authors should strive to provide more recent and nationally representative estimates (look at the WHO on Global Database on Body Mass Index).

   - Updated based on the WHO on Global Database on Body Mass Index: page 4, lines 73-74; new reference 1 – page 15, lines 349-351.

2. The 2nd sentence on page 5 is missing the word “not”, to make sense.

   - Added as suggested by the reviewer: page 5, lines 95-96.

Methods

Major Compulsory Revisions:

1. Please clarify what is the meaning of “singleton spontaneous deliveries” (last sentence, 2nd paragraph, page 5). Did the author exclude all women who had induced or elective, antepartum cesarean deliveries? This should be clearly stated.

   - We excluded women with multiple pregnancy as well as those who had induced deliveries or any type of cesarean section (CS) including intrapartum CS.

   - Addressed: page 6, lines 120-121.

2. The exposure variable (BMI) is very well defined but the outcome variable (spontaneous PTB) needs to be better defined by the authors. On page 6, 2nd paragraph, it is unclear whether the authors included only women who presented with spontaneous onset of labor before 37 weeks with intact membranes or whether they also included those with preterm ruptured membranes too, as long as they were in spontaneous labor.

   What about those with spontaneous onset of labor < 37 weeks who were delivered by intrapartum CS? On Figure 1, it is unclear whether the authors excluded all women who were delivered by CS before 37 weeks (including those who initiated preterm labor spontaneously) or only those that had an elective CS before 37 weeks, for any reason. This should be clearly stated.
Among those included into the study, all deliveries: with intact membranes or with preterm ruptured membranes, were considered as long as the onset was spontaneous. Those who had spontaneous onset of delivery, but delivered by intrapartum cesarean section were excluded from the study.

Addressed: page 6, lines 120-121 and page 6, lines 133-136; figure 1, box 3.

3. The authors need to report what was the exact definition used for “excessive gestational weight gain”, which was one of their confounders (page 7).

Excessive weight gain is a diagnosis that is stated by a doctor (O26.0 according to ICD 10). It is based on a combination of pre-pregnancy BMI, total weight gain during pregnancy and/or rates of weight gain 2nd and 3rd trimesters (average range/week). This information is obtained from obstetric journal.

Addressed: page 7, line 159.

Minor Essential Revision: For the sake of clarity, education should be presented in years of schooling, instead of “basic”, “secondary” and “vocational”, which are unclear for readers of other nationalities.

Addressed: page 7, lines 152-153.

Results

Minor Essential Revision: The 2nd foot note of table 2 should be reviewed: the total N for term deliveries is 20,064 (29,209 women – 1645 PTB).

- 29,475 (number we have in the table) is the total number of subjects included into this particular model with MPTB (29,709 women all together minus 234 women with VPTB).

Addressed: page 23, line 459.

Discussion

Major Compulsory Revisions:

1. The statement on the 2nd paragraph of page 10 regarding the findings of the systematic review by McDonald is misleading: “According to the review, overweight and obese women had an increased risk of VPTB (<33 weeks of gestation) with relative risks of 1.16 (95% CI: 1.05-1.29), 1.45 (95% CI: 1.23-1.71), and 1.82 (95% CI: 1.48-2.24) for overweight, obese, and very obese women, respectively”. These data refer to PTB in general and not specifically
to spontaneous PTB. In fact, McDonald states that “The risk of spontaneous preterm birth did not differ (0.93, 0.85 to 1.01, 15 studies)”. His Table 3 clearly depicts the specific OR for spontaneous PTB according to maternal BMI, from studies with crude and adjusted OR; they are all non-significant.


2. Similarly, in their discussion of the findings of the study by Salihu (2nd paragragh, page 11), the authors report the results of the association between low maternal BMI versus PTB in general. The crude and AOR for this association with spontaneous PTB are different from the values presented in the Discussion (see Salihu’s Table 3).

- Rewritten: page 11, lines 242-245.

3. The authors are encouraged to compare and discuss their results with the findings of those reported in two other systematic reviews (Honest 2005, in their reference list and Torloni et al 2009 not in their list) that specifically analyzed the interaction between maternal BMI and spontaneous PTB.

- Added to the discussion: pages 11-12, lines 257-265 (Torloni et al 2009) and page 12, lines 266-274 (Honest 2005). The Torloni’s paper has been added to the reference list – ref. 22, page 18, lines 415-417.