Author's response to reviews

Title: Perinatal mortality by gestational week and size at birth in singleton pregnancies at and beyond term: a nationwide population-based cohort study

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Author's response to reviews:

To the Editor-in-chief,

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Dear Sir,

Thank you for giving us the opportunity to comment on the posed concerns and submitting a revised version of the paper entitled: “Perinatal mortality by gestational week in singleton pregnancies at and beyond term: a nationwide population-based cohort study” for your consideration.

We have in the current version changed the title to: “Perinatal mortality by gestational week and size at birth in singleton pregnancies at and beyond term: a nationwide population-based cohort study”.

The manuscript was reviewed and some concerns were posed by the two reviewers. We have addressed the comments in the revised version (all changes are marked with red font color) and below in this covering letter we provide a point-by-point response to the concerns from Reviewer #1 and #2, respectively.

Reviewer #1

Major compulsory revisions

1) The authors focus not only on perinatal mortality at and beyond term but also on the difference in case of SGA and AGA. This should be mentioned also in the title of the article.
Response: We agree and have added to the title that also size at birth is an issue in this paper.

2) The methods used in the article are appropriate and well described although the standard used for estimation of due dates, ultrasound measurements at 18 weeks of gestation, should be explained in detail. On what measurements duedates are calculated in Norway at around 18 weeks (BPD, HC, FL, TCD ...)? Moreover, the 18-weeks protocol may lead to some bias as the authors mentioned in the discussion.

Response: We agree and have added a description of the method used by the vast majority of all obstetric departments in Norway up until the end of the study period (Methods section under definitions). BPD was the ultrasound measurement used to calculate gestational age and estimate due date. We have also added a reference.

Discretionary revisions

3) In case of SGA caused by IUGR, it might be of interest to distinguish perinatal mortality in fetal and (early) neonatal mortality. Was there a reason why the authors didn’t make this difference?

Response: Thank you for this important comment. In line with this comment and also the comment made by Reviewer #2 below (4) we have added data in Table 5 analyzing stillbirth risk alone using fetus at risk approach. There was only 77 early neonatal deaths and therefore it was difficult to analyze these alone (based on the numerous categories we used: 37-42+ and SGA or Non-SGA). The latter is also stated in the manuscript Results section when presenting data from table 5.

Reviewer #2

Major Compulsory Revisions

1) The abstract is difficult to follow. It is not as clearly written and organized as the rest of the paper. In particular the Results & Conclusions sub-sections are confusing.

Response: We have rewritten the abstract and in particular the entire results and conclusion section. Hopefully, this is now more clear and easy to grasp.

2) In the Introduction, the authors should state their hypothesis/motivations for asking these questions. The study questions themselves are outlined fairly clearly at the end of page 5, but the reader would benefit from a clear explanation of why these questions matter.
Response: We have added an explanation/hypothesis why we are asking these questions and why they are important (in the Introduction section).

3) In particular, what is the motivation for the interaction analysis of SGA and post-term delivery?

Response: Hopefully based on the earlier presentation of the hypotheses/explanation for asking the study questions it is clearer why we did the interaction analysis. We have also in the result section where these analyses are presented added a short statement that hopefully adds to outlining the motivation for this analysis.

4) Methods: It is now accepted that stillbirth and neonatal/infant death require different analytical techniques. Specifically, the population at risk for IUFD at any given week is the ongoing pregnancies beyond that week (i.e., fetuses at risk), whereas the risk set for neonatal death is the population of neonates born that week. This complicates perinatal death as an outcome. The authors need to address this in any revision.

Response: Thank you for this valuable comment. We agree and have in the subset of data 1999-2006, where the in depth analyses of differences between LMP and ultrasound-based estimates are possible also analyzed risk of stillbirth alone using ongoing pregnancies as the denominator in accordance with the fetus at risk approach. Table 5 is added to the paper. We have also decided, based on that rather few early neonatal deaths occurred and that we had many categories, not to present early neonatal deaths alone. Also, in the discussion we have added a section commenting on the fetus at risk approach.

Minor essential revisions

5) The Results section reads like a list in places. Because the hypothesis/study questions are not clearly stated, it is difficult for the reader to know what s/he should be taking away from the findings, or which findings to focus on.

Response: We have stated a hypothesis earlier in the Introduction section, outlining that the main focus of this paper is in particular the effect on post-term pregnancies. Hopefully, it is now easier for the reader to know what to take away from the findings. Also, the splitting of the Tables may have added to this. We have also added sub-headings to the results section that hopefully makes it easier to read.

6) The clinical implication about closer attention/monitoring to pregnancies with discrepant LMP and US delivery dates is sound.

Response: We agree.
7) Tables: The tables are busy/overloaded with information, particularly Table 1. Can they somehow be split out into multiple tables, or altered so they are more digestible?

Response: We agree and have split table 1 into three tables and also removed the unadjusted estimates and stated in the text that they were little affected by the adjustments. Hopefully this makes the numbers more accessible and digestible. Also, we have reorganized the old Table 2 into a new table 4.

8) Figure 1: Odds ratio y-axis needs to be on a log scale.

Response: We agree and have revised the figure and changed the y-axis to log scale.

We would also like to add that two more issues came up during the revision process:

1) We recognized that the rates in the old tables 1 and 2 were calculated using the total number of pregnancy in each period. These rates were not the ones that were used in the logistic regression analyses originally. We have in the current version put in the rates that originally were used and think that they now in a much better way and more clearly reflect the association estimates by each week (Please see current tables 1-4).

2) We also checked the interaction analyses once more. The previously reported p-value in the section starting in the last paragraph page 10 to 11 was correct but the odds ratios reported were for some reasons not the correct one. These have been changed into the correct values and outline a statistically significant interaction term with somewhat stronger risk estimates in the stratified analyses (please see manuscript, last paragraph page 10 continuing to top of page 11).

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