Author's response to reviews

Title: Low birth weight: comparison of two birth cohorts in Sao Luis, Northeastern Brazil, 1997/98 and 2010

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Author's response to reviews: see over
Dear 
Dr Peter O'Donovan 
Editor 
BMC Pregnancy and Childbirth 

Please find enclosed the revised version of the manuscript entitled MS: 1531277689948638 - Low birth weight: comparison of two birth cohorts in Sao Luis, Northeastern Brazil, 1997/98 and 2010. Please also find below a point-by-point response to the reviewer’s concerns. Changes were marked in red in the manuscript.

We hope you will find this revised version of the manuscript suitable for publication in BMC Pregnancy and Childbirth.

Best regards

Heloisa Bettiol

Reviewer's report 
Reviewer: Cynthia Ferre

Overview: This manuscript compares low birth weight (LBW) rates and changes in associations of LBW risk factors with LBW at two time points in Sao Luis, Brazil using two local cohort studies (convenience samples). The authors also utilized data from the Brazilian Nation Birth Registry to assess changes in stillbirth (fetal death) rates and LBW rates from 1996 to 2010.

The cohort studies were population based and not convenience samples. We added more explanations to the methods section to make it clearer.
Major Compulsory Revisions

1. Please clarify the research question, study design, and choice of data in the Methods section. Since the SINASC data show increasing and then decreasing trends, and the 2 cohorts show stable, non-significant changes in LBW rates at only 2 time points, the cohort datasets cannot provide appropriate information about the SINASC trends. This is a major flaw in this study. I suggest doing a paper solely on the SINASC data and a separate one on the comparison of the 2 cohorts. Otherwise it is confusing and misleading the reader. Analyses of the SINASC data should utilize 3-year moving averages or assessment of yearly variability in the rates (e.g. trend modeling via Joinpoint or other similar software).

The initial research question was to compare the low birth weight rate in the two birth cohorts. However, since there was no difference in the rates and we were aware that birth registry (SINASC) data indicated a rise and later fall in the LBW rate we thought it would be interesting to interpret LBW rates in the two birth cohorts including registry data. Otherwise it would give the false impression that LBW rate was static, which was not the case. Of course the cohort datasets cannot provide appropriate information about the SINASC trends. Therefore we used registry data to study trends in LBW assessing them using 3-year moving averages as suggested and cohort data to analyze factors associated with LBW in two time points.

The research question, study design, and choice of data were clarified the Methods section. This section has been completely modified.

2. Please provide a comparison of maternal demographic factors, including maternal race or ethnicity, and perinatal outcomes in the cohort data and the SINASC data. It is unclear how comparable the cohort data is to the SINASC data. In Figure 2, the 2010 cohort has a LBW rate lower than the rate in the SINASC data. It is not clear in the manuscript how representative the cohorts are of the Sao Luis births.

In new supplementary tables 1 and 2 we compared maternal socioeconomic and demographic characteristics and birth weight from birth registry data (SINASC) and the two birth cohorts in 1997/98 and 2010.
Please see methods page 9:

Selected data on maternal socioeconomic, demographic variables and birth weight from the two birth cohorts were compared with birth registry data by the chi-square test to assess how representative the cohorts are of the city births.

Results pages 11 and 12:

In 1997, cohort data did not differ from birth registry data regarding birth weight, maternal age and type of delivery. Males were slightly overrepresented in the cohort compared to females (p=0.010). Although there were differences with respect to maternal schooling, missing data were too high in birth registry data for a meaningful comparison (Supplementary table 1). It was not possible to compare marital status in 1997, because this information was not available in the birth registry. In 2010 newborn’s sex, birth weight and maternal age did not differ significantly comparing birth registry with cohort data. Low schooling, married mothers and those born by cesarean delivery were slightly underrepresented in the 2010 cohort (Supplementary table 2).

Discussion page 16

Another limitation is that there was slightly overrepresentation of male births in the 1997/98 cohort and underrepresentation of low schooling and married mothers and those born by a cesarean section. However, there are some concerns regarding quality of registry data, especially in the earlier period [29].

Data from the cohorts are population based and not convenience samples. This is now stated in the methods section (page 6)

Data from the two birth cohorts are population based. Hospital births comprised 96.3% of all births in 1997/98 and 98% in 2010. Maternity hospitals where less than 100 deliveries were performed were excluded from the study. This represented only 2.2% of the deliveries in 1997/98 and 3.3% in 2010. Thus, the sampling frame consisted of 94.1% of all births in 1997/98 and 94.7% in 2010.

The cohort LBW was not lower than birth registry based LBW. Although the point estimate was somewhat lower, 7.5% in the cohort and 8.03 in birth registry data, the
cohort’s confidence interval was 6.8 – 8.3, and thus includes birth registry estimate. This is now clearly shown in figure 2.

3. Methods, paragraph 12: What was the reference curve used in the calculation of the IUGR measure? Was it a standard national curve, a local curve, or one generated from the subjects in these cohorts? Also, please clarify what “with or without restriction” means.

The reference curve used in the calculation of the IUGR measure was a Canadian reference curve. The reference was added to the text. We replaced “with or without restriction” by IUGR (yes or no).

Please see methods page 7:

The classification of IUGR by Kramer et al. [17] is based on the birth weight ratio (BWR), which was obtained by dividing the newborn’s birth weight by the median sex-specific weight for gestational age of the Canadian reference [18].
In regression models IUGR was dichotomized into yes, when BWR<0.85 and no otherwise.

4. Methods, paragraph 4: It is unclear what the procedures were for selecting cohort participants. Was it a stratified random sample? What does “order of birth” mean here? Is it referencing a date? To a U.S. reader who works with perinatal vital statistics, “order of birth” refers to parity – what number of birth is this to the mother? For example, her first birth, second birth, third birth? It is not clear what “control cards” are. This is probably not necessary to describe in detail. Not clear why the interval between births and interview was relevant here or how this was used to select mothers to participate, especially since it is stated in paragraph 6 that the interview was conducted within 24 hours of delivery.

The procedures for selecting cohort participants were described in detail in this revised version. Order of birth was replaced by order or occurrence of births.
The sample was stratified by maternity hospital with sharing proportional to the number of births at each facility. In each maternity hospital sampling was systematic and all live births and stillbirths were listed in order of occurrence. The sampling interval was seven in 1997/98 and three in 2010. A random number from 1 to 7 in 1997/98, and from 1 to 3 in 2010 was drawn to determine the starting point for each study unit. Thus one out of seven births in 1997/98 and one out of three births in 2010 were randomly selected for interview. Losses due to refusal or early discharge from hospital occurred in 5.8% of cases in 1997/98 and in 4.6% in 2010.

In the present study only data from mothers residing in São Luís, liveborns and singletons were used. In 1997/98, after exclusion of births from non-residents (n=290), stillbirths (n=48), multiples (n=50) and missing information on study variables (n=17), 2426 cases remained for analysis. In 2010, after exclusion of stillbirths (70), multiple births (99) and missing information on study variables (n=27), data from 5,040 births remained for analysis.

5. A sensitivity analysis should be conducted to examine the effect of imputation of gestational age on the findings reported. This can be done by taking out the imputed cases and reexamining the findings where this variable is used to see if there are substantial differences in the findings. This data doesn’t have to be presented but should be commented on in the discussion.

Preterm birth and intrauterine growth restriction were not included in the regression models. We only presented univariate analysis of PTB and RCIU in relation to LBW. Results of univariate analysis without imputation were also presented in the results.

Please see page 12:

Results regarding preterm birth and intrauterine growth restriction rates did not change appreciably using unimputed gestational age data (Supplementary tables 3 and 4).
6. Regarding the 2 cohort comparison, there were mixed findings on risk factor changes. Similar to other published reports of perinatal trends, some adverse risk factors decreased and some increased. Some factors thought to be protective remained stable or increased. However, the reader cannot assess if these changes are in the population or are due to selection biases in the cohorts’ construction.

We believe by including a clearer description of the methods used to select births in the two birth cohorts it is now evident that the cohorts are population based.

7. Any information on maternal body mass index?

BMI was not available in 1997/98. Since the main objective of this paper is to compare the factors associated with LBW in the two birth cohorts and since BMI is only available in 2010 we did not include this information.

8. If Items 1, 2, and 7 above cannot be addressed, then these issues should be discussed as study limitations. The limitations should also discuss other variables which were not available for analyses, such as maternal race/ethnicity, antenatal and chronic diseases and nutritional factors.

We discussed that lack of information on maternal BMI, maternal race/ethnicity, and mother’s diseases in the 1997/98 birth cohort were study limitations.

Please see discussion page 16:

Lack of information on maternal body mass index, maternal race/ethnicity and mother’s diseases for the 1997/98 birth cohort prevented us from using these variables in this study, since our objective was to compare risk factors for LBW in the two birth cohorts.

Minor Essential Revisions

1. Please clarify the definition of “cohort” in this study. Do you mean a prospective or retrospective cohort? 2010 seems to be a stratified convenience sample.

The term birth cohort was used because the participants are being followed up at other time points. The 1997/98 birth cohort was reinterviewed at school age and the 2010 birth cohort was followed up at the second year of life. However, data presented in
this paper is cross-sectional with a retrospective component. The study is population based and not a convenience sample.

2. Please clarify that the SINASC data were from Sao Luis and not all of Brazil. This needs to be explicitly stated in the methods.
This is now explicitly stated in the methods.

3. Methods, paragraph 7: Which data was abstracted from medical records?
Medical indication for cesarean section and Apgar score were abstracted from medical records. Since these data were not used in the present study we deleted this passage from the manuscript.

4. Methods, paragraph 8: Clarify if the baby was weighed at delivery or at interview.
Please see methods page 7:
The newborns, wearing no clothing, were weighed on a baby scale with 5-gram graduations, shortly after delivery.

5. Methods, paragraph 10: Type of delivery should be “vaginal” or cesarean. This needs to be corrected here and in the rest of the paper.
Thank you very much for spotting this error. Corrections were done as suggested.

6. Methods, paragraph 11: It is unclear what the reference time period for the comparison of minimum wages between Brazil and the U.S. In the U.S., this is usually a dollar per hour amount. As written in this paragraph, it is unclear what the “per” is.
It is now stated that we are referring to monthly minimum wage.

7. Methods, paragraph 13: Please replace the use of the word “Ignored” with “Unknown” or “Missing” here and in the rest of the paper.
Ignored was replace by missing thought out the document.

8. Discussion, paragraph 12. It is not clear how better dating would influence cesarean section
Previous studies conducted in Brazil have shown that incorrect late ultrasound dating
of gestational age was associated with increased iatrogenic preterm births. An explanation and appropriate references have been added.

Please see discussion pages 15 and 16:

Previous studies conducted in Brazil have shown that incorrect late ultrasound dating of gestational age was associated with increased iatrogenic preterm births [2, 27].

Discretionary Revisions

There are a lot of spelling and phrasing issues that need to be addressed by the authors or an editor.

Spelling and phrasing issues were reviewed.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.

Reviewer: Deanne Wilson-Costello

This is a well-written article which analyzes factors associated with low birth weight in Brasil. The authors have made the requested revisions and I recommend acceptance.

Thank you very much for the positive comments.
Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.