Author’s response to reviews

Title: The relationship between the different Low Birth Weight strata of newborns with Infant Mortality and the influence of the main health determinants in the extreme south of Brazil

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Reviewer reports:

Reviewer #1:
This paper could be an interesting one in the area of infant mortality and low birth weight. However, there are many limitations in the methodology that are of concern. First, underreporting of live births who die very close to childbirth was not considered in the study. Frequently, they are classified as fetal deaths and are not informed to SINASC (the Live Birth Information System). Therefore, those deaths were not analyzed in the study.

Reply: The study prioritized the investigation of infant mortality related to birth weight extracts in a time series not considering stillbirth rates. To perform an analysis of the underreporting of live births who die very close to childbirth it is necessary to link the Mortality Information System (SIM) with the Hospital Information System (SIH) verifying the information on childbirth and its outcomes, as shown already published in previous studies (1) (2).

However, officially, these newborns who die in the early hours should generate a death certificate and therefore be included in the Mortality Information System. Thus, we will include this consideration among the limitations of the study.

Secondly, I could not understand the temporal trend analysis. According to the authors: "Based on the number of live births and annual deaths presented in these two databases, a temporal analysis of the mortality trends for each weight stratum in the period studied (2000-2015) was performed."
Preliminarily, the Average Annual Percentage Change (AAPC) was calculated, with a 95% confidence interval. This temporal trend was performed through the Join Point program (version 4.1.1.1). Subsequently, chi-square tests for trend were carried out to evaluate Infant Mortality Rates”.

The temporal evolution of mortality in each weight stratum was calculated annually by the APC while the temporal trend was evaluated by the Joint Point Program.
In contrast, the weight strata were analyzed together for each year evaluated, while the determinants in health were also assessed togheter but for the entire time series by Poison Regression.

The main focus of the study was to stratify weight ranges and to verify their relationship with mortality, even though it seems obvious that it will be higher among lower birth weight infants. However, in addition to the well-known historical association of low birth weight with infant mortality, the study mainly proposes an individualized analysis of the three LBW weight ranges related to some of the major health determinants. Thus, it was possible to have a broader approach on the subject allowing the identification of modifiable risk factors to support more specific policies in the area of maternal and child health.

Although secondary data were used, they were obtained directly from the information systems (SINASC and SIM) provided by the General Coordinator of Health Surveillance of the city of Porto Alegre during the study period. Mortality incidence rates for the various weight extracts were calculated from the information in both systems. In addition, this is a study with a retrospective cohort design and therefore the incidence rate can be used.

Reply: As to results presented in Table 2 (“Incidences of infant mortality”), I could not understand either. Furthermore, I do not think that the time effect was analyzed as mentioned in the methodology, as the multivariate results are presented for the whole period regardless of the year of analysis.
The translation of the technical terms is very poor, and this may have hindered the analysis of the paper. In addition, the results presented in the article do not show any relevant information besides what is already known.

Again, we highlight that the temporal evolution of mortality in each weight stratum was calculated annually by the APC while the temporal trend was evaluated by the Joint Point Program.
In contrast, the weight strata were analyzed together for each year evaluated, while the determinants in health were also evaluated together but for the entire time series by Poison Regression.

Reply: The technical terms have been corrected in the Methods to make the text clearer and more informative to facilitate manuscript analysis. Although, as known, some outcomes would already be known or even predictable, the originality of the article refers to a stratified analysis of the various birth weight categories, particularly LBW (less than 2,500 grams) relating them to the main determinants of health. Somehow, our intention was to revise the concept of risk generically attributed to LBW since, effectively, according to the results of the study, a significantly greater vulnerability of morbidity and mortality is among newborns in strata weighing less than 1,500 grams.

My recommendation is that the article be thoroughly revised, both data analysis and translation, so that the results become more interesting and could provide relevant information to reduce low birth weight, and consequently, infant mortality.

Reply: The important considerations and suggestions were accepted. The manuscript was revised and restructured qualifying its final text.

Reviewer#2:
This paper is an analysis of mortality within the first year of life in a region of Brazil using new-borne data linked prospectively to mortality records. The linkage seems, as far as I can tell, robust. It is a broad brush statistical analysis with no particular hypothesis in mind. Perhaps this is a weakness, in that it lacks focus.

The statistical analysis is based primarily on Poisson regression the results of which are presented in Table 2, which is much too large. Details of the regression are scant and need to be improved. For example, it is described as "a Poisson sequential regression". I have no idea what sequential means here.

A Poisson model allows the possibility of multiple deaths! Why not use logistic regression for binary (death) outcome?

Reply: The text in the Methods has been corrected to explain the use of Poison Regression in the analyzes. Multivariate analysis was performed using Poisson regression with robust variance, as this is one of the best alternatives for the analysis of longitudinal studies with dichotomous outcomes (3). It also provides a good estimate of the incidence ratio.

In table 2, the crude analysis was removed and only the adjusted analysis was maintained, as suggested by the reviewer.

Also, the introduction of the manuscript included a new paragraph to highlight the focus of the study on mortality in different strata of birth weight, especially among newborns with LBW, related to the main determinants of health.

Further, Table 2 presents birthweight "strata" as six columns. It is unclear to me what is meant by this. Were separate Poisson models created for each birth-weight band? If so, I would question why the researchers did not develop a single model with birthweight (either as categorical or perhaps preferably actual birthweight) as a predictor variable? It seems only sensible to me to fit 6 separate models if there are clear interaction effects.

Reply: Mortality risk for newborns with lower birth weights is well known in the literature and clinical practice. However, one of the objectives of the study was to seek a better understanding of the influence of different health determinants on each of the weight strata, especially among those newborns with low birth weight.

Thus, it was verified the association of mortality for each weight stratum through the interaction with the main determinants in health. Also the text has been adjusted to better understand this.

Although the time-trend aspect is clearly important to the authors, it is not included in the Poisson modelling. It probably should be.

What are the dots (.) in Table 2 meant to signify?

The temporal evaluation of the eleven major determinants in health and their various variable values would bring a very complex analysis model. Similarly, in the time period analyzed (2000-2015), in view of the socioeconomic stability experienced in Brazil, it is also known that no major changes were observed between these determinants in health. For these reasons, therefore, an analysis of the interaction of these determinants year by year with mortality in the various weight strata was not performed.

Other points:
Figure 1 and 2 traces can barely be distinguished in black and white. Dashed or variable width lines would be better. Furthermore, in Figure 1, a log-scale for the vertical axis would be preferable. "Gross" would better be "un-adjusted" or "crude". "RI" is in table 2, but presumably you mean IR (incidence ratios).

A simple spline plot of probability of death versus birthweight would be useful.
Reply: Suggestions and modifications to the illustrations (Tables and Figures) were made.

References: