Author's response to reviews

Title: Gestational age at birth and morbidity, mortality and growth in the first 4 years of life: findings from three birth cohorts in Southern Brazil

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Author's response to reviews: see over
Point-by-point answer to the queries and requests of the Editor and the two Reviewers.

Dear Editors,

This is a point-by-point answer to all queries and requirements made by the editor and the two reviewers. The queries and requirements are marked with Q.: and our answers are marked in yellow. We have left aside all parts of the reviews that did not need any answers.

Summarizing, the Editor made one request, Reviewer 1 just required an improvement in the written English, while Reviewer 2 made a number of comments and requests, and finished with one major compulsory review, and minor essential reviews. We provide below, a point-by-point answer. The summary of our answers: we satisfied all requirements, with the exception of the reviewer 2 request to add breastfeeding as a confounder in the multivariate analysis. As breastfeeding is not a confounder, but a mediator in the association between gestational age and outcomes such as morbidity, mortality and growth, we did not add this variable to the equation, but explained the reasons in the Methods section. In addition, in this paper breastfeeding is also one of the outcome variables.

We made two major changes in this version, as compared to the previous. The first in which we excluded all outcomes which were not available for the three cohorts, to satisfy the reviewer’s request. The second one is that we decided to use the same criterion for estimation of gestational age – date of last menstrual period - to guarantee the comparability of the results across the cohorts.

Editor

Q.: Provide further comments on the comparative differences of 42+ wk vs 39-41 wk gestational outcomes and implications of those findings.

Answer: We have added comments on these differences both in Results and Discussion, comparing the outcomes of these two groups.

Reviewer 1

Title: Biological, mental and cognitive outcomes at four years of age of preterm and early term babies of three birth cohorts in Southern Brazil

Version: 1 Date: 30 June 2012

Reviewer: Felix A Okah
Q.: Quality of written English: Needs some language corrections before being published.

Answer: The written English was fully revised and we hope that this version will satisfy the reviewer.

Reviewer 2

Reviewer’s report

Title: Biological, mental and cognitive outcomes at four years of age of preterm and early term babies of three birth cohorts in Southern Brazil

Version: 1 Date: 7 September 2012

Reviewer: Carlos Duran

Reviewer’s report:

Q.: It is of particular note that the authors’ main interest appears to be that of “evaluating the risk of children born with 37 and 38 weeks gestation…” yet they describe much more than this in their study. They also describe the infant mortality of various groups defined by their gestational age.

Answer: we have changed the focus of the paper, to cover the outcomes of children of all gestational age groups. This now appears in all parts of the paper, including the title. As the Editor rightly mentioned, the outcomes of post-term children are also reason for concern, as well as those of preterm babies (<34 and 34-36 weeks). Therefore, we introduced a number of comments, both in the Results and in Discussion, about all gestational age groups. However, we still think that the major finding of the paper is the unfavorable outcomes of children with 37 weeks of gestation, who are still considered as born at term, and we give more emphasis for this group, as findings about the other gestational groups have been already well described.

Q.: The data collection methods and data analysis are appropriate and well described. This is partially described in the article, but more specifically described in the individual cohort study presentations. There are clearly some difficulties with the data collection that are mentioned but not specifically
described as possible limiting factors in the discussion or conclusions.

**Answer:** we have added in Discussion a commentary on the limitations of the paper, including losses to follow-up (which we consider as small, considering what is observed in other birth cohort studies). On the other hand, we changed the method of estimation of gestational, to make it more consistent in the three cohorts and also to minimize missing values. This is clearly described in Methodology.

Q.: Regarding potential confounding factors, there is no discussion of breast feeding. This is something that the authors can adjust for, since they do have this data available.

**Answer:** we did not adjusted for breastfeeding because this variable is a mediator in the relationship between gestational age and the outcomes, and not a confounder. In addition, in this paper we also considered breastfeeding as an outcome. Because of this we did not add breastfeeding to the multivariate model, but we explained the reasons in the Methods section.

Q.: There is a significant loss to follow up in the first cohort study, double that of the 2004 cohort, yet there is no analysis of the possible effects this may have on the overall data. Is this loss associated with a certain group of patients, or does it reflect the broad group?

**Answer:** We have now added in the Discussion, in the part of limitations of the study, that losses to the first follow up of the 1982 cohort were more frequent among the richest and the poorest groups, as middle-class families are more easily found.

Q.: At the same time, the authors clearly state that morbidity data as well as cognitive assessments are only available for the 2004 cohort study; yet, the title of their manuscript implies that “mental and cognitive outcomes” will be presented for all birth cohorts. The same can be said of the presented objective and methods noted in the abstract.

As already mentioned, their main purpose also appears to be different than what is reflected by their title and what is the focus of their conclusion. It seems that this manuscript could be better represented either as “Biological, mental and
cognitive outcomes at four years of age of preterm and early term babies of the 2004 birth cohort in Pelotas, Southern Brazil, or as a study of Neonatal and Infant mortality of the three described birth cohorts in Pelotas, or some other title to accurately represent the study.

Answer: due to these comments of the reviewer, we decided to change substantially the paper, including the title, and we excluded all outcomes which were not available for the three cohorts. Doing so, we had to exclude all information regarding neonatal morbidity, mental health, and cognitive function. We did it with sadness, as we really liked the paper as it was before, and could not see any problem in having information for only one cohort for some outcomes. But the reviewer’s request was satisfied, as we are very interested in publishing the paper in BMC Pediatrics.

Q.: At the same time, although they mention that there has been a significant increase in prematurity over the three cohort periods, and how this could possibly be attributed to the increase in cesarean births; there is no specific note of the improvement in overall neonatal mortality in Pelotas. It is clear that the infant mortality in Pelotas has decreased by almost 50% from 1982 to 2004. At the same time, the cesarean section rate has increased from 28% to 45%. It would be fascinating to see how, or if these factors have affected mortality in the late preterm and the 37 week gestation infant.

Answer: we agree that this is a fascinating subject, but it is not the focus of the present paper, and we have discussed these issues in a previous publication which is cited when we discuss this topic (Barros, FC et al. Lancet 2005;365;847-854)

Q.: In summary, this study presents clear detailed data of their cohort children, but the title needs to be changed to more accurately reflect the plan as well as data presented in this study by the authors involved in this long term study.

Major Compulsory Revision: I believe the title needs to be changed to more appropriately describe the purpose as well as data presented in the manuscript, and then the discussion and conclusions can be adjusted and would more accurately reflect the title.

Answer: we have changed the paper and the title according to the reviewer’s request.
Q.: Minor essential revisions: It would be of significant interest to have breastfeeding adjustment when assessing both morbidity and mortality in the various outcomes by gestational age.

Answer: as already mentioned, we consider that breastfeeding is not a confounder, but a mediator. Because of this we did not add this variable to the multivariate analysis, and explained our reasons in Discussion section of the paper.