Author’s response to reviews

Title: GESTATIONAL AGE AT BIRTH AND BEHAVIORAL PROBLEMS FROM FOUR TO ELEVEN YEARS OF AGE: BIRTH COHORT STUDY

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REPLY TO THE REVIEWERS

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GESTATIONAL AGE AT BIRTH AND BEHAVIORAL PROBLEMS FROM FOUR TO ELEVEN YEARS OF AGE: BIRTH COHORT STUDY

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BMC Pediatrics

Dear Dr Castro-Fornieles,

Thank you very much for the opportunity to submit a revised version of our manuscript. We are very thankful to the Reviewers for their careful reading, comments and suggestions that contributed to the improvement of our paper. Our answers to the Reviewers comments are in italic blue below. All the comments and suggestions have been addressed in the revised version.

On behalf of all the co-authors, thank you and best wishes.

Iná S. Santos
Elizabeth Asztalos (Reviewer 1): Thank you for asking me to review this manuscript. I commend the authors for conducting this in-depth population study looking at the factors that may contribute to attention and behavioral issues in children and the role of gestational age at birth. The authors presented a very nicely organized follow-up study with a good follow-up rate.

I have a few minor points and most of it is related to the discussion:

1. The study does bring out that the issue of attentional and behavioral issues is multi-factorial and may vary between countries. I think this aspect needs to be brought out more as it does differ from some of the current literature, as evident by a relatively recent publication looking at similar gestational age grouping in the US (Richards JL et al Nov 2016).

Response: Thank you for driving our attention to the need of further discussing the reasons for differences in findings from studies conducted in settings with different confounding factors structure. We included two paragraphs at the Discussion section (lines 12-22, page 8) to address this issue:

“A higher social risk, represented by low parental educational level, younger maternal age, and low socio-economic status, is strongly associated with increased behavior problems.[1, 34-36] Maternal clinical depression and anxiety have a negative influence on mother-infant interaction and this in turn affects the behavioral outcome of the children.[37-39] All these risk factors are more prevalent in low and middle-income settings. Such characteristics of the confounding structure were controlled for in the current study.”

“Medical factors, such as the length of stay in a neonatal intensive care unit, a prolonged need for artificial ventilation and postnatal corticosteroid exposure may negatively affect behavioral outcome.[1] The access to full intensive care technology and the survival rate after intensive care management are higher among preterm children born in high-income than among those born in low and middle-income settings. Lack of adjustment for such characteristics may positively confound the association between age at birth and behavioral outcomes of the children.”

2. A limitation of this study is the fact that the number of infants <34 weeks is 2.3% which is very small when one wants to evaluate the effect of significant prematurity; this, again, is related to the fact that this is a regional population that is being studied but this does need to be addressed. Most of the discussion focuses on the later preterm and does not address the more preterm infants.
Response: We totally agree with the Reviewer. Based on the paper by Richards JL et al, 2016 (that was included at the revised manuscript reference list under the number 43) an additional limitation was added to the Discussion section (lines 17-19, page 9):

“Additionally, children with different risks may have been inappropriately pooled into the < 34 weeks group thus impairing the study capacity of assessing their behavioral outcomes.[43]”

3. I think that there needs to be more in the discussion as to why its results are different. This is a regional population cohort study which in itself can be and is a limitation and it may be prudent to include a discussion why the socio-demographic situation plays a heavier role compared to the other studies to date.

Response: Please, see the answer to the comment number 1 above.

4. What actions or recommendations can be drawn from this manuscript?

Response: A sentence was added to the Conclusion section (lines 24-27, page 9) highlighting the need of targeting preterm children from low socio-economic families with the aim of preventing behavioral problems in childhood and adolescence:

“This study highlights the importance of targeting children from families with less favorable socio-economic conditions, a risk factor that co-occur with preterm birth in low and middle-income settings, with the aim of preventing behavioral problems in childhood and adolescence.”

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Answers to Reviewer 2:

Bede Ibe (Reviewer 2): accept without revision.

Response: Thank you very much.