Author's response to reviews

Title: Optimal fetal growth for the Caucasian singleton and assessment of appropriateness of fetal growth: an analysis of a total population perinatal database

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Author's response to reviews: see over
Dear Editors

Re: 'Optimal fetal growth for the Caucasian singleton and assessment of appropriateness of fetal growth: an analysis of a total population perinatal database

We would like to resubmit this paper for your consideration. We have thoroughly rewritten the paper following the valuable feedback we have received. We would particularly like to thank the reviewer for his careful review, which we believe has helped us to greatly improve the manuscript. As a result we believe the paper is now much more readable, and we hope it will be acceptable to your journal.

We have addressed all of the reviewer’s points as indicated below:

1. The manuscript is not presented in a traditional scientific report style

This has now been addressed as per the reviewer’s suggestions. The paper has been completely re-written to fit into the standard style.

2. It would be much better to focus the introduction on the specific research objective at hand, concluding with a succinct statement of study purpose, in perhaps at most 3 pages.

The Introduction is now 2.5 pages long and focused on a statement of study purpose (see pp3-5).

3. Results (such as on bottom of p 10) should be confined to the results section, and presented there objectively and without discussion

These results have now been moved to the results section.

4. Instead of “turning points” use mathematically accepted terms, ie “inflection” points.

This has been done.

5. The results section could be simplified

This has been done.

6. The equations given in the text are repetitive of results in Table 7 and can be eliminated.

We have chosen to retain these equations because we believe that this communication will be of interest not only to people with a statistical background but also to clinicians may not be familiar with generating equations from Tables of the results of regression analyses. We therefore believe that the presentation of the results in the form of an equation as well as in tables of co-efficient estimates will cater for a wider audience. However, if you disagree with our assessment of our audience, we are quite happy for
you to remove the equations, as suggested by the reviewer, or include them as an 'Additional' file.

7 Since these are regression equations, include additional statistics (standard errors not C.I.s for each parameter estimate!, overall adjusted R-square, p-values for each term).

All of the additional statistics have been supplied, see Tables 4, 5 and 6.

8 The discussion should focus first on the statistical utility of the proposed method, then compare it with the work of others. A detailed discussion of the limitations of these results should be included. It's extension to other populations should be discussed especially for publication in an international journal.

This has been done, see Discussion pp 12-22.

9 Why not include all births from 1998-2003

We are happy to say that since we originally submitted the paper, additional data for the years 2000, 2001 and 2002 has become available. Unfortunately the data from 2003 are not yet finalized. However we have re-analysed the 1998-2002 data, increasing the sample size by a factor of 2.5.

10 A significant weakness of this study is …… the severe restrictions due to exclusion criteria…… the authors only study ……about 50% but undoubtedly represents some systematic biases due to the exclusions.

We acknowledge that the original manuscript was not sufficiently clear in describing the rationale for these exclusions, and we thank the reviewer for bringing this to our attention. We trust that the much-revised version will clarify the rationale for these exclusions. We select a sample with optimal intrauterine growth, so that observed growth may be compared with optimal growth rather than what might be expected given whatever prevalence of growth restricting disease happens to exist in the reference population.

11 and present a table showing how the included and excluded cases compare on key demographic and reproductive health characteristics?

As requested we have included an additional table. We were not entirely sure of the reviewer's objective in requesting such a table. We assume that it is to demonstrate that we have indeed excluded neonates having inappropriate intrauterine growth. We have therefore limited Table 3 to Caucasian singletons so that differences in distributions in gestational duration and birth weight can be attributed to excluding pregnancies influenced by exclusion criteria other than race and multiplicity.

12 [With only 26K births, this is smaller than the population studied by Brenner, not much larger than Usher, and] very difficult to use as a basis for generalization for western Australia or elsewhere around the globe.

As we anticipate will be clearer in the revised version, it is the primarily the method that we wish to generalize rather than the results. Nonetheless, we have more than doubled
the size of the dataset used for the analysis. While this has had trivial impact on the estimated model parameters, it has served to increase the statistical precision of the results.

13 **The writing style of this manuscript could be improved by attention to use of active voice wherever possible.**

This has been done.

14 **What are the additional files referenced at the end of the manuscript?**

BMC formatting allows additional files. For the previous submission there were no additional files. Possible additional files for this revised submission are the equations and the Table of the gestation-specific birth weight cut points above which we would exclude a subject on the grounds of an erroneous gestational datum.

15 **The authors should carefully review the references, both for journal formatting and completeness.**

This has been done.

16 **Of special note are book chapters, refs 1-3 where the page numbers are repeated,**

We have checked these references. The page numbers are sequential and not repeated. We believe these refs to be correct.

17 **and ref 15 where the last author is someone with no last name**

This has been fixed.

18 **and ref 23 where the word “transformations” is incorrectly capitalized.**

This has been fixed.

19 **In Table 1, why are some entries included if they are NA,**

These entries have been excluded from the Table and are now discussed in the text.

20 **and is it really likely that no cases of TORCH or high altitude (however that may be defined) occurred?**

The cases affected by TORCH infections have now been enumerated and included. I don't know how Resnik defines high altitude, but we can safely say that however it is defined it would not be met by any WA births, see footnote to Table 1.

21 **The column heading is really part of the title.**

The column heading has been removed.

22 **What is the relevance of Table 2? Surely this is part of the results of the current study, so why does it appear before the study has been developed and presented?**
Table 2 has now been moved to the Results section.

23 Table 3: compare the included and excluded with respect to other characteristics, like maternal age, education, prenatal care, parity, etc. and provide p-values for these statistical comparisons.

As mentioned above, a comparative table has now been included, however we do not have total population data concerning maternal education or prenatal care. We anticipate that the reviewer wishes to have some kind of measure of socio-economic status (SES). We have presented a comparison of our most general measure of socio-economic disadvantage. This is based on SEIFA (Socio-Economic Indexes For Areas) derived from census data averaged over a collection district, which covers an average of about 250 dwellings, reference supplied. We would expect SES to be lower among those excluded due primarily to the exclusion of smoking mothers, since this is strongly associated with social class.

24 Is Table 4 necessary? Given that only 25 cases are excluded couldn’t this be mentioned in a sentence in the text instead?

Since we are interested in the distribution of birth weight within each gestational age category (primarily in order to relate POBW to percentile position, since the exclusion of such small numbers will have a negligible effect on the value of the central estimate), it is dangerous to have exclusion criteria that arbitrarily truncate that distribution, see Discussion, under 'Advantages of ratio method'. The reason for giving the actual birth weight cut points was to allow readers to assess for themselves whether they were indeed reasonable cut points given the stated objective. However we are happy to exclude this Table, if its inclusion is considered to err on the side of excessive caution, or to include it in an Additional file if this is considered appropriate.

25 Table 5 could be incorporated into the suggested expanded Table 3.

This has been done.

26 Table 6 could be included in Table 7 in the relevant cells.

In order that the Tables should remain easy to read with the additional requested statistics, we have now created one table for each predicted variable, Tables 4-6. These new tables include the material in the original Table 6.

We trust that these revisions meet with the approval of the editors and the reviewer and that this revised paper may be considered for publication in BMC Paediatrics. Once again we would like to thank you and the reviewer for your thoughtful attention to our paper and the helpful comments offered.

Yours sincerely,

Eve Blair

on behalf of E Blair, Y Liu, N deKlerk and D Lawrence.