Author’s response to reviews

Title: Thinking Outside the Curve, Part II: Modeling Fetal-Infant Mortality

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Version: 4 Date: 7 July 2010

Author’s response to reviews: see over
07 July 2010

Dear Mr. Aldcroft,

We appreciate having the opportunity to revise our manuscripts. Our responses to the reviewer comments are provided below. We hope that the revised versions are acceptable for publication.

Best Regards,

Richard Charnigo

Associate Professor of Statistics and Biostatistics

Director of Graduate Studies, Ph.D. in Epidemiology and Biostatistics

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MS: 1675492990329176

Technical advance

Thinking Outside the Curve, Part I: Modeling Birthweight Distribution

Richard Charnigo, Lorie W Chesnut, Tony LoBianco and Russell S Kirby

BMC Pregnancy and Childbirth

MS: 1206841582329185

Technical advance

Thinking Outside the Curve, Part II: Modeling Fetal-Infant Mortality

Richard Charnigo, Lorie W Chesnut, Tony LoBianco and Russell S Kirby

BMC Pregnancy and Childbirth

Dear Dr. Charnigo,

Please accept our sincere apologies for the delays in processing your two submissions to BMC Pregnancy and Childbirth. As you are aware we had some difficulties finding qualified referees to judge your manuscripts, and we sincerely apologize for the delay that caused to your submissions. Additionally, once we received the reviews the Associate Editor was unavailable to comment immediately, and we felt that his advice was essential in our decision. Again, please accept our apologies for the delays, and we are pleased to now provide you with our decision.

Please see the comments below for the peer reviewers’ reports. As the two manuscripts are highly related we sought advice from the same Associate Editor and reviewers on both submissions. The reports on both manuscripts are below the signature of this e-mail. We would be grateful if you could address the comments in two revised manuscripts and provide a cover letter giving a point-by-point response to the concerns. As you will see, the reviewers were both quite positive in their assessments, and should you address all points in sufficient detail in both your cover letter and revised manuscript, we do not anticipate a delay in formal acceptance of your manuscript.
While there were some concerns raised regarding whether the two manuscripts should be combined and whether the manuscripts fit within the scope of BMC Pregnancy and Childbirth, the Associate Editor overlooking the manuscripts supported the idea that the manuscripts be kept separate and also felt they were within the scope of the journal.

Please also highlight (with ‘tracked changes’/coloured/underlines/highlighted text) all changes made when revising the manuscripts to make it easier for the Editors to give you a prompt decision on your manuscript.

We have used the track changes feature of Microsoft Word to identify modifications from the originally submitted versions.

Please also ensure that your revised manuscripts conform to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals ). It is important that your files are correctly formatted.

Specifically, we ask that you include the sections listed as Methods as an additional file, or incorporate some of it under the Results and the rest as an additional file.

For each of the two manuscripts, the material previously listed under the heading of Methods has been relocated to a Technical Appendix in a separate file.

We look forward to receiving your revised manuscripts by 8 July 2010. If you imagine that it will take longer to prepare please give us some estimate of when we can expect it.

You should upload your cover letter and revised manuscripts through http://www.biomedcentral.com/manuscript/login/man.asp?txt_nav=man&txt_man_id=1206841582329185 and http://www.biomedcentral.com/manuscript/login/man.asp?txt_nav=man&txt_man_id=1675492990329176. You will find more detailed instructions at the base of this email.

Please don't hesitate to contact me if you have any problems or questions regarding your manuscripts.

With best wishes,
Reviewer's report for ms 1675492990329176: This is a well presented manuscript as part one of a two-part series of a detailed technical study exploring the important topic of birthweight distribution and fetal-infant mortality. I have no major concerns.

Major Compulsory Revisions
Nil

Minor Essential Revisions
References: Ref number 22, Pilla et al may need revision.

The reference is correct as listed; that manuscript has been submitted for publication but not published.

Discretionary Revisions
a) The reference list appears a little dated with the most recent being from 2007.

We have added three new references from years 2008, 2010, and 2010 respectively.

b) Consider cutting back reference to paper two throughout the text. I found this unnecessary and possibly inappropriate in parts eg last sentence of the discussion and of the conclusion.

We have removed three of the references to the companion paper, including the one in the last sentence of the discussion. However, we have retained the reference in the last sentence of the conclusion to emphasize that the contribution of the present paper is best understood in the context provided by the companion paper.

c) Frequent reference to paper two and the technical nature of the manuscript made me wonder whether the two papers should be combined, including more of the technical aspects as appendices.

We feel that our work is best presented in two manuscripts, first because a single manuscript would be extremely lengthy and second because there really are two distinct (though related) aspects to the statistical modeling: (i) describing a birthweight distribution; and, (ii) making inferences about fetal-infant mortality in relation to that birthweight distribution. In addition, we note that the Associate Editor supports the idea of our work being presented in two manuscripts. On the other hand, we have followed your suggestion to move the more technical aspects (specifically, those which had previously appeared under the heading of Methods) to a separate Technical Appendix that may be skipped, skimmed, or
reviewed carefully by a reader according to his/her own preference.

Level of interest An article whose findings are important to those with closely related research interests
Quality of written English Acceptable
Statistical review Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests I declare that I have no competing interests

Reviewer’s report for ms 1206841582329185: This is a well presented manuscript as part two of a two-part series which describes an enhanced approach to estimation of birthweight specific mortality. I have no major concerns.

From the perspective of a clinical epidemiologist, mention of fetal growth restriction (mortality and measurement issues including constitutional factors and gestation) in the context of this work would enhance understanding, particularly for the non statistician.

We have added new material to the discussion that mentions intrauterine growth restriction (IUGR), related measurement issues, and the potential to assess IUGR within a statistical modeling framework similar to that described in our paper.

Major Compulsory Revisions
Nil

Minor Essential Revisions
Nil

Discretionary Revisions
As mentioned in the review of paper one, for the general BMC audience, the readability of this body of work may be improved by combining the two papers including more of the technical aspects in appendices.

As noted in our response to your review of the first paper, we feel that our work is best presented in two manuscripts. However, we have followed your suggestion to move the more technical aspects to a separate Technical Appendix.

Level of interest An article whose findings are important to those with closely related research interests
Quality of written English Acceptable
Statistical review Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests I declare that I have no competing interests

Reviewer’s report for ms 1675492990329176 & 1206841582329185 (combined): These comments apply to both Part I and Part II (and the supplementary file if they are being considered for publication.

1. According to my biostatistician the statistical modeling is sound and that it is adequately described.
   
   We appreciate the corroboration.

2. The examples are limited to white singleton births, a group that has fewer adverse birth outcomes than
minority groups such as blacks. Granted the authors chose "heavily smoking" birth mothers (no definition), but from an overall standpoint, issues such a prematurity and low birthweight are more prevalent among minority populations. It would be desirable, therefore, to see how the authors' model performs with data from such a population.

Heavily smoking mothers are defined in Section 2a of the first paper as those smoking at least twenty cigarettes per day.

The newly added Section 3c of the first paper provides another example, this one using data from black singletons. The new example shows that the Flexible Information Criterion (FLIC) chooses a 6-component birthweight distribution model over a 4-component model for black singletons, in contrast to the 4-component model preferred for white singletons born to heavily smoking mothers (Section 2b of the first paper) and for white singletons in general (Section 3b of the second paper). To provide some insight into why a 6-component model is chosen for black singletons, we have also included a new graphic (Figure 4 in the first paper) that juxtaposes the fitted 4-component and 6-component models. Our impression is that, roughly speaking, the two extra components are needed to capture patterns in the far left and right tails of the birthweight distribution for black singletons. In any event, our examples demonstrate that an appropriate model for birthweight distribution may vary from population to population, which underscores the importance of not relying on a one size fits all approach to modeling birthweight distribution.

Regarding fetal-infant mortality, we respectfully defer examination of the black singleton experience and its comparison with the white singleton experience to a future manuscript. Especially given the major qualitative difference in birthweight distribution between black singletons and white singletons (in particular, the fact that a 6-component model is preferred for the former population while a 4-component model is chosen for the latter population), such examination and comparison seem to warrant a more detailed and thorough investigation than would be appropriate in the context of an additional illustrative example for our second paper. We hope that the multiple illustrative examples already present in our second paper sufficiently demonstrate our methodology for fetal-infant mortality modeling.

3. While well written, I have serious reservations that this the appropriate journal for these two manuscripts (and the supplemental material if that actually was for publication). A more statistically oriented journal might be considered. Few clinicians and only a small percentage of epidemiologists will have the appropriate training to comprehend these works.

We had no little discussion among ourselves about what would be an appropriate journal for these manuscripts. We selected the open source approach because we wanted our methodological developments to be accessible; computational statistics and biostatistics journals are sometimes difficult even for academic researchers to access. We also wanted our work to be available to an international audience. In addition, our papers were too technical for many public health journals. Ultimately, we chose *BMC Pregnancy and Childbirth* because it has emerged as a top tier journal publishing work that moves the fields of obstetrics and gynecology, as well as perinatal epidemiology, forward. The journal has published numerous papers on topics similar to or related to ours, some comparably theoretical. Here are a few examples:

*Centile charts for birthweight for gestational age for Scottish singleton births*

*Bonellie S, Chalmers J, Gray R, Greer I, Jarvis S, Williams C*

*BMC Pregnancy and Childbirth 2008, 8:5 (25 February 2008)*

*Measuring perinatal complications: methodologic issues related to gestational age*

*Caughey AB*

*BMC Pregnancy and Childbirth 2007, 7:18 (30 August 2007)*
Customized birth weight for gestational age standards: Perinatal mortality patterns are consistent with separate standards for males and females but not for blacks and whites
BMC Pregnancy and Childbirth 2005, 5:3 (20 February 2005)

A parsimonious explanation for intersecting perinatal mortality curves: understanding the effects of race and of maternal smoking
Joseph KS, Demissie K, Platt RW, Ananth CV, McCarthy BJ, Kramer MS

A parsimonious explanation for intersecting perinatal mortality curves: understanding the effect of plurality and of parity

Our hope is that clinicians and epidemiologists who are interested in our work but who are less familiar with some of the methodological content will, perhaps in collaboration with biostatisticians in their institutions, use this as an opportunity to add to their methodological repertoires.

Level of interest An article of limited interest
Quality of written English Acceptable
Statistical review Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests I declare that I have no competing interest.

To submit your revised manuscript

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When you have revised your manuscript in light of the reviewer's comments and made any required changes to the format of your paper, please upload the revised version by following these instructions:

1. Go to http://www.biomedcentral.com/manuscript/login/man.asp?txt_nav=man&txt_man_id=1206841582329185 and log on with your email address and password. For the other manuscript, please go to http://www.biomedcentral.com/manuscript/login/man.asp?txt_nav=man&txt_man_id=1675492990329176

2. With the 'Manuscript details' tab, please update the title, abstract and author details if they have changed since the previous version. It is very important that all changes are updated on this page, as well as in the manuscript file as the information on this page will be used in PubMed and on BioMed Central if your manuscript is accepted for publication.

3. With the 'Cover letter' tab, please provide a covering letter with a point-by-point description of the changes made.

4. With the 'Upload files' tab, please upload the revised version of the manuscript and press 'Submit new version'. Please wait for the confirmation page to appear - this may take a few moments.