PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	**Association of Maternal Age with Infant Mortality, Child Anthropometric Failure, Diarrhoea, and Anaemia for First Births in Low- and Middle-Income Countries**
AUTHORS	Finlay, Jocelyn; Ozaltin, Emre; Canning, David

VERSION 1 - REVIEW

REVIEWER	***Amina Khambalia, PhD.*** Epidemiologist University of Sydney Australia
REVIEW RETURNED	01-Jul-2011

THE STUDY	1. Of the 55 countries examined there must be countries where maternal age at first birth has shown an increase over time (1990-2008). Have th authors examined whether the outcomes studied (i.e. infant mortality, stunting, underweight) showed an adjusted decrease that coincides with increased maternal age at first birth that would further the investigators' conclusions? 2. In Intro please define terms "minors" and "majors" in Raj et al. study. 3. Websites references in methods can be cited as other references in the reference list using referencing for websites rather than including webpage links in the actual paper. 4. Importantly, how is the main outcome infant mortality measured? Questionnaire of birth histories from mother, medical records, or death certificate? 5. Unclear how wealth index was created, need more detail. Is this a common, validated measure used for these surveys? 6. Discussion in Results section on differential effects of maternal and paternal indictors should be in the Discussion section because it is of an interpretative nature. 7. Unclear why religion is thrown into the sensitivity analyses which is performed to examine maternal height. Given that the sensitivity analyses did not detect change, Table 5 could be an appendix table.
RESULTS & CONCLUSIONS	1. What is the rationale for creating a categorical variable for maternal age instead of using a continuous outcome? And for the categorical variable for maternal age, the choice of reference group seems to change (27-29 or 24-29) and appears arbitrary. To reduce reader concern that choice of maternal age categories affected results, could the investigators describe in a few sentences rationale for using a categorial versus continuous variable and for using 2

	year intervals rather than say 3 or 4 years? Would using different categories for maternal age significantly alter the findings? Looking at Figure 1, it appears as though stunting and underweight decrease until ~age 30 and then levels off, whereas, diarrohoea, wasting and infant mortality are pretty flat between maternal ages 14 onwards. This creates more uncertainity in results and the age ranges that are of lower risk and others that are at higher risk. Not convinced that creation of pre-defined categories for maternal age is best way to determine optimal age for delayed first birth (i.e. age 27 as reported in this study). I think a break-point analysis would be needed to accurately determine a particular cut-off age where largest effects are observed from the data. 2. What do the results mean? Not sure how policy-makers and governement could apply results for program and change. The results seem to determine various maternal age ranges at first birth that minimize risk, such as 18-32 for infant mortality, 27-35 for stunting, and 21-35 for underweight. How is one to interpret different maternal age intervals for particular risks? Under age 21 is ok for infant mortality but not for stunting or underweight risk? Over 32 years is not good for infant mortality but ok for stunting and underweight up until age 35. 3. Of concern, are the many important factors that contribute to infant mortality that are not taken into account in the present study. Four diseases—pneumonia, diarrhoea, malaria and AIDS— account for 43% of all deaths in children under-five. Many of the countries studied in this paper are greatly affected by malaria and AIDS, not adjusted for this is a major limitation. Also what about variables from the Demographic Health Surveys on birth interval, breastfeeding, and pneumonia? How can the reader be certain that the risk of infant mortality from such a large time period (1990-2008) is due to maternal age at first birth and not some other factor not examined? There have been major improvements/interventions between 1990 and 2008 that could be explaining change in outcomes over time. 4. Would be useful to have a table in the paper that shows the country, year of DHS, number of women surveyed, mean (SD) of maternal age at first birth, infant mortality rate and children under-five mortality rate. 5. Need to mention in limitations potential for ecological fallacy from using cluster-level variable for measles vaccination in model. Lack of data on malaria, AIDS, place of delivery, birth attendance (trained/untrained), birth interval and breastfeeding also limitations.

REVIEWER	***Joanne Katz*** Professor Johns Hopkins University, Bloomberg School of Public Health USA I have no competing interests.
REVIEW RETURNED	05-Jul-2011

THE STUDY	The manuscript is generally well written but there are various typos (see those listed in the review below). Page 5, line 32-33 ...show that children BORN to mothers...

	Page 9, line 14 ...interest IS mother's... Page 22 line 9 ...we observe IS confounded... Page 25 line 51 ... that applies TO low- to middle-income countries... There is one reference that is not correctly cited (Zou is cited as reference #9 but that is listed as Villar 1982). Zou's paper does not appear to be listed in the references.
RESULTS & CONCLUSIONS	Page 26 and table 3. Not sure I totally agree with the conclusion that 27-29 is the lowest risk age group, and that early twenties women present higher enough risk to warrant recommendations to delay child bearing to late twenties. For example, for the mortality outcome, the real risks come in those < 18. Even for the other outcomes which do present a higher risk for higher age groups, it is largely the < 20 or the < 22 that are at higher risk, and it is important to look at the size of the relative risk itself, not just whether the RR confidence interval does not cover 1.
GENERAL COMMENTS	Question about Table 5: it was not clear if these results were adjusting for the covariates (used in the prior adjustment) or just for height and religion. This could be clarified in the text.

VERSION 1 – AUTHOR RESPONSE

In response to Amina Khambalia

1. Of the 55 countries examined there must be countries where maternal age at first birth has shown an increase over time (1990-2008). Have the authors examined whether the outcomes studied (i.e. infant mortality, stunting, underweight) showed an adjusted decrease that coincides with increased maternal age at first birth that would further the investigators' conclusions?
• Response: In this paper, we aimed to examine the cross sectional nature of the effect of mother's age at first birth on child health outcomes. Towards this end, we controlled for year of birth fixed effects that would capture any idiosyncrasies associated with the year of birth of the child. However, one might also suspect that the effect of mother's age at first birth may be changing across time. To explore this, we inserted an extra table (Table A4 page 37) that shows the adjusted results for each outcome using DHSs from 2000-2005 only. These results show that the age effects are similar in the restricted year range (Table A4) to those using all surveys (Table 4). With this addition, we feel that we have illustrated that the time trend is not dramatic, and we reserve the time series analysis for another paper where summary statistics will also draw out the time trend element as opposed to the cross sectional association we focus on in this paper.

2. In Intro please define terms "minors" and "majors" in Raj et al. study.
• Response: We have added clarification for the definitions of "major" and "minor" (see highlighted sections on page 4).

3. Websites references in methods can be cited as other references in the reference list using referencing for websites rather than including webpage links in the actual paper.
• Response: We have converted the website references to the reference list as recommended (see page 5)

4. Importantly, how is the main outcome infant mortality measured? Questionnaire of birth histories from mother, medical records, or death certificate?
• Response: The explanation of the variable for infant mortality has been extended (see page 7)

5. Unclear how wealth index was created, need more detail. Is this a common, validated measure

used for these surveys?
• Response: The wealth index is now explained in greater detail on page 8.

6. Discussion in Results section on differential effects of maternal and paternal indictors should be in the Discussion section because it is of an interpretative nature.
• Response: We have moved the discussion of the differential effects of the maternal and paternal indicators to the discussion section. (See page 28 for its placement in the Discussion)

7. Unclear why religion is thrown into the sensitivity analyses which is performed to examine maternal height. Given that the sensitivity analyses did not detect change, Table 5 could be an appendix table.
• Response: An explanation of why we add religion as a control variable has been added on page26. In addition, we have moved Table 5 to the web appendix where it is now Table A5 page 39.

1. What is the rationale for creating a categorical variable for maternal age instead of using a continuous outcome? And for the categorical variable for maternal age, the choice of reference group seems to change (27-29 or 24-29) and appears arbitrary. To reduce reader concern that choice of maternal age categories affected results, could the investigators describe in a few sentences rationale for using a categorial versus continuous variable and for using 2 year intervals rather than say 3 or 4 years? Would using different categories for maternal age significantly alter the findings? Looking at Figure 1, it appears as though stunting and underweight decrease until ~age 30 and then levels off, whereas, diarrohoea, wasting and infant mortality are pretty flat between maternal ages 14 onwards. This creates more uncertainity in results and the age ranges that are of lower risk and others that are at higher risk. Not convinced that creation of pre-defined categories for maternal age is best way to determine optimal age for delayed first birth (i.e. age 27 as reported in this study). I think a break-point analysis would be needed to accurately determine a particular cut-off age where largest effects are observed from the data.
• Response: The rationale for creating a categorical variable for maternal age instead of a continuous age variable is now explained in detail. See the additional text on page 8, and Table A2.

2. What do the results mean? Not sure how policy-makers and government could apply results for program and change. The results seem to determine various maternal age ranges at first birth that minimize risk, such as 18-32 for infant mortality, 27-35 for stunting, and 21-35 for underweight. How is one to interpret different maternal age intervals for particular risks? Under age 21 is ok for infant mortality but not for stunting or underweight risk? Over 32 years is not good for infant mortality but ok for stunting and underweight up until age 35.
• Response: The general meaning of the results is now explained on page 27. The policy implications of the results are discussed on page 30 (highlighted in green instead of yellow as this paragraph was in the original submission and is not an addition as those text marked in yellow are).

3. Of concern, are the many important factors that contribute to infant mortality that are not taken into account in the present study. Four diseases—pneumonia, diarrhoea, malaria and AIDS— account for 43% of all deaths in children under-five. Many of the countries studied in this paper are greatly affected by malaria and AIDS, not adjusted for this is a major limitation. Also what about variables from the Demographic Health Surveys on birth interval, breastfeeding, and pneumonia? How can the reader be certain that the risk of infant mortality from such a large time period (1990-2008) is due to maternal age at first birth and not some other factor not examined? There have been major improvements/interventions between 1990 and 2008 that could be explaining change in outcomes over time.
• Response: Controlling for many child health characteristics was not possible, as much information on the health of the children who have passed away is not available. Moreover, we have added a table that shows the results for a limited year range (2000-2005 only) (Table A4 page 37). These

results show that the effect of the mother's age at birth on child health outcomes is similar in the restricted year range as it is in all the surveys over time. It seems that Table 4 and Table 4A suggest that the relationship between age of mother and child health outcomes is not changing over the time period analysed in this paper.

4. Would be useful to have a table in the paper that shows the country, year of DHS, number of women surveyed, mean (SD) of maternal age at first birth, infant mortality rate and children under-five mortality rate.
• Response: We have added a table that shows the country, year, number of observations, then weighted statistics for age of mother at first birth, and infant mortality. In addition, instead of another column with child mortality we add columns with averages (and 95% CI) for the 5 other child health outcomes. See Table 1.

5. Need to mention in limitations potential for ecological fallacy from using cluster-level variable for measles vaccination in model. Lack of data on malaria, AIDS, place of delivery, birth attendance (trained/untrained), birth interval and breastfeeding also limitations.

• Response: The ecological fallacy concern has been addressed on page 9. The limitations section of the study has been expanded to include those limitations raised by the referee (page 29).

In response to Joanne Katz

The manuscript is generally well written but there are various typos (see those listed in the review below).
Page 9, line 14 ...interest IS mother's...
Page 22 line 9 ...we observe IS confounded...
Page 25 line 51 ... that applies TO low- to middle-income countries...
Page 5, line 32-33 ...show that children BORN to mothers...
• Response: The typos have been fixed. We have also been through the document carefully to see that there are no other typos. These changes are tracked.

There is one reference that is not correctly cited (Zou is cited as reference #9 but that is listed as Villar 1982). Zou's paper does not appear to be listed in the references.
• Response: The Zou reference has been fixed. See page 9 and page 32.

Page 26 and table 3. Not sure I totally agree with the conclusion that 27-29 is the lowest risk age group, and that early twenties women present higher enough risk to warrant recommendations to delay child bearing to late twenties. For example, for the mortality outcome, the real risks come in those < 18. Even for the other outcomes which do present a higher risk for higher age groups, it is largely the < 20 or the < 22 that are at higher risk, and it is important to look at the size of the relative risk itself, not just whether the RR confidence interval does not cover 1.
• Response: The interpretation of the results has been expanded, see page 27

Question about Table 5: it was not clear if these results were adjusting for the covariates (used in the prior adjustment) or just for height and religion. This could be clarified in the text.
• Response: The query has been clarified in the text, see page 26.

VERSION 2 - REVIEW

REVIEWER	***Joanne Katz***

REVIEW RETURNED	22-Jul-2011

THE STUDY	There are some minor typos, mostly words that have no spaces between them and some word that are capitalized but are not at the start of a sentence.

REVIEWER	***Amina Khambalia***
REVIEW RETURNED	26-Jul-2011

GENERAL COMMENTS	Reviewer completed checklist only. No further comments were made