PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Antenatal Care Services and its Implications for Vital and Health Outcomes of Children: Evidence from 193 Surveys in 69 Low- and Middle-Income Countries
AUTHORS	Kuhnt, Jana; Vollmer, Sebastian

VERSION 1 – REVIEW

REVIEWER	Laura Oakley London School of Hygiene and Tropical Medicine, UK.
REVIEW RETURNED	30-May-2017

GENERAL COMMENTS	1. It would be useful to include a list of all countries included in the dataset, and the year. This could be provided as supplementary information 2. There is considerable missing data for all outcomes, particularly for low birthweight. Figure 1 suggests that among those with valid data on confounders and ANC use, nearly half had missing data on birthweight. The proportion of those with missing outcome data was also high for the stunting and underweight outcomes. Missing data should be discussed as a limitation of this study. 3. I think it would be useful to report separate estimates for other antenatal care exposures, primarily ≥4 antenatal care visits with a skilled provider. I had expected this to be reported in the manuscript, but it only seems to have been included as an additional variable in the models. Indeed, I found it confusing that all three ANC variables were included in models 4 and 5 (Table 3). How would one interpret the estimate for “at least 1 ANC visit” adjusted for “at least 4 ANC visits”? 4. I can understand the rationale for controlling for birth characteristics as ‘potential transmission channels’ when looking at mortality outcomes (though there is considerable debate about the appropriateness of adjusting for mediator variables

	– see https://academic.oup.com/ije/article/42/5/1511/619987/Mediation-analysis-inepidemiology- methods), but I do not think that these should be in the model looking at low birthweight and longer-term nutritional outcomes. How does caesarean delivery lead to low birthweight? 5. Did the authors consider breaking down the results by world region? 6. The authors need to add a sentence about ethical approval. Abstract 1. Page 2 line 39: “pp” needs spelling out. Thank you, Introduction 1. Page 4 lines 10-11: I suggest these two sentences are joined together “Nearly three million babies….month of life: many of these deaths occur in low- and middle-income countries and are easily preventable”. 2. Page 4 line 54: unneeded apostrophe after “services” 3. Page 6 line 31: As of 2016, WHO recommends a minim of eight antenatal care visits. 4. Page 6 line 31: I believe that the WHO recommendation also specifies the antenatal care should be delivered by a skilled provider. Methods 1. Did you include a maximum of one birth per woman, or did some women contribute more than one birth to the analysis? 2. Presumably the infant death analysis was restricted to children aged at least one year at the time of survey? If yes, this should be stated. 3. Page 7 lines 34-42: I am not convinced that these variables should be included as possible mediators for all outcomes. Also, adjusting for mediator variables in this way is usually not recommended. Results 1. Page 9 line 30: Revise “If the mother chooses to have at least one ANC visit…” (it might not be much of a choice!) 2. Page 9 line 41: Typo, change “looses” to “loses”. Discussion 1. Page 10 lines 36-37: This statement suggests that the association is especially strong almost everywhere. This would be easier to interpret if there was a table in the supplementary section listing the included countries by region. 2. Individual DHS surveys were conducted over a 23 year period. Comparing data from 1990 (and births as earlier as 1985?) to those in 2013 is not without problems.

	The possibility that this may have affected results should be discussed in the manuscript. 3. It is also worth noting that the effect of antenatal care will depend on the quality of care, which in term might be influenced by other factors (e.g. whether it is private or public sector). Tables 1. Table 1: It would be useful to present the frequencies in this table, as the sample varies for different outcomes. 2. Table 1: Typo in Column 2 header, “leat” needs to be changed to “least”. 3. Table 2: Models 4 and 5 could be moved to a supplementary table. 4. Table 2: I suggest the row heading “Controls” is changed to “Adjusted for confounding”. 5. Table A2: The reference group for “Maternal age at birth” is not clear (I think it is ≤17?) 6. Table A2: Are these results from model 4? I think it would be more consistent to use estimates from model 2, or possibly 3. The authors should specify as a footnote that all estimates are adjusted for other variables in the table.

REVIEWER	Vrijesh Tripathi Department of Mathematics and Statistics The University of the West Indies, St Augustine campus Trinidad and Tobago No Competing Interest
REVIEW RETURNED	27-Jun-2017

GENERAL COMMENTS	The article is statistically sound and publishable. Abstract: the authors are advised to use verbs in their abstract. We need full sentences. Add at least One more point each in Strengths and Limitations. Please proof read correctly and check for spellings and grammar: e.g. Page 6: line 17, age at death of the child Page 6, line 31, visit to a doctor Page 8, line 21: average less educated Page 9, line 32: if the mother chose Page 10, line 4: explain LBW Outcomes: why are the authors stating they used data for 0-59 months while their focus is on neonatal and infant mortality, along with low birth weight, stunting and underweight. Why was child mortality left out? There is also no clear explanation why they used one ANC visit as the lowest common denominator, rather than the WHO recommended 4 visits.

	Results: there is no specific indication if the data would have allowed the authors to assess the quality of the provider apart from quantity. Besides rewording the last line on page 8, they need to supply a more valid reason to believe that even one ANC visit is necessary. Discussion Why use U5M indicator when you have not modeled child mortality? The authors are advised to connect up the points. References Should be updated with 2015, 2016, and 2017 articles. Also there is little mention of sustainable development goals.

VERSION 1 – AUTHOR RESPONSE

Response to Reviewer 1

Comment 1. It would be useful to include a list of all countries included in the dataset, and the year. This could be provided as supplementary information.

Response: We thank you for this suggestion and we now included a list of all countries and the respective survey years included in the analysis in the appendix.

There is considerable missing data for all outcomes, particularly for low birthweight. Figure 1 suggests that among those with valid data on confounders and ANC use, nearly half had missing data on birthweight. The proportion of those with missing outcome data was also high for the stunting and underweight outcomes. Missing data should be discussed as a limitation of this study.

Thank you for this remark. We have clarified the extent of missingness by excluding the surveys from our initial sample that did not systematically collect information on our dependent and independent variables (because those are not missing but rather not available). Hence, we only included surveys in our initial sample that could have potentially collected the necessary information. We then re-calculated our final analytical samples.

We further acknowledge your concern and have added it as a limitation in the discussion section of the study.

Comment 3. I think it would be useful to report separate estimates for other antenatal care exposures, primarily ≥4 antenatal care visits with a skilled provider. I had expected this to be reported in the manuscript, but it only seems to have been included as an additional variable in the models. Indeed, I found it confusing that all three ANC variables were included in models

4 and 5 (Table 3). How would one interpret the estimate for “at least 1 ANC visit” adjusted for “at least 4 ANC visits”?

Response: Thank you for this comment. We acknowledged your concern and adjusted the regressions to ease their interpretation. Instead of adding quality and number of ANC visits separately to the regression, we now created a variable that more accurately reflects the WHO recommendation: a dummy variable indicating whether the mother received at least 4 ANC visits while having at least once seen a skilled provider during her pregnancy. Its interpretation is similar to an interaction term: it gives the additional effect as the variable overlaps with the variable indicating the mere attendance of ANC.

Hence, it shows the additional effect of attending at least 4 ANC visits while having at least once seen a skilled provider as compared to merely attending ANC (less than 3 visits and not necessarily at a skilled provider). We made an effort to explain this more explicitly in the study. Please note that this definition is still different from the WHO recommendation, but information on skilled provider is not available for all visits. With this definition we come closest to the WHO recommendation with the data that is available.

Comment 4. I can understand the rationale for controlling for birth characteristics as 'potential transmission channels' when looking at mortality outcomes (though there is considerable debate about the appropriateness of adjusting for mediator variables – see https://academic.oup.com/ije/article/42/5/1511/619987/Mediation-analysis-inepidemiology-methods), but I do not think that these should be in the model looking at low birthweight and longer-term nutritional outcomes. How does caesarean delivery lead to low birthweight?

Response: We agree that the analysis and interpretation of mediator variables should be done with caution. Though, we still believe that it can provide insightful information. We have moved the mediator analysis to the appendix.

Comment 5. Did the authors consider breaking down the results by world region?

Response: Thank you for this suggestion. We have analyzed the results (association between mere ANC attendance and outcome variables – model 2) by the 5 world regions. Unfortunately, we are limited by the BMJ word count but have included the figures in the appendix and are shortly referring to them in the discussion part of the study.

Comment 6. The authors need to add a sentence about ethical approval.
Thank you. We have added this information.
Abstract
1. Page 2 line 39: "pp" needs spelling out.

Response: Thank you, we corrected this.

Introduction
1. Page 4 lines 10-11: I suggest these two sentences are joined together "Nearly three million babies….month of life: many of these deaths occur in low- and middle-income countries and are easily preventable".

Response: Thank you, we followed your suggestion.

2. Page 4 line 54: unneeded apostrophe after "services"

Response: Thank you, we corrected this.

3. Page 6 line 31: As of 2016, WHO recommends a minim of eight antenatal care visits.

Response: Thank you for this comment. We have included this information in the study. As we are only using data of women attending ANC visits before 2016, we continue to focus on 4 ANC visits (at a skilled provider) as this represents the WHO recommendations at the time of the surveys. Hence, the number of women attending 8 ANC visits would represent a highly selective sample of women that were actively seeking care beyond and above what the WHO was recommending.

But for future DHS rounds that will come out soon it
would be interesting to consider studying the effect of the newly formulated WHO recommendations and possibly also comparing the old WHO recommendation to the new one.

4. Page 6 line 31: I believe that the WHO recommendation also specifies the antenatal care should be delivered by a skilled provider.

Response: We have taken your comment into consideration and changed our analysis by specifying an adjusted variable “at least 4 ANC visit while at least once seen a skilled provider”.
Herewith, we try to better proxy the WHO recommendations (prior 2016). Unfortunately, we do not have provider information regarding every ANC visit but only on whether the woman at least once has seen a skilled provider.
But it is reasonable to argue in most cases that the woman continues her ANC visits with the same provider throughout her pregnancy.

Methods
1. Did you include a maximum of one birth per woman, or did some women contribute more than one birth to the analysis?

Response: As we only have information on the ANC visits of the last-born child, the analysis is based on the last-born child of the women. Hence, each woman only contributed one birth to the analysis. In the analysis we control for birth order. We made an effort in clarifying this in the study.

2. Presumably the infant death analysis was restricted to children aged at least one year at the time of survey? If yes, this should be stated.

Response: Thank you for this comment. Yes, the infant death analysis is restricted to children that aged at least one year and it excludes neonatal deaths. We made an effort in explaining it in more detail in the study.

3. Page 7 lines 34-42: I am not convinced that these variables should be included as possible mediators for all outcomes. Also, adjusting for mediator variables in this way is usually not recommended.

Response: We agree that the analysis and interpretation of mediator variables should be handled with caution. Though, we still believe that it can provide insightful information. Hence, we have moved this analysis to the appendix.

Results
1. Page 9 line 30: Revise “If the mother chooses to have at least one ANC visit…” (it might not be much of a choice!)

Response: Thank you, we corrected this.

2. Page 9 line 41: Typo, change “looses” to “loses”.

Response: Thank you, we corrected this.

Discussion

1. Page 10 lines 36-37: This statement suggests that the association is especially strong almost everywhere. This would be easier to interpret if there was a table in the supplementary section listing the included countries by region.

Response: Thank you for this comment. We added a table listing all countries and surveys included in the analysis as well as a figure displaying the associations between ANC attendance and the outcome variables by world region.

2. Individual DHS surveys were conducted over a 23 year period. Comparing data from 1990 (and births as earlier as 1985?) to those in 2013 is not without problems. The possibility that this may have affected results should be discussed in the manuscript.

Response: By adding PSU level fixed effects that are phase and survey specific, we absorb all factors within the PSU that are similar within that locality and respective survey and get our variation only within these PSUs. We now also acknowledge that the magnitude of the association could change over time and that we estimate an average effect across countries and years.

3. It is also worth noting that the effect of antenatal care will depend on the quality of care, which in term might be influenced by other factors (e.g. whether it is private or public sector).

Response: Thank you for this comment. Unfortunately, we are unable to use further quality indicators of the ANC received by the women due to many missing values (e.g. was the women weighted, blood pressure taken or urine/blood sample taken). But as we control for PSU level fixed effects and we hence, estimate the variation within PSUs. A PSU is the smallest geographical survey statistical unit within the DHS surveys. It consists of a number of adjacent households. Hence, we believe that the quality of ANC available to the women within the same PSU is comparable.
Still, we added this as limitation in the discussion part.

Tables

1. Table 1: It would be useful to present the frequencies in this table, as the sample varies for different outcomes.

Response: Thank you for your suggestion. We have adjusted the table and added an additional category “at least 4 ANC visits and seen skilled provider” and show simple differences to “no ANC visit”. With these changes we also try to follow the suggestions of the other reviewer. We fear that adding frequencies could make the table too complex, especially as the respective variables are not balanced across exposure categories.

2. Table 1: Typo in Column 2 header, “leat” needs to be changed to “least”.

Response: Thank you, we corrected this.

3. Table 2: Models 4 and 5 could be moved to a supplementary table.

Response: Following your suggestions, we have adjusted the tables. We also moved the mediator analysis to the appendix.

4. Table 2: I suggest the row heading “Controls” is changed to “Adjusted for confounding”.

Response: We followed your suggestion.

5. Table A2: The reference group for “Maternal age at birth” is not clear (I think it is ≤17?)

Response: Thank you for this comment. We adjusted the table formatting (which cut off this information)

6. Table A2: Are these results from model 4? I think it would be more consistent to use estimates from model 2, or possibly 3. The authors should specify as a footnote that all estimates are adjusted for other variables in the table.

Response: Following the suggestions within the review process, we have changed the main models. The results in Table A2 are from model (3) and include the standard set of control variables and PSU fixed effects. We have also stated this at the bottom of the table.

Response to Reviewer 2

1. Abstract: the authors are advised to use verbs in their abstract. We need full sentences.

Response: Thank you for this comment. We adjusted this and hope that it is now easily readable.

2. Add at least One more point each in Strengths and Limitations.

Response: We added more points to the strengths and limitations section.

3. Please proof read correctly and check for spellings and grammar: e.g.
Page 6: line 17, age at death of the child
Page 6, line 31, visit to a doctor
Page 8, line 21: average less educated
Page 9, line 32: if the mother chose
Page 10, line 4: explain LBW

Response: We apologize for these typos and have conducted further proofreading to improve the manuscript and appendix.

Outcomes

1. Why are the authors stating they used data for 0-59 months while their focus is on neonatal and infant mortality, along with low birth weight, stunting and underweight.

Response: We are sorry for the misunderstanding. In our dataset, the information on our main outcome and explanatory variables has only been collected for the last-born children in the previous 5 (and in some surveys 3) years to the survey. Hence, we only have data available for children between 0 to 59 (36) months. For some outcome variables, e.g. anthropometric measures, we use the full range of children’s age groups. We have made an effort to clarify this further in the study.

2. Why was child mortality left out?

Response: In order to analyze child mortality we would have to limit our analysis to only those children that already aged 5 years (to observe survival until age 5).

As our dataset only includes information on the children born in the previous 5 (3) years, this would starkly reduce our sample. Hence, we decided to focus our analysis on neonatal and infant mortality outcomes.

3. There is also no clear explanation why they used one ANC visit as the lowest common denominator, rather than the WHO recommended 4 visits.

Response: We adjusted our analysis to improve our proxy of the WHO recommendations (prior 2016) with regard to prenatal care: We added a variable indicating whether the woman attended at least the recommended 4 ANC visits and whether she has at least once seen a skilled provider. Comparing this variable to the lower bound of whether the woman has attended any ANC visit at all gives us the additional effect of the WHO recommendation. We made an effort to clarify this in the study.

Results
1. There is no specific indication if the data would have allowed the authors to assess the quality of the provider apart from quantity.

Response: We tried to proxy for the quality of the provider by defining “skilled” and “unskilled” provider types. Skilled providers include: doctor, midwife, nurse, auxiliary midwife, obstetrician, health professional, or trained (traditional) birth attendant. Due to many missings, we were not able to assess the quality of the ANC services provided further (e.g. blood pressure/height/weight taken during ANC visit). By using PSU level fixed effects we control for variation of quality across PSUs and it is reasonable to believe that the quality of ANC services available to women of the same PSU is comparable.

2. Besides rewording the last line on page 8, they need to supply a more valid reason to believe that even one ANC visit is necessary.

Response: We have rephrased this and made an effort to explain these results further in the paper. We hope that we were successful in adding a more straightforward explanation.

Discussion
1. Why use U5M indicator when you have not modeled child mortality? The authors are advised to connect up the points.

Response: We are sorry for the misunderstanding. We have deleted all information from the study referring to U5 mortality rates. We only analyze neonatal and infant mortality as well as low birthweight and U5 anthropometric measures (stunting and underweight).

References
1. Should be updated with 2015, 2016, and 2017 articles.

Response: Thank you for this comment. We made an effort to update the literature review and references with the most recent articles.

2. Also there is little mention of sustainable development goals.

Response: Thank you, we followed now updated the study by referring to the SDGs in the introduction and discussion.

VERSION 2 – REVIEW

REVIEWER	Vrijesh Tripathi Faculty of Science & Technology The University of the West Indies, St Augustine, Trinidad and Tobago
REVIEW RETURNED	01-Sep-2017

GENERAL COMMENTS	All my concerns have been addressed. This is an important study that quantifies the effect of ANC on child health outcomes. I recommend that it is published.