Author's response to reviews

Title: Country Characteristics and Acute Diarrhea in Children from Developing Nations: A Multilevel Study

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Author's response to reviews: see over
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BMC Public Health
Attn. Celine Zapanta
Journal Editorial Office
BioMed Central

Dear Celine,

We are resubmitting for publication the manuscript “Country Characteristics and Acute Diarrhea in Children from Developing Nations: A Multilevel Study” with the suggested corrections. We would like to express our appreciation to the reviewers for their very useful comments and wonderful feedback, which have contributed to improve the quality of the paper.

You will find below answers to the reviewers’ suggestions and concerns. Please let us know if you require any additional information.

Sincerely,

Angela M Pinzon-Rondon

Reviewer: Rachel Burke

Major compulsory revisions

1. Please justify the use of the missing indicator in the birthweight variable. Use of a missingness indicator has been shown to create a selection bias. Therefore, I would recommend leaving these values as missing and then either utilizing multiple imputation or other methods of simulation to conduct a sensitivity analysis.

Answer: We agree that the use of a missing indicator is not ideal. However, after an attempt to impute the data and taking into consideration that 46% of the information was missing, we concluded that it was better to include it. This is explained in the text and recognized as a limitation.

2. The statistical analysis section requires clarification. By “hierarchical linear modeling Bernoulli regressions” do you mean mixed effects logistic regression? If
so, utilize this terminology, as it will be more familiar to the reader. If not, then report a source for this type of model for the interested reader. In lines 141 – 147, it is unclear if you ran different models, or used the same model to calculate different effects.

Answer: The model was included in the text as an appendix and a couple of references are given.

3. In the Methods section, lines 148 – 149, clarify data weighting. Were data weighted to be representative within countries, or also across countries? If within countries, then it doesn’t seem appropriate to report simple proportions in Table 1—these should be weighted by each country’s relevant population.

Answer: The data weighting was clarified.

4. Tables should be clarified—it seems like one column has the fixed effects, and the other has the random effects (for table 4)? You might just want to present overall ORs and then the parameter estimates for the random effects. Table 5 is unclear. I cannot tell why there are two different variances? Consider referring to other published articles for other ideas on how to most clearly present results from multilevel models. E.g., http://www.plosone.org/article/fetchObject.action?uri=info%3Adoi%2F10.1371%2Fjournal.pone.0109930&representation=PDF

http://www.equityhealthj.com/content/13/1/95

Answer: we modified tables 4 and 5 using the examples provided by the reviewer. They are easier to understand now.

5. Discussion should assess meaningfulness of significant associations that seem rather weak (e.g., OR of 0.98), especially since study is over-powered. This is relevant particularly for the country-level effects.

Answer: This is true. It was included as a limitation in the discussion session.

Minor compulsory revisions

1. Methods section, line 101-102 – does permanent residents refer to residents of the household? If so, clarify.

Answer. Yes, it refers to household residents. We have clarified it in the text “permanent household residents”.

2. In the Methods section, line 108 – clarify DHS definition of diarrheal depositions – was it just “high frequency and low consistency” or was there a more specific definition (e.g., “3+ depositions per day, of looser than normal consistency”)?
Answer: The definition of diarrhea given by the DHS does not distinguish by severity or number of episodes. It is defined by increased frequency of depositions and/or low consistency of feces per child’s mother report. This has been written in the text.

3. In the Methods section, line 174, it is unclear which pregnancy is being referred to. Is the analysis with “index” children only, or with all children in the household? Which of the pregnancies was unplanned?

Answer: The analysis was done with the index child. The variable planned pregnancy refers only to the pregnancy in which the index child was the outcome. Wording clarifications have been made.

4. Overall, please clarify if all children were used or only one index child per household. If multiple children per household, then this should also be included in the analysis (random effect for household given correlations).

Answer: Only one child per household was included. If the households had more than one child, the youngest was included. This has been explained in the text.

5. Consider shortening Discussion section. I think it can be condensed so that it does not repeat results so much.

Answer: We have shortened the discussion.

6. Could probably shorten discussion of prevalence of ADD – other studies are not fully comparable since they have addressed a totally different population (different countries).

Answer: We have deleted the discussion on diarrhea prevalence

Discretionary revisions

1. Consider using the abbreviation of “AGE” (acute gastroenteritis) instead of ADD (acute diarrheal disease) throughout, as this is an abbreviation I have seen more commonly.

Answer: The abbreviation ADD, has been changed to avoid confusion in terms of its similarity with Attention Deficit Disorder. The condition is now referred throughout the text as Diarrheal Disease and diarrhea. The Acute Gastroenteritis (AGE) suggestion was not used considering that AGE is a condition that presents only with vomiting.

2. How is a family that is nuclear + grandparents (or other relatives) coded?
Answer: Nuclear family refers to a social unit conformed exclusively by two parents and one or more children. Family groups including other family members (e.g. grandparents) were coded as non-nuclear (0 = non-nuclear family, 1 = nuclear family). This definition was clarified in the manuscript.

3. Is wealth index relative to one’s own country? I would imagine so.

Answer: Yes, This is now clear in the text.

4. How was the model’s validity assessed (line 133)?

Answer: We used HLM residual files and reliability indicators. We have included the information in the text.

5. For the models used, it may be helpful to the reader to show the form of the model (formula / equation).

Answer: The formula was included.

6. Tables 1 and 2 can be combined.

Answer: The tables were merged.

7. Wealth index should be better contextualized (range).

Answer: We contextualized better wealth index and provided the range.

Minor Issues not for Publication

1. In the Methods section, line 89, correct country “Albany” to Albania

   Answer: Albany has been changed for Albania.

2. Line 179 in Methods – false cognate - change “stretch” to “narrow.”

   Answer: Stretch has been changed for narrow.

3. Overall, you will want to do another read-through for minor typos and grammatical errors.

   Answer: We appreciate the reviewer’s recommendations. We have read the final version again looking for possible typos or grammatical errors.
Reviewer: Niko Speybroek

1. The models are developed based on the available data and not on a conceptual model. This creates the risk of a mis-specified model. I would like to see such a conceptual model, based on a literature review followed by estimating those parameters (of this conceptual model) that the data allow for. Such a review will also allow understanding which important variables were omitted.

Answer: We have included a brief summary of the factors associated with diarrhea on the background. We have specified that the model bases on these factors in the methods. We had to exclude two of them for collinearity but the rest were included.

2. Two levels are considered in the models uses, namely country and individuals. In a multilevel analysis the household should be considered as a level, separate from the individual level. Furthermore, the authors say that a stratified sampling procedure is used. However, this survey design characteristic is not taken into account in the model.

Answer: we only included one child per household. This has been specified on the text. Initially we considered three levels of analysis but most of the households had only one child so it was decided to include only one child per household, i.e., the youngest.

3. The authors mention that they have been “Using hierarchical linear modelling”. This is too vague. The exact model, with the random effects etc… should be specified.

Answer: We have included the equation of the statistical model. We have also included some references.

4. It is unclear how the interaction effects were estimated.

Answer: Interaction terms were calculated for Duration of breast feeding and maternal education, Duration of breast feeding and maternal employment, immunization and maternal education, and wealth index and immunization. No interaction effects were found.

5. A map, indicating the differences between countries may be needed.

Answer: Changes were made to the tables and we believe that these changes address this point. It is now easy to see the differences between countries. There are not many differences.
Reviewer: Shannon Majowicz

Major compulsory revisions.

1. Throughout the paper, results (e.g., CI's, OR's) are reported to two decimal places; however, as the authors note there are instances where this is not enough to demonstrate the difference between the values. I suggest the authors report a greater number of decimal places so the reader can see how the values differ.

Answer: We have placed three decimal places in tables 4 and 5.

2. Please provide more details as to the source of the DHS and World Bank Data (e.g., reference or website).

Answer: This has been included.

3. I am unfamiliar with the Bernoulli regressions mentioned in the methods. Can you please explain more or give a reference?

Answer: The model has been included as well as a couple of references.

4. Page 7, paragraph 2, what does this mean?

Answer: We have explained the weights more clearly.

5. There is great repetition of the results between the text and tables, and again in the Discussion. Please consider having your results in the text or tables, but not repeated in both. Throughout the discussion, the link between your findings and other literature, as well as discussion about what the results mean was limited. Please consider including deeper discussion of the meaning of your findings. For example, you suggest that interventions should be tailored depending upon the country characteristics; how specifically would we do this based on your results? Can you give some specific suggestions about what policy makers could do differently based on your findings?

Answer: We have deleted some results and have modified the discussion to include more on interventions and policy implications.

6. Did you look at interactions in your regression models? If yes, what did you find? If no, why not?

Answer: Yes we did but we didn’t report because we didn’t find anything. This has been clarified in the text.
7. I am not sure I agree that your results support the importance of social determinants of health as 'causally' as you state in the discussion. It would be good to explore this further... how might GDP and income inequality lead to diarrhea as you observed? This is a very powerful study in terms of sample size and data, and a deeper discussion of the results would be helpful. Are there possible biological mechanisms that may differ between groups? Can you suggest reasons for these observed differences? What kind of expenditure WOULD you expect to decrease diarrhea, if not money invested in health? Infrastructure investment? And could you have looked at those data (i.e., was there other economic information you could have included, not just health expenditure?)?

Answer: We agree. Thank you for pointing this out. The results don’t support the importance of social determinants of health in this way. We have made this clear in the paper. We have also included possible mechanisms to explain our results in the discussion.

8. Please be clear in your results why you’re discussing the results of the bivariable analysis and not focusing on the multivariable results. It seems to me that you should focus on discussing results of the multivariable model only, as that adjusts for the presence of other factors. Why would you also discuss the bivariable results?

Answer: We have deleted the discussion of the bivariate analysis.

Minor essential revisions.

1. I suggest you use the term 'diarrhea' in place of the abbreviation "ADD", since ADD is a common abbreviation for Attention Deficit Disorder (and not commonly used for diarrhea), and may be confusing.

Answer: The abbreviation ADD, has been changed to avoid confusion in terms of its similarity with Attention Deficit Disorder. The condition is now referred throughout the text as Diarrheal Disease and diarrhea.

2. This paper would benefit from an editor to improve the overall English, conciseness, and flow (e.g., ‘Albany’ in para 2, page 4; ‘data’ as plural). Additionally, please spell out acronyms the first time they are used (with the abbreviation in brackets, e.g., ‘gross domestic product’ on page 3).

Answer: Numerous changes have been included in the paper to address issues of language, conciseness and flow. Additionally, Albany has been changed for Albania. Acronyms were spelled out the first time they were used on the text for World Health Organization (WHO) and Gross Domestic Product (GDP), respectively.
3. Please report ORs in the Abstract along with CI's

Answer: In the abstract, the odds ratios and the confidence intervals were included, for the mentioned variables.

4. In the intro you reference a paper by Christa Fishcer-Walker, as being from industrialized nation(s). Is this correct?

Answer: No, thank you. As mentioned by the reviewer, this study does not take place in developed nations. In fact, it includes low and middle income countries, mostly in Asia and Africa. This has been corrected.

5. The way the variables are described, starting on page 5, is difficult to read. Consider displaying in a Table? or describing in full sentences?

Answer: We have modified the definition of many variables to clarify them.

6. Page 6, please give the year instead of 'current' US dollars. Is it 2014?

Answer: It has been changed.

7. How does your work relate to the work of the WHO's FERG and CHERG groups?

Our work aims to provide scientific information to help design productive public health initiatives. None of the authors or our institution has any relation with any of WHO's CHERG or FERG groups, other than sharing common interests. Their work is now mentioned in the discussion.