Author's response to reviews

Title: Health, poverty and cognitive function in pre-school children: a cohort study in a middle income urban context

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Author's response to reviews:

Dr. Annabel Phillips
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Dear Dr. Phillips

First of all I and my co-authors very much acknowledge the careful review and insightful recommendations to our paper 'Health, poverty and cognitive function in pre-school children: a cohort study in a middle income urban context' made by Dr Guerrant and Dr. Caughy. We have made our best efforts to follow all their recommendations and we think that the manuscript is now a lot more readable than it was before. (All additional material or modifications are highlighted in yellow.) We are sending herewith a new version of our paper revised in accordance with the referees' comments, answering the points made by each referee as follows...

A: Comments by Richard Guerrant

Principal concerns

1. What were the rates of diarrhea episodes, and were these correlated (only days of diarrhea are mentioned)?

Answer: Longitudinal prevalence - that is, the fraction of days of follow-up with
diarrhea - has been shown to be more closely associated with long-term health effects such as weight gain and mortality than incidence measures, and was used in this study to measure diarrhea burden. This information has been added to the text.

2. Was the HAZ of the children at 2 years old separately assessed for correlations with cognitive performance? This may be an excellent 'surrogate' measure of sanitation, enteric infections or malnutrition after birth, especially if analyzed independently of birthweights/lengths.
Answer: Yes, this was effected in the univariate analysis (Table 1)

3. A few typos need clarification; such as "careers" on page 6 (do they mean Caregivers?)
Answer: Revised

Minor essential revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

4. The authors should look for interaction effects--especially how their model applies within the lowest income group.
Answer: We tested product terms for the socioeconomic and environmental levels (Model D), as well as for the socioeconomic, environmental and child-health levels (Model G). The results did not show statistical significance, suggesting that the socioeconomic level did not act as an effect modifier for the associations analyzed.

5. The authors need to show how the factors may be weighted differently as influences to negative outcomes. Within the factors that adversely effect outcome is there a difference or do they contribute differently?
Answer: Our analysis was based on a previous defined conceptual model as an alternative to the more traditional analysis used in epidemiology. Consequently the variables in the model were previously defined according to their potential role in the studied outcome. The final model was defined in a hierarchical way. We are not sure that if other conceptual models or other strategies of inclusion of the independent variables were applied, this would change the weight of these variables regarding the negative outcomes. But this question was addressed in our discussion.

Discretionary Revisions (which the authors can choose to ignore)


Quality of written English: Needs some language corrections before being published
Answer: This has been addressed
INTRODUCTION

1. I found the introduction to be unusually short. Again, perhaps my perspective is different, but introductory sections are usually 4-5 times as long as the introduction for this paper. Because of the brevity of the introduction, I did not feel I had a very good idea of the primary goal of the analysis. It appears the authors may be focused on contrasting the importance of poor early health with the importance of early stimulation as predictors of cognitive competence in young children, but it is not explicit. I am not familiar with such studies of determinants of cognitive competence for children in countries such as Brazil, and it would be useful to have a fuller explication of that literature as a foundation for the current investigation.

Answer: We have expanded the introduction including reference to Brazilian studies in the field, and clarified our aim of assessing the socioeconomic effects on children’s cognitive development that are mediated by environmental and health variables.

2. With regards to the conceptual model for this study, although I appreciate the contextual perspective, I am not sure I agree with the presentation in the figure. Specially, all of the more distal factors are seen as being mediated by psychosocial stimulation. I could see arguments for a number of the factors that are not mediated in such a way. For example, I would suggest that the impact of child health status (at least as measured by the factors in this study) on cognitive competence is not mediated by psychosocial stimulation as measured by the HOME score or preschool attendance. In order for that to be the case one would have to argue that compromised child health status results in significant disruption of the quality of the home environment and or pre-school attendance. Although it's not outside the realm of possibility, there are likely other, more direct paths of influence.

Answer: The conceptual model has been reformulated and psychosocial stimulation now integrates environmental variables at an intermediate level between children’s personal health and socioeconomic determinants. We also consider that early cognitive performance was correlated with late cognitive score and should be the object of a separate study.

METHODS:

1. Although the figure delineating the study sample is helpful, I would like additional information regarding those who refused and or lost to follow up. Were they different or similar to those who are included in the analysis in terms of demographics, child characteristics, etc?

Answer: Revised details were added in the text.

2. More detail should be provided regarding the details of data collection.
Specifically, although the children were under age 42 months before 1999, what was their age range at the time when the Bayley was administered? If that range is very wide, it might be problematic. Where did data collection occur and by whom? Was the data collection in the home or in a clinic setting? I assume that because the HOME was administered, at least part of the data collection occurred in the child's home. Were the medical data collected via self report or from the child's medical record?

Answer: Revised details were added in the text

3. I'd like to see more rationale for how the infectious illness variables were operationalized. As detailed at the bottom of page 8, there are four different measures of infectious illness - 3 related to specific organisms and one related to experience of diarrhea. For the 3 measures specific to organisms, 2 are measured on a four point intensity scale, and one is a yes/no variable. The diarrhea variable is dichotomous (0-6 vs 6+ days/year). In terms of rationale, I'd like more justification for these variables specifically in terms of how they are seen to be related to child cognitive competence. Perhaps if the literature review had been more extensive, this formulation of variables would be apparent to the reader. However, speaking as a developmentalist, it is my assumption that these variables are supposed to provide an index of the burden of ill health experience during the child's early years. If so, I don't understand the need for separate variables as opposed to some sort of combination which more accurately captures the overall burden of illness.

Answer: These variables were presented in the standard way of the epidemiological literature. Many of them were eliminated in the initial stage of the analyses, leaving those that are more common in cognitive studies. References support the way they were operationalized, as for example the use of longitudinal prevalence to measure diarrhea. We reinforced these aspects in the text.

4. Likewise, I'd like to see further explication of the breastfeeding variables. The authors decided to create three groups - 0-7 days, 8-60 days, and 61+ days of breastfeeding. I am not sure why these cut points were chosen, that is, whether these cut points are seen as important determinants of cognitive functioning. I suppose that depends on whether the authors see breastfeeding as having a direct effect or an indirect via reductions in infectious illness. Also it would be helpful to have more information about how breastfeeding was determined. Was it any breastfeeding or more breastfeeding that formula? For example, a mother could have breastfed her infant for 9 months but only partially, with half or more of the infant's nutrition coming from formula. Again if the introduction were more extensive, then it might be apparent why the authors are including breastfeeding in a model predicting cognitive functioning. This rationale would, in turn, inform the construction of the breastfeeding variable.

Answer: We examined the literature more carefully and because there is controversy over the association between breast-feeding and cognitive outcomes, this factor was excluded from the model.

STATISTICAL ANALYSIS:
1. The approach to the analysis was unusual in some regards, and I think there are more effective ways of presenting the information. Specifically, in the first column of table 2, the authors present univariable analyses in the form of R2. A more informative analysis would be to present an intercorrelation matrix of the WPPSI-R scores and all of the covariates. Such a matrix would provide the identical information as what is presented in column 1 plus the added information of the intercorrelations of the predictors. The intercorrelations of the covariates themselves are important in trying to disentangle the different domains of factors and their influence on child cognitive functioning.

Answer: In epidemiological analysis the emphasis is on the association between the covariates and the outcome. The intercorrelation of the covariates was done from the beginning but we found that the process to construct each block of variables excluded the highly correlated ones.

2. The additional information that could be provided by such an intercorrelation table would help inform model building that I believe would more effectively address the study questions. Although there is nothing technically wrong with the multivariate regression analyses presented in step 3, I felt as though I was left with more questions than answers. If the purpose of the analysis was to disentangle these factors in terms of confounding, mediation, etc, then a more systematic approach to model building would have been more illuminating as opposed to presenting all covariates in a single multivariate model.

Answer: We adopt an effect-decomposition strategy to fit seven linear regression models (A, B, C, D, E, F, G) by including step-by-step blocks of potential risk factors, following references in the epidemiological literature (Genser et al, 2006, Victora et al, 1997).

3. Although I think the message that the early psychosocial environment appears to be a more potent predictor of cognitive functioning than burden of illness, I believe there is, potentially, a significant limitation in the paper’s findings as currently presented. In the multivariate analysis presented in table 3, early cognitive performance as measured by the Bayley is included as a covariate. This presents a problem for concluding that poor early health doesn’t compromise cognitive function at age 5. If early cognitive functioning mediates the association between burden of illness and later cognitive functioning, including, including the Bayley in the multivariate regression model would mask the association between illness and later cognitive functioning. Such would argue for a more systematic approach to model building.

Answer: The early cognitive performance has been excluded from the conceptual model and from the analysis.

4. A minor point: I think that some of the rows of coefficients in the Step 3 regression are shifted up. They are not lined up with the variables I think they are supposed to be for.

Answer: Revised