Author's response to reviews

Title: Blood pressure in primary school children in Uganda: a cross-sectional survey

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Author's response to reviews: see over
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The Editor
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Dear Sir or Madam,

MS: 6879355951413607
Blood pressure in primary school children in Uganda: a cross-sectional survey
Farah Kidy Diana Rutebarika Swaib A Lule Moses Kizza Amos Odit Emily L Webb and Alison M Elliott

Thank you very much for giving us the opportunity to respond to the reviewers comments regarding our manuscript. Please find our responses detailed below. We do hope that you will now find our article suitable for publication.

Yours sincerely,

Alison Elliott

Response to reviewers

Reviewer:Fernando Guerrero-Romero

Reviewer's report:
In this school-based cross-sectional survey, conducted in Uganda, author address the procedures required to assess blood pressure accurately in primary school children, and investigated risk factors for high blood pressure associated with rural or urban environments.

Comments
This is an interesting and well-conducted study. However, data about how many
schools as well as about characteristics of the general children populations in the urban and rural selected areas are needed. A table showing characteristics of target population breakdown by gender in the rural and urban areas is needed.

We have added information about the primary school population in Uganda, including the gender distribution (Lines 101-102) and about the number of eligible schools from which the selections were made (Lines 111-113). For participants, an additional table (new Table 1) describing general characteristics including gender and age has been provided.

Was Tanner stage estimated? A Table showing the characteristics of target population breakdown by pubertal and prepubertal stage also is needed. The 14 participants who were diagnosed as hypertensive were adolescents or prepubertal children? Is necessary to discuss the role of sex hormones on the increase of blood pressure. So, population in study should be stratified according their pubertal status.

We did not estimate Tanner stage or assess puberty. We have added discussion of this point among the limitations of the study. Lines 282-283.

Reviewer: Telmo Pereira

Reviewer’s report:
Kidy and colleagues present an interesting and quite pertinent paper, addressing the prevalence and determinants of high blood pressure (HBP) in children and adolescents in Uganda. They report a prevalence of 17.1% at the initial evaluation, with age, female gender, body mass index (BMI) and soil-transmitted helminths as the main determinants for HBP. The prevalence of HBP was reduced to 3.8% when repeated measurements were considered for those with HBP at the first evaluation, a phenomenon already reported in previous papers, that stresses the need to perform several blood pressure measurements for an accurate definition of the BP profile at these ages. HBP at these young ages is clearly under-studied and poorly described, although there’s a consensual knowledge that it results from a complex and multi-componential physiopathological process, incorporating the interaction amongst genetical, environmental and behavioural factors. The interaction amongst these interplaying factors makes it extremely difficult to isolate single determinants, or to identify the individual weight for each isolated factor. Moreover, other aspects emerge as crucial towards a good characterization of BP at these early stages in life. One Major aspect refers to the blood pressure methodology, not only in terms of overall procedure, but also regarding the devices used for measuring BP. On the other hand, the criteria for blood pressure classification are also crucial for identifying accurately HBP. So, notwithstanding the merits of this investigation by Kidy and colleagues, some major questions should be carefully addressed before publication should be considered.

1. The device used for BP measurement in this study (OMRON M6) is not yet been validated for the measurement of BP in children and adolescents. Although the device was validated for adults, its accuracy cannot be extrapolated for the paediatric populations, and therefore the internal validity of the study is seriously compromised. In a recent study, Flynn argues that “BP values obtained using
Oscillometric devices should not be used for the diagnosis of hypertension in children. (1) This has led the US and European guidelines to recommend that BP elevation in children should be confirmed by auscultation, preferably with a standard mercury sphygmograph. (2,3) There’s no evidence in the paper indicating that such recommendation was followed.

We acknowledge this limitation. The Oscillometric devices were used because of their ease to use and also to minimise inter-observer variability and digit preference. Although no local validation of Omron M6 was done, a palpation method of blood pressure determination was used in addition for the few children sent to Mulago hospital before recommendations were made upon management. This information has been added to the text. Lines 146-150.

2. The classification of BP based on the US percentiles could not be appropriated for this population, as there are biological idiosyncrasies that could make such extrapolation highly imprecise. This has for example motivated the publication of BP percentile tables in several European countries, not just for BP but also for height and BMI. Ideally, there should be an effort for creating specific tables for African paediatric populations, as the US tables could lead to under or overestimations of the real dimension of the problem.

We agree that population-specific tables would be preferable, but these are not available. It was interesting, therefore, that our findings suggest that the US tables were not unreasonable for this setting – given that you would expect about 5% of a population to have readings above the 95th centile if the tables were applicable. This is why we commented upon this in both the conclusion of the abstract and the first paragraph of the discussion. We have now extended the latter comment to make it clear that population-specific normograms would be desirable. Lines 261-262.

3. Characterization tables with descriptive statistics must be provided for the all sample and for the subgroups considered in the analysis. The prevalence of overweight should also be provided, and the prevalence of HBP stratified according to the BMI classification. It must also be described the representativeness of each age stratum, overall and for gender, as we cannot appreciate whether the sample is well balanced across the all age range.

We have included a new Table (Table 1) showing the characteristics of study participants, stratified by urban/rural school. This includes information on age and gender as requested, and also on BMI Z-score, categorised using the WHO suggested cut-offs for overweight and obese. Note that we use BMI Z-score as a continuous covariate in regression analyses for blood pressure outcomes, which is why we do not present the prevalence of HBP stratified according to BMI classification. To avoid confusion we have removed the text “92/539 (17.1%)”, which is the overall proportion of children with HBP, from the original Table 1 (now Table 2) for the variable BMI Z score.

4. The authors provide data regarding the HBP condition, but not regarding the intermediate BP classification – pre-hypertension or high-normal BP classification (BP between 90 and 95 percentile), or the stages of HBP (stage 1 or stage 2). These data must be provided, and additional multivariable analysis performed.
In order to classify all the children correctly with regard to pre hypertension it would have been necessary to see all of them at all visits over the three month period. We think it might be unsatisfactory to classify those with blood pressure between the 90th and 95th percentile as pre-hypertension based on a single visit and so we have confined ourselves to the simpler definition.

Of the 14 who were found to have persistent HBP, three and eight had diastolic blood pressure above the 95th and 99th percentile, respectively, and three had systolic blood pressure above the 99th percentile. This information has been added to the text. Lines 235-237.

5. It would have been interesting to check the BP change over time of the first visit prehypertensive children and adolescents, as some could progress to HBP classification.

Unfortunately we did not repeat the measurements for children with “prehypertensive” readings at the first assessments.

6. Socioeconomic data would have added valuable information, as well as nutritional information, in terms of caloric intake, nutritional balance and importantly, salt ingestion. Also, physical activity data is an important absence in this study.

We agree that this was a limitation of our study and have further emphasised the need for further investigation of such factors in such populations. Lines 313-315.

7. No reason for the higher prevalence of HBP in female is presented.

This result was rather borderline, being “statistically significant” (at p<0.05) only for systolic blood pressure and only after adjustment. We have mentioned this in the discussion, rather than entering into possible explanations that might not be justified by the data. Lines 282-283.

8. The Odds Ratios are sometimes different in the text comparing with table 1 (e.g. see the adjusted OR for age, in the abstract and table 1). A thorough revision of the results must be done. Also, in the abstract the BMI is not indicated as a major determinant of HBP, and it should be, considering that BMI has been identified as an independent determinant of HBP at these young ages in practically all related-research.

Thank you for noticing this. We have corrected the errors and checked the data.

9. In table 2, the legend indicates b) as adjusted Odds Ratio, but the data presented are Mean and Adjusted Mean differences, indicating that a parametric hypothesis statistical test was applied, supposedly the Student t test or the One-way ANOVA. This table must be clarified.

Thank you, we have corrected this.
10. Much of the identified arguments strongly limits the external validity of the research, notwithstanding its merits and indisputable scientific relevance.

We had initially proposed to present this as a pilot study, and had included in the title. At the editor’s discretion we would be willing to reinstate this, to reflect the preliminary nature and limitations of the work.