Author's response to reviews

Title: Factors associated with asthma among under-fives in Mulago Hospital Kampala Uganda: a cross sectional study.

Authors:

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Author's response to reviews:

Responses to reviewer’s comments

Title: Magnitude and factors associated with asthma among under-fives in Mulago Hospital Kampala Uganda: a cross sectional study.

Version: 1 Date: 8 May 2013
Reviewer: Paul Mullan
Reviewer’s report:

• Major Compulsory Revisions
The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical mistakes, errors in interpretation.

Comment: For readers who want to reproduce the study, the “questionnaire that was administered by the study nurse” should be an included figure.

Response: Thank you very much for this comment. A copy of the questionnaire that we used has been included as figure 1.

Comment: Pg 7. Please state where these case definitions came from. Major guidelines? Local expert consensus?

Response: Thank you for this very important observation. In this study of children aged 2-59 months, we modified the GINA (Global Initiative for Asthma) guidelines for diagnosis of asthma. The following modifications were made:
1) We excluded “chest tightness” as a symptom because it is not easily expressed by children less than five years (1).
2) We excluded peak expiratory flow measurements/spirometry because children less than five years are not able to perform these test effectively (2).
3) We also included chest x-rays to distinguish asthma from pneumonia. Pneumonia is common in Uganda and its presentation is similar to that of asthma
The case definition for pneumonia was based on “Pocket Book for Hospital Care for Children: Guidelines for the management of common illnesses with limited resources 2005” by World Health Organization (5). We also included chest x-rays and blood culture tests to aid in distinguishing bacterial and viral pneumonia (6-7).

Details on how the case definitions were derived have been included under methods section.

Comment: Pg 10. Confused by the children recruited and who these 372 were dropped from. Please either make into a figure or clarify language.

Response: We screened 986 children aged 2 to 59 months who presented with cough and/or difficulty in breathing during the study period. Of these, 614 were recruited. The remaining 372 children were dropped because; 189 (50.8%), did not fulfil inclusion criteria, 150 (40.3%), declined to participate, and 33 (8.9%) died before investigations were done.

Comment: Kappa for xray reviewers is mentioned in the methods but I did not see the kappa in results.

Response: Cohen’s kappa statistics were used to determine the degree of agreement between the primary radiologists regarding the chest x-ray findings. The primary radiologists agreed on the chest x-ray findings in 79.4% of cases (Cohen’s kappa 0.72, p=0.0000). This was statistically significant, indicating good agreement on the chest x-ray findings. We have included this information in the results section.

Comment: Pg 13, line 9: “thus reducing the role…” This and many other statements in discussion appear to state causality from risk factors identified to the outcomes tracked in the study. This type of study design can only imply association and not causality. Change wording to reflect the study design’s inherent limitations in this regard. Other examples are pg 14 line 1 (“demonstrated”). A better expression of results is pg 14 line 11 “no association…”.

Response: Thank you very much for this comment. We have revised the whole manuscript and improved on the language to indicate scientific writing.

Comment: Pg 16 last sentence. I believe you meant to write “Diagnosis” instead of “management” as the whole article was about mis-diagnosis (you were not comparing salbutamol to epi to mag… etc.)

Response: Thank you for the comment. We have changed the sentence in accordance with the reviewer’s comments. The recommendation about improving diagnosis of asthma among children with acute respiratory symptoms followed the findings of a much higher asthma prevalence compared to that from a study which looked at doctor-diagnosed asthma. Hence, further assessment on
diagnosis of asthma in this age group would contribute towards understanding some of the reasons for under-diagnosis of asthma among under-fives in Mulago hospital, which is a tertiary care setting.

• Minor Essential Revisions
Comment: The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.
Response: Thank you so much for this observation. The labels on the figures and tables have been revised to reflect the corresponding results.

Comment: OR and AOR. OR is mentioned in methods but AOR in results. Please clarify distinction or keep uniform.
Response: Thank you very much for this comment. The crude Odds ratios were determined using bivariate analysis. We then performed multivariable logistic regression to determine factors that were independently associated with asthma, a process that adjusts for any potential confounders. The corresponding confidence intervals and adjusted Odds ratios are presented.

We have revised the section on statistical considerations. We also present the results on both bivariate and multivariable analysis in table 2 to highlight all the factors that were studied.

Comment: Background: Cite Bitimwine reference more formally per journal guidelines.
Response: The citation has been revised in accordance with journal guidelines (ref 7)

Comment: Pg 7. Sentence “Children who needed…” should be after reference 23 or sounds like research > clinical priority.
Response: Thank you so much for this comment.

Upon arrival at the emergency unit, the children were triaged and potential participants identified. Through triage, we were able to identify children who need urgent care, which was provided before proceeding with enrolment. We have revised this sentence in accordance with reviewer’s comments.

Comment: Pg 7 “expert panel.” State whether these people include study authors.
Response: The panel of experts were is not part of authors of this manuscript. Their role was to review the participants’ case reports and make a diagnosis. We have acknowledged their contribution in the section on acknowledgement.

The main author participated in the meetings as a minute secretary and was responsible for documenting the proceedings of the discussions. She did not in
any way contribute to the discussions that culminated into assigning diagnoses to the participants.

Comment: Pg 11 4th line: “allergy in a child”; is this the patient or a sibling? Clarify.

Response: Thank you for this observation. The child referred to in this statement is the study participants. We have revised the statement accordingly.

Comment: Pg 12 4th line: Please add reference for 0.1% stat.

Response: This reference has been deleted because the information in this reference focus on children aged 2 months up to 12 years and was part of routine records at the paediatric unit of Mulago hospital. We have provided a more appropriate reference (ref 30) in which the study focused on children aged 2 to 59 months.

Comment: Pg 12 12th line: “asthma in the offspring” - Confusing. Offspring meaning this patient or the patient and their siblings. Please clarify.

Response: Offspring refers to the study participant. This sentence has been rephrased to clarify the meaning.

Comment: Pg 12: “regardless of the geographic setting.” This statement is too broad as the mother and child do live in the same geographic setting as well as share genetic traits. Soften this conclusion.

Response: We have revised this statement in line with the reviewer’s comments.

Comment: Pg 12: 2nd to last line: “The reverse is true in Africa.” Africa is so big and diverse that I would be hesitant to make this broad of a statement and instead state specific areas where this is true. Other instances of “In Africa” are noted elsewhere and should not be stated as this study was based in one area of one of Africa’s 47 countries.

Response: Thank you so much for this comment.

In Ghana, the comparative studies which were done among school going children showed that the proportion of asthmatics that were atopic was low compared to that in industrialised nations. However, it was noted that the prevalence of atopy among children with asthma is increasing. We have provided details in the 2nd paragraph under discussion of genetic factors associated with asthma.

Comment: Pg 15 last 6 lines: Clarify as it seems to state that the expert panel had limited access in one sense but later states that they had “full access.” Explain exactly what they did and did not have access to.

Response: Thank you so much for this observation. The expert panel did not have access to the study participants at all. They used information on case reports and results of test results to make a diagnosis. This process was guided
by the study definitions. This point has been clarified in the methods section as well as the discussion.

Comment: Pg 16 6th line: “there are no studies...”. I questioned the validity of this statement as I have come across related articles. On a pubmed search of “asthma severity AND environmental and genetic factors” there are 148 articles as of 7 May 2013 (clearly some of these are not specific to this exact topic but to say there are no articles on this topic might be inaccurate).

Response: Thank you so much for this observation. This statement was made in error and has been revised.

- Discretionary Revisions
These are recommendations for improvement which the author can choose to ignore. For example clarifications, data that would be useful but not essential.

Comment: Abstract Results: delete “representing 8% of total participants.”

Response: The abstract has been revised and only presented the most useful results. Issues such as study design, and case definitions that were used in the study have been clarified.

Comment: Pg 7 after nasal epithelium add “and removed.”

Response: This section has been revised. The nasopharyngeal epithelium was collected and stored according to the manufacturer’s instructions. A summary of the procedure of collecting nasopharyngeal swabs has been provided.

Comment: Pg 7: Please confirm it was an ultrasonic nebulizer that was used and not a pressurized baffle or electronic nebulizer.

We used an ultrasonic nebulizer. This has been clarified in the methods section.

Comment: Pg 9 : After Pakistan, add “by”

Response: The sentence has been revised in accordance with reviewer’s comments.

Comment: Pg 15 line 3: delete “only”.

Response: The word “only” has been deleted.

References

5. WHO. Pocket Book of Hospital Care for children. Guidelines for the management of common illnesses with limited resources. 2005.
