Author's response to reviews

Title: Insufficient access to oral paediatric medicines in Ghana: A descriptive study

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Author's response to reviews: see over
The Editor-in-Chief
BMC Health Services Research.

Dear Sir/Madam,

RE: AN UNMET NEED IN THE ACCESS TO ORAL PAEDIATRIC MEDICINES IN GHANA: A DESCRIPTIVE STUDY.

Thank you for reviewing my manuscript. All the comments raised have been addressed. The title has been revised. It now reads, “INSUFFICIENT ACCESS TO ORAL PAEDIATRIC MEDICINES IN GHANA”. The full response to reviewers’ comments is attached below.

I trust that the next steps in the publication process will start soon.

Yours faithfully,

Daniel N. A. Ankrah (first author, on behalf of all co-authors).
RESPONSE TO REVIEWERS’ COMMENTS

REVIEWER 1
Reviewer's report:

Minor essential revisions:
1. I have made some specific comments on the attached version of your manuscript.
2. In table 1, would it be possible to add a column showing the distance in Km between the treatment centre where the prescription was written and the hospital where the prescription was dispensed?

Response
This has been done.

3. In table 2, why are there '-' in the column labelled 'Prescription registered for oral paediatric use'? This isn't clear to me, I think a footnote explaining this would help.

Response
This has been done

Major compulsory revisions:
1. Presumably, the fact that the pharmacies that can dispense the necessary medicines are few and far between means that some children are unable to obtain the medicines? Moreover, how much of a strain on families is having to pay for medicines? Again, is it the case that a number of children will not be receiving their medicines because the family cannot afford or chooses not to buy them? I think these are important issues that you should directly address in the introduction section.

Response
The Korle-Bu Teaching Hospital (KBTH) is the most popular referral hospital in Ghana. All prescribers and all pharmacists are aware that extemporaneous medicines are prepared at the KBTH. The preparations are also heavily subsidized because the KBTH is a government hospital. For example, a 100ml suspension from Martindale in the United Kingdom may cost about £120.00 but the same is sold for £2.00 at the KBTH. The main problem is the inconvenience of having to travel long distances just to have your prescription filled. Formal courier systems are not in place to reduce the burden, and even if they were, they would be more expensive than the medicine cost.

The biggest problem we have is treatment persistence among those on long term medication. Sometimes they break treatment for a few days which may affect treatment outcomes. To partly address this, we have made available to all those on long term treatment, a mobile number to call a day before you intend to pick up a prescription in order to reduce the waiting time.

A statement has been made in the introduction section:
“This may lead to late treatment initiation among new patients and non-persistence among those already on treatment”.

2. Would it have been possible to obtain all prescriptions written for children over the study period and compare these with the prescriptions obtained? It would be interesting and important to know the rate of written prescriptions dispensed as this would have a major public health implications. If this was not something that was possible for you to do, I think you need to explain about this in the limitations section of the discussion.
Response
At this point we have missed that opportunity and would not be possible to get all prescribed medicines. It is a point well noted and a statement has been made in the limitations section.

3. The first aim stated in the final paragraph of the introduction is clear but the second aim is not. On what basis can this study make recommendations for interventions? The study is not designed to do this and it cannot achieve this. You should remove this as an aim. You can make suggestions for future research in the discussion section which may include the investigation of specific interventions but this is all.

Response
Well noted. This has been done.

4. Please explain why the cut off was children aged 9 years and under. Is this an important age in terms of children being able to take adult versions of medicines?

Response
Age 9 years was not necessarily a cut-off point. It was the oldest age we formulated medicines for. The statement has been revised and it now reads: “All prescriptions for extemporaneous oral preparations for children presented to the LPU from November 2013 were eligible for the study”.

Reviewer 2

Reviewer's report:
Major Compulsory Revisions
1. In Abstract-Results: Give data to support statements put forward

Response
This has been done

2. Abstract- Conclusion: Does not follow from results presented

Response
The statement has been corrected. It now reads: “Paediatric prescriptions including off-label medicines are prescribed and formulated extemporaneously in this setting. Steps should be taken to improve access and monitor benefit-risk profiles of paediatric medicines in order to improve treatment outcomes among children”.

3. Aim: The recommended interventions presented are not dealt with in detail. It is difficult to identify suggestions for improving access to medicines.

Response
Based on suggestions from Reviewer 1, our aim to recommend interventions needed to improve availability of paediatric medicines and reduce undue hardships to caregivers, have been dropped.

4. Method: Lines 67-69: transfer to results section

Response
Similar information already exists in the results section. Lines 67-69 (under Method) have been dropped.

General comment: The paper presents superficially the data gathered and does not describe in detail areas of concern of off-label use of medicines. Recommendations are not clearly proposed.

Response
Data for this study were collected from prescriptions forms. This paper was on access to medicines. The issue of off-label use was an observation we made. It is being tackled in another study and we did not want to go too deep in this paper.

The conclusion has been reframed and now reads:
“In conclusion, a number of paediatric medicines are being formulated in limited facilities in Ghana using adult tablets because pre-formulated paediatric medicines are not available. This creates problems for access to medicines among children. Some of these medicines are neither present on the WHO Children’s Medicines list nor registered with the FDA Ghana, emphasizing the possibility of off-label use of medicines. Steps should be taken by policy makers and all involved to improve public health among paediatric patients”.

Minor Essential Revisions
1 Keywords: include off-label use of medicines

Response
This has been done

2. Table 1: Only data at baseline is presented- update title of table to better describe content

Response
This has been corrected. The title of table 2 now reads:
“Prescribed medicines at baseline with ATC codes”.

REVIEWER 3

Thank you for the opportunity to read this manuscript- An important area for research and communication.
I do have a number of issues that I believe must be addressed and clarified before this paper is suitable for publication. These relate both to the focus and content of the paper, and also the written English expression.
1. Is the question posed by the authors well defined?
The research topic is not well defined. It is unclear if this paper is an audit and a descriptive analysis of prescriptions written for paediatric patients; or, whether this is a study of off-label prescribing; or if this is a study of aspects of extemporaneous preparations and a commentary about the lack of available paediatric formulations of prescribed medicines.
It seems to me that this may be an audit, and based on the results of this audit a number of issues have been identified- including need for formulations for paediatric patients. (Note – definition of the use of the term 'off label' needs clarity here. It seems the authors are referring to the formulation and the use of 'adult' preparations for 'young' children, rather than the use of a particular medicine in paediatrics. This should be clarified and defined for the purpose of this manuscript.)

Response
First of all, we are using adult tablets to compound medicines for a different sub-group of patients. Secondly, people have to travel long distance in search for their medicines, not because there are no pharmacists to serve them, but because the medicines are not there. If the medicines are not available, accessing them becomes an obvious unmet need that should be addressed.
Table 2 shows the list of medicines predominantly formulated. It also shows the regulatory status of the medicines. So our use of the term off-label may not be for the wrong reasons.

2. Are the methods appropriate and well described? See above - depending on a clearly stated aim- the methods need to be appropriate to achieve that aim.
Note that reference is made to the Australia PBS in terms of cost/pricing guidance. Note that the Pharmaceutical Benefits Scheme is a national subsidisation program for medicines, based on efficacy/safety and cost effectiveness criteria. While that approach does influence costs to patients/and the country it is not a price guide per se, and would not seem to be as relevant to the comment in the manuscript, unless this is comment on national medicines policy and access.

Response
In citing the Australian PBS, our intention was on best practices. This sentence has been rephrased and now reads:
“In Ghana, there are no guidelines for paediatric extemporaneous preparations in contrast to places like Australia [3], for instance. There is no particular mechanism on how the price of such products should be calculated. To make matters worse, such products are not represented on the national health insurance medicines list, and patients must pay for these medicines out-of-pocket”.

3. Are the data sound? Unclear until the terms of the study are better defined.

Response
Reviewer 1 suggested the addition of a column on Table 1 for clarity. This has been done and may address this concern.

4. Do the figures appear to be genuine, i.e. without evidence of manipulation? N/A
5. Does the manuscript adhere to the relevant standards for reporting and data deposition? Little detail provided. Note that although IRB/Ethics clearance is stated, the paper refers to collection of the patients' names. Data for research needs to have been either re-identifiable (coded) or non-identifiable.

Response
Because we were using repeat prescriptions we needed the names for identification of patients. The data we used are routinely captured at the extemporaneous preparations unit. Names of patients were anonymized before data analysis. A statement to that effect has been inserted. It reads: “The data were anonymized for this study”.

6. Are the discussion and conclusions well balanced and adequately supported by the data? As above.

7. Are limitations of the work clearly stated? Limitations are noted.

8. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? N/A

9. Do the title and abstract accurately convey what has been found? No, as discussed above.

Response
With our explanation in comment 1 above, in addition to the suggestion to insert a column on Table 1 showing the distances travelled by patients to access their medicines, we hope that the message is clearer now.

10. Is the writing acceptable? The English expression does need editing before this work is suitable for publication.

Response
This manuscript was edited by Editage, a division of Cactus Communications before submission for publication. However, based on your recommendation, the manuscript has been re-submitted to Edanz for English editing.