Author’s response to reviews

Title: Intestinal Parasitic Infections In Children Presenting With Diarrhoea In Outpatient And Inpatient Settings In An Informal Settlement Of Nairobi, Kenya.

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Author’s response to reviews: see over
To The Editor-in-Chief

BMC Infectious Diseases

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Dear Editor,

I am writing to re-submit our enclosed revised manuscript entitled “Intestinal Parasitic Infections In Children Presenting With Diarrhoea In Outpatient And Inpatient Settings In An Informal Settlement Of Nairobi, Kenya.” for publication in BMC Infectious Diseases journal. The paper demonstrates that intestinal parasitic infections are common in children aged five years and below, presenting at outpatient clinics and those admitted in paediatric wards in urban slums of Nairobi, Kenya. The main parasites isolated being Cryptosporidium spp, E. histolytica and G. lamblia.

All the issues raised by the 2 reviewers have been addressed accordingly as per the uploaded file above, also detailed below.

REVIEW COMMENTS/RESPONSE FOR MS: 4148707069141637
Intestinal Parasitic Infections In Children Aged Five Years And Below In An Urban Informal Settlement Of Nairobi, Kenya.

REVIEWER 1

- There are punctuation errors throughout the manuscript and need to be corrected. This has been corrected.

The authors should be consistent with use of the following terms in the manuscript:

- “intestinal parasitic infection” or “intestinal parasite infection”- We chose to use intestinal parasitic infection(s)
- “urban informal settlement” or “urban slum”- We prefer urban informal settlement/s
- “Polyparasitism” or “multiple parasitic infection” or “co-infection” or “mixed
parasitic infection” or “mixed intestinal infection” - We have used polyparasitism

ABSTRACT:
Results: Correct “intestinal parasites infection was” to “The Prevalence of intestinal parasitic infections was….” - Done

INTRODUCTION
First paragraph: correct “impair cognitive functions” to “impaired cognitive functions” - Done
Third paragraph: Correct typographical error ‘18)’ - Done

MATERIALS AND METHODS
Data processing and analysis:
Remove the duplicate "for analysis" at the end of second sentence.- Done

Results
Last line: Remove “up to” - Done
b) Cryptosporidium spp.
Second line: remove ‘more than’ - Done
c) Giardia lamblia
First line: modify: “had 3 times” to “had approximately 3 times” - Done

- Discretionary Revisions:
It will be interesting to include a descriptive + comparative table on the presenting symptoms and signs of patients - We already have 5 tables in the manuscript and we plan to include the table in the next paper

ABSTRACT:
Methodology:
First line: Remove ‘prospective’. - Done
In the last line, mention direct test also. - Done

Results: The first line should mention the overall prevalence of intestinal parasitic infection in the study population followed by the comparative analysis. - Done
For comparison of prevalence among two or more groups, it is better to use the p values of multivariate analysis than the p values of univariate analysis. This also applies to the discussion section. - This has been incorporated throughout the document

RESULTS
In table 1 under the parasite infection, add information on ‘any’ and ‘none’. - This has been done and incorporated in table 1.

Title misrepresents the study, which is a comparison of two groups (in patients and outpatients). Since this study is not based on a representative sample randomly taken from the population of the specified slum; therefore, the title should be modified accordingly. - We have changed the title to read “Intestinal parasitic infections in children presenting with diarrhoea in outpatient and inpatient settings in an informal settlement of Nairobi, Kenya

The odds ratio should be interpreted uniformly throughout the manuscript as there are inconsistencies. - This has been addressed and have used “less likely or more likely” accordingly.

INTRODUCTION
Third paragraph:
To make the point clear, please rephrase the sentences "In spite of
this……………………and other antiseptics”.- The sentence has been rephrased to read “Less attention has been given to .......antiseptics.

Last paragraph: Reference is missing for the 'little published data'. Either the authors should give the reference(s) to the study/studies or write ‘To our knowledge there is no information available…..’- This has been put into consideration and adopted your suggestion.

Last sentence, the study objective should be modified in line with the comments Above- This has been done, mentioning the inpatients and outpatients.

MATERIALS AND METHODS
Study site and patients:
Since all the children presented with diarrhoea, were they not looked for bacterial or viral infections, need to be mentioned somewhere?- For the purposes of this project, we only did the parasite profile for all the samples.

Did the patients recruited from the hospital belong to the same slum area? The authors say that the patients were recruited from the selected outpatient clinics located in Mukuru slums. How this sample was representative of that slum? It would be informative if they could give a total number of outpatient clinics and then why they selected three among those (randomly?). The three outpatient clinics from which patients were recruited are the only public dispensaries in Mukuru informal settlement, that are open to the public for general treatment, hence this is a representative of the study area. The patients who are seen in these outpatient clinics and require admission are normally referred to Mbagathi district hospital, which serves patients not only from Mukuru but other informal settlements, and low income areas in Nairobi. The inpatients recruited from the study were from Mukuru informal settlements, though it is important to note that most of the informal settlements border each other, and the living conditions are almost similar, with poor overcrowded housing, poor sanitation and lack of clean water among others..

The children admitted to the hospital must have some serious issues requiring hospitalization? Why were they compared with the patients coming to the outpatient clinics? This needs to be discussed.- This is the initial part of a larger project that seeks to establish genetic diversity of Cryptosporidium and Giardia, and compare the differences between inpatients/outpatients, HIV positive and HIV negative in the study area, and we were recruiting patients aged 5years and below, who were presenting with diarrhoea, either as the only complain or diarrhoea among other symptoms.

What are the inclusion and exclusion criteria (if any)? – Children from Mukuru aged 5 years and below, and presenting to the participating clinics/hospital with diarrhoea.

Data processing and analysis:
Rephrase the sentences for clarity:
"Frequencies,proportions……………………correlates of parasitic infection.”- This has been rephrased

RESULTS
Second paragraph: Check the numbers in the statement and rectify if incorrect:
“The prevalence of intestinal parasites was 613/1577(38.9%), among children from outpatient clinics and 113/535(21.1%) among those admitted in hospital”. 
Rectify the errors in numbers and corresponding percentages: “Other parasites isolated include *I. belli*, 35 (5.7%), *A. lumbricoides*, 26 (4.24%), *H. nana* 12 (1.96%).” – The wrong percentages have been corrected

Among inpatients, *I. belli* is also isolated but not mentioned? and it should be. This has been corrected

In the last paragraph regarding the mixed parasitic infections, either the information be put in the table 1 or it must be mentioned as “Data not shown”. - We have clarified that the details of data on polyparasitism is not shown in this paper.

Associations of patient characteristics and infection with 3 common parasites

a) *Entamoeba histolytica*

Remove the repetition: “Children within 37-48 months age group were four times likely to get the infection than those below 12 months old (OR, 4.02,CI,2.57-6.29, p<0.001)” – Repetition has been removed

Rephrase the second last line: “The odds for *E. histolytica*……………..”- We have rephrased this to read ‘The HIV seropositive children were more likely to get infected……

Last line: Put the p-value of multivariate model instead of univariate analysis.- This has been corrected to include p-values from multivariate analysis

b) *Cryptosporidium spp.*

Second sentence: correct/rephrase “the highest risk” to interpret the odds ratio.- This has been rephrased accordingly

For patients aged 37-48 years, the odds ratio is inverted, therefore should be interpreted separately and may be discussed in the discussion.- This has been addressed.

Immunosuppression and infection with parasites

This section is a repetition of the information given already; therefore, needs to be deleted.- This has been deleted

Discussion

Second paragraph: IPIs should be unabbreviated- Done.

Adjusted odds ratios should be given instead of crude ones- We have done this to give Adjusted ratios instead of Odds ratios.

Third paragraph: “It is likely that most of the children admitted in hospital may have been treated elsewhere in outpatient clinics in the community before being admitted in hospital”. Was information on past medical history not obtained for these patients? We have data to show that most inpatients were put on treatment immediately upon admission, or had been treated before, but was not included in this paper

Fourth paragraph: “Similar findings have been reported in Uganda with prevalence of 73.6% and 5.9%, in HIV positive and HIV negative children respectively [47]”.- The percentages and the difference in percentages are not similar to the current study and should be properly discussed. This was noted and has been rephrased and discussed appropriately.

“*Cryptosporidiosis was highest among children 13–24 months of age*. Add the
comparison group.- We have added the comparison group which is 12 months and below.

Fifth paragraph:
Second line: Correct the “whose prevalence among inpatients’’ to “whose prevalence among outpatients’’- This has been corrected.

Sixth paragraph: “G. lamblia was common among both outpatients and inpatients (5.8% and 1.3%) respectively’. No, As per table 2c, Giardiasis was significantly lower in inpatients- This was noted and corrected.

Last paragraph
“In conclusion…….” If the sample is not representative then the results can not be generalized. This needs rephrasing accordingly- As explained above the sample is representative of Mukuru informal settlement, which is one of the largest informal settlements in Nairobi as patients were recruited from the three only public dispensaries open to the public for general treatment ..

REVIEWER 2

- Standardize out-patients or outpatients, in-patients or inpatients- This has been done and adopted outpatients, inpatients

- Abstract, second last line, to exclude ‘and’- Done

- Page 4, second line typo error 18)- Corrected (18)

- Page 4- All kids were admitted with diarrhoea or other cause?- As explained above, recruited children may have presented either with diarrhoea as the only presenting symptom, or with diarrhoea among other symptoms, our main interest was diarrhoea.

- Page 6, second line, exclude previously.- This has been done to read “...as described by Cheesbough)

- Page 6- Results, 1st line- upto 5years and below- We have agreed to use 5years and below for uniformity to include all children aged five years and below.

- Page 6- Results, 2nd paragraph- interquartile range (IQR) Typo error corrected

- Page 9- giardiasis not associated with HIV status. The reports regarding this issue are different from different studies. However most studies in developing countries have concluded that this protozoan does not present relevant expression in the HIV population (e.g Cardoso VL et al., 2011, Iqbal et al., 2012, Getachew et al., 2004). Our study similarly did not show significant association between HIV and giardiasis.

- Page 11, Discussion line 8- Comparing with total parasitic infection or just E. histolytica....- The quoted study(Gatei et al) reported a wide range of intestinal parasites from the studied children, and just like in our study, The three(Cryptosporidium spp., E. histolytica and G. lamblia were the most common parasites reported, among others, hence the comparison.

- Page 12- What is IPIs- Intestinal Parasitic Infections, this has been unabbreviated for clarity

- Page 12- Typo errors ‘%..p and ]’- Corrected

- Page 12- The prevalence in HIV negative patients in China [48] was 3.0%, this has been included in the text.

- Page 13- Typo errors “p and )” – Corrected

- Page 14- Giardia common in both outpatients and inpatients at 5.8% and 1.3%.....- This has been rectified and discussed accordingly to show that Giardia was more common among outpatients than inpatients.
As such this paper remains to be of interest to a broad readership including those interested in infectious diseases in children.

We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal. All authors have approved the manuscript and agree with submission to *BMC infectious diseases*. The authors have no conflicts of interest to declare.

Thank you for receiving our revised manuscript, and we look forward to hearing from you at your earliest convenience. Please address all correspondence to cmkathure@yahoo.com.

Sincerely,

Cecilia Mbae