Author’s response to reviews

Title: Factors associated with tungiasis among primary school children: a cross-sectional study in a rural District in Rwanda

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Author’s response to reviews:

Kigali, Rwanda
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Dear Editor-in-Chief:

On behalf of our study team, I would like to submit a revised version of the manuscript PUBH-D-19-01149R1 “Factors associated with tungiasis among primary school children: a cross-sectional study in a rural District in Rwanda”. We would like to thank you for the opportunity to revise our article and appreciate the positive points cited in your letter. We have responded to the reviewers’ comments below.

We hope the concerns raised by the reviewers have been addressed adequately and that the manuscript will meet your approval for publication in the Journal.
Looking forward to hearing from you.

Sincerely,

Jerome Nsanzimana  
Butare University Teaching Hospital, Rwanda  
Email: ihozauwacu@gmail.com

Reviewer 2’s Comments

Page 3-4: The new part with general information about the biology, development and transmission which you added in the section "Background" has to be rewritten. There are some imprecisely and/or unclear information. Some sentences are grammatically incorrect. The structure is confusing; maybe you should try to start with explaining that the life cycle consists of an on-host and an off-host part. Then you describe the on-host part clearly, then the off-host part. You speak about the biology in a very detailed way. Is this relevant for your study? I think you should focus more on the pathology so that the reader can imagine why it has an impact on the school performance of affected children. Describe symptoms like itching, pain, impairment of walking... acute and chronic pathology. How long remains the flea in the epidermis? Please indicate co-infections like tetanus, gangrene or even HBV. (You describe some aspects later in the method section. I think I would fit better to give the information in the section background).

Authors’ answer to the comments

Thank you for the relevant comments and suggestions. In the revised version of this manuscript, the background section has been rewritten. Additional information and edits suggested were considered.

Reviewer 2’s Comments

The unfertilized eggs stop developing while those fertilized progress to development and become larvae 1 within 6 days (-> Leave this out because it is not relevant/interesting: The unfertilized eggs stop developing while; the supplement that it is larvae 1).

Authors’ answer to the comments

We appreciate this comment and have considered it when revising the background.

Reviewer 2’s Comments

These larvae feed on organic material in place (-> Please add information about the favored places for larvae to feed and develop like cracks and gaps in houses, shady places etc).

Authors’ answer to the comments
This comment was considered when revising the background

Reviewer 2’s Comments

Female of sand flea enters the host through the skin ("enters the host through the skin" could mean everything. Does the flea enter the body until the gut? Better: female sand fleas penetrate into the epidermis of its host) in unfertilized stage and copulation with the male occurs at that level (what level do you mean? Better: Copulation with the male sand flea occurs on the host after penetration). (Please add an appropriate reference).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

The fertilised (choose if you write fertilised or fertilized) female become hypertrophic (why? What happens? intestines grow, eggs mature) and expel eggs (to where? to the outside). (Please add an appropriate reference).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

The development of larvae 1 to larvae 2 takes a minimum of one day, and this larva will start pupation stage within 4 to 10 days or more (Leave this out because it is not relevant/interesting: The supplement that there is larvae 1 and 2).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

The adult fleas developed inside the pupation within 9 to 15 days (it should read: develop).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

Once the adult female fleas reach the skin of the host begin to suck the blood within 5 minutes and prepare to penetrate (it should read: Once the adult female fleas reach the skin of the host they begin to suck blood ...).

Authors’ answer to the comments
The revised background took into consideration of this comment.

Reviewer 2’s Comments

Two thirds of the body of the flea is inside the skin after 24 hours of penetration, while complete penetration will be after 40 hours (-> Leave this out because it is not relevant/interesting: Two thirds of the body of the flea is inside the skin after 24 hours of penetration).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

By feeding, there is enlargement of the flea (-> the enlargement of the flea is not due to feeding alone, see above), which is complete on the sixth day and then the eggs are expelled (-> for a period of several days).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

Ejected eggs reach the ground and are developed into larvae, pupae and then immediate adult form (-> it is not true that they develop immediate to adults - larvae and pupae can last for a long period, up to months until they hatch to adults under good conditions/circumstances).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

The life cycle of sand flea is partially or totally complete in human and domestic or wild animals depending on the tropical surroundings (-> it cannot be true that the cycle is totally completed in humans or animals as there is an on-host and off-host part in the life cycle of sand fleas! Obviously the off-host part takes outside the host).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

This risk is increased in some countries like Uganda, where domestic animals such as goats, sheep, and
pigs are kept in the same house with family members over night for preventing them to be stolen (-> it would be nice to add information in this regard about the situation in Rwanda; do people there keep animals inside their house?).

Authors’ answer to the comments
The revised background took into consideration of this comment.

Reviewer 2’s Comments

Sand flea is among the parasites that can complete its life cycle when the person is sleeping (-> this sentence is very wired. of course, a complete life cycle does take a lot of more time! You are speaking about the place of transmission and not about time. Please make this clear).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

Afterwards, eggs are transported to the fissure and cracks when the floor is clean (-> you mean cleaned?).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

The adult sand flea emerges from pupae and penetrates the skin of the person when he deposes the naked feet on the ground (-> if you want to keep the right order, you first have to speak about the larvae which feed from the organic material in the fissures and cracks).

Authors’ answer to the comments

The revised background took into consideration of this comment.

Reviewer 2’s Comments

Concerning the programs aiming preventing at treating tungiasis: You cited two publications, but you did not write any word about the content.

Authors’ answer to the comments

We appreciate this comment. In a revised manuscript we provided two references related to the current programs aiming at preventing tungiasis in Rwandan setting. However, the information on tungiasis remains scarce in a Rwandan context because of lack of publications.
What do you mean with "over time"?

Authors’ answer to the comments

In a revised manuscript “over time” was replaced with “during the study period”

Reviewer 2’s Comments

Methods, setting:
it should read: primary schools located in a remote rural area ...

Authors’ answer to the comments

We appreciate this comment. This was addressed accordingly

Reviewer 2’s Comments

Methods, setting:
All three schools had cemented floors and walls. (-> this information is a contradiction to the information you gave just before. Please give more information about the condition of the floors. Did they have a lot of fissures, cracks and holes?)

Authors’ answer to the comments

We thank you for raising up this comment about the characteristics of schools’ environment. We have mentioned the lacking information in a new version of the manuscript.

Reviewer 2’s Comments

Methods, data collection:
... children, who were included in the study were clinically assessed by inspection on the whole body to ascertain whether they had skin lesions suggesting tungiasis infestation. (-> is this true? How did you observe the whole body? In a classroom? Were other pupils present by that time? Did the pupils take all the clothes off?)

Authors’ answer to the comments

Thank you for this comment. A thorough assessment for tungiasis infestation was done by inspection of any abnormal lesions on the body during home visits of children included in our study. However, since all lesions were located on feet, we had already noticed these lesions when we met children at schools for the first time.

Reviewer 2’s Comments

Methods, data collection:
loss of toenails and deformed nails as signs of chronic tungiasis...
This comment was addressed. We moved the clinical information related to tungiasis to the background section, as suggested.

Reviewer 2’s Comments

Methods, data collection:
children who had any body part embedded by sand flea but without clinical manifestation were not considered as cases. (¬) this does not really make sense as each embedded sand flea causes clinical signs sooner or later. In a very early stage (in the first few days) an embedded sand flea may not cause any symptoms but in the course of time the show a clinical manifestation. So, you did not count children with early stages as cases? Even if clinic will have developed later? Please, indicate how many embedded sand fleas were necessary for the case definition. At least one or more?)

Authors’ answer to the comments

We thank you for this comment and apologise for providing a confusing information regarding our diagnostic approach for tungiasis in this study. In a new version of the manuscript, we have elaborated on the case definition for tungiasis in order to avoid any confusion. Any suspicious lesions for tungiasis were taken into consideration during our assessment even at early stages of infestation.

Reviewer 2’s Comments

Methods: Outcome and independent variables:
In a Rwandan educational system, secondary school last 6 years. After that, a student may pursue studies in undergraduate and postgraduate program... (¬) Leave at least the last sentence out, because not really relevant).

Authors’ answer to the comments

Thank you for the comment. We have addressed it accordingly.

Reviewer 2’s Comments

Methods: Outcome and independent variables:
Situation at school was assessed through school attendance (regular attendance, missing less than two days per week, missing more than two days per week). (¬) please leave the information in brackets out. Otherwise it is doubled).

Authors’ answer to the comments

We appreciate this comment. We have taken care of deleting the doubled information.

Reviewer 2’s Comments

Results:
…those whose families shared houses with domestic animals, especially goats... (¬) very interesting. Are there studies about tungiasis in goats?)

Authors’ answer to the comments
Thank you for raising up this comment. We apologise for the confusion regarding our description of study population, which caused some misunderstandings. In this piece of sentence, we wanted to highlight the highest proportions of children infested with tungiasis, which were found in families sharing houses with goats compared to other domestic animals (pigs, cows, hens etc.) (see Table 1). In a revised manuscript, we removed “goats” to avoid any confusion.

Reviewer 2’s Comments

Comparison with other studies:
- Poor hygienic and housing conditions as major predictors of tungiasis infestation were echoed by other authors. (-> the content of this sentence is found in the sentence before and after. So, it is a doubled information.)

Authors’ answer to the comments

We appreciate this comment. The doubled information was deleted.

Reviewer 2’s Comments

Comparison with other studies:
Increasing body of literature... -> what does this mean?

Authors’ answer to the comments

This comment was addressed in a revised manuscript.

Reviewer 2’s Comments

Conclusion:
it should read: ...including dirty feet, wearing dirty clothes, ...

Authors’ answer to the comments

Thank you for the relevant comment. We have addressed this

Reviewer 4’s comments

The authors continuously refer to incidence (number of new cases divided by number of people at risk) as prevalence (total number of cases in a population divided by the total population). This should be corrected.

Authors’ answer to the comments

Thank you for the comment. In our study we considered the prevalence [the proportion of a population that has the condition (here: tungiasis) at some time during a given period (in our study: a 3-month period July-October 2018], which includes people who already have the condition at the start of the study period as well as those who acquire it during a given period. We did not use an incidence, which is a measure of only new cases arising in a population over a given period.
Regarding the population at risk of tungiasis, we considered the school children, who have been sampled and included in our study. The size of this population was used as a denominator when calculating the prevalence of children infested with tungiasis (children already having tungiasis at the start of our study plus new cases who acquired it over a study period).

Reviewer 4’s comments

Page 3: If the presented results are based on multivariable logistic regression, then present the adjusted odds ratio as AOR.

Authors’ answer to the comments

Thank you for the comment. This was addressed, as suggested.

Reviewer 4’s comments

Line 20-40: The description of the statistical techniques is cumbersome. The tow-step analysis is not clear. The authors said, "When carrying out logistic regression, two models were created based on the type of variables."

Please revise this part. You may replace line 20-40 with the following:

The association between independent variables and outcome was analysed using logistic regression. Bivariate logistic analysis was used to determine the strength of association between independent variables and outcome at the first instance. Variables with significant association in the bivariate analysis were included in the multivariable logistic regression. The independent variables were grouped into two categories- potential factors leading to tungiasis such as dirty feet or clothes and consequences of tungiasis such as poor performance at school. Two models were formulated based on the two types of variables, the results were presented as adjusted odds ratio (aOR) and 95% confidence interval (CI).

Authors’ answer to the comments

We incorporated edits in a revised manuscript, as suggested.

Reviewer 4’s comments

Page 12 Line 24: This study on prevalence and factors....

The results presented in this study were not based on prevalence, the authors did not present any prevalence rate of tungiasis rather they presented incidence rate of tungiasis. If they want to present prevalence, they will need to adjust for the population of the study area.

Authors’ answer to the comments

Thank you for the comment. However, we believe that the prevalence calculated in this study is reflecting the proportion of school children, who had tungiasis among children sampled for our study, i.e. the number of children with tungiasis at the start of our study plus the number of those who acquired it during the study period divided by the total number of all children included in the study. We were not interested in calculating the prevalence of tungiasis among the population in the study area,
which was out of the scope of our study. Our study only covered three schools located in a rural district in Rwanda.

Reviewer 4’s comments

Page 13 line 20: 87/384 (23%). This is not a prevalence

Authors’ answer to the comments

Thank you for the comment. The proportion provided considered the old cases of tungiasis found in the beginning of study as well as the new cases, which occurred during the study period. Thus, we believe that this proportion reflects the prevalence of tungiasis in this specific population of school children included in our study.

Reviewer 4’s comments

Strengths and limitations could come at the end of the discussion. Also, there is no need to have subheadings for "Strengths and limitations", and "Comparison with other studies" in the discussion

Authors’ answer to the comments

We made the suggested corrections accordingly.