Author's response to reviews

Title: Parasite threshold associated with clinical malaria in areas of different transmission intensities in north eastern Tanzania

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Author's response to reviews: see over
Cover letter

1st October 2009

Dear Editor,

Re: MS 2021230647268477.
Attached is a revised manuscript entitled - Parasite threshold associated with clinical malaria in areas of different transmission intensities in north eastern Tanzania.

We have gone through the comments of the reviewers and responded to the comments of our reviewers accordingly. Some of the comments from reviewer3 were already covered in the previous two versions.

With this letter, we attach our responses.

On behalf of all authors,

Bruno P. Mmbando

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Enclosure:
Responses to reviewer
Version: 3 Date: 29 September 2009
Reviewer: Jean Gaudart

Reviewer's report:
Since the first submission, the manuscript has been significantly improved.
- Major Compulsory Revisions: None
- Minor Essential Revision: None
- Discretionary Revision: as the model 3 seems to be the best one, Authors should provide more results for this model, particularly for tables 1, 2 and 3.

Response: Table 1 and 2 was aimed at simulation and AICs, respectively, to compare model 1 and 2 as well as with the classical model (table 2). Model 3 is extension for model2 where age is considered as a continues variable. So, we included results of model3 in figure 4. Finding specificity and sensitivity for model3 (table3) will be very interesting, but not covered in this paper.

Referee 3:

Minor revisions

The authors could give the number of previous malaria attacks before the study (if they have the data) per age groups in order to confirm the theory of acquisition of immunity in the two strata highlands and lowlands of Tanzania.

Response: Unfortunately we don’t have previous data, but the pattern is shown in Figure 1 of this manuscript.

Page 5: Model (2): the explanation ?where pi, ?> 0, ? and ? is slope and intercept parameters.? Is not clear. The authors should reformulate

Response: This was also raised and corrected in the previous version.

Page 5 last sentence : did the authors mean: ?where the joint distribution of such n observations with probability of occurrence ?i ,and yi a realization of a fever in individual i = 1, . . . , n, is?

Response: The phrase containing this sentence was also revised in the previous version.

Page 6: Estimation of threshold by regression second sentence ? change testing to tested

Response: The phrase containing this sentence was also revised in the previous version, and now it reads “..., and then test if there is significant difference in the slope parameter”.

Page 6: Estimation of threshold by regression. Could the sentence be: ?If we let the mean age of group j be Aj , j = 1, . . . , J, and assume ? to show a similar trend as parasite rate shown in Figure 1, which was also shown elsewhere [12], and A?j be the mean age squared of group j, then ? can be modeled as a function of Aj and A?j with parameters ? = (?0, ?1, ?2)?.

Response: This is now corrected as suggested.
Page 8: In a statistical model where the estimates of parameters are unknown, the MSE is a random variable whose value must be estimated.

Response: This is now corrected and it reads “The MSE is unknown and can be estimated by a sample mean.”

Page 8: Last sentence: The authors write that model(2) was doing well in almost all age groups? but this is not the case for lowlands in the 4-6y age group where it is model (6) which have a better AIC and in the highlands in the 0-1y age group with model (1).

Response: This was also raised and was well discussed in the previous version

Page 9: Sentence before the last paragraph: Change ?There was more or less similar OR in the highlands..? to ?There were more or less similar ORs in the highlands..?

Response: This is changed as suggested

Page 10: The following sentence is not understandable ?The acquired malaria immunity varies with the level of exposure to parasite; hence individuals living in endemic areas tend to acquire immunity sooner than those in hyperendemic areas.? Especially in the light of the previous sentence which seem to mean the opposite. The definitions of endemity usually accepted are:

? Holoendemic: transmission occurs all year long
? Hyperendemic: intense, but with periods of no transmission during dry season.
? Mesoendemic: regular seasonal transmission
? Hypoendemic: very intermittent

Did the authors mean ?holoendemic? rather than ?endemic??

Response: The word “endemic” is now changed to “holoendemic”

Discretionary revisions

Page 2, last sentence: change considerable to considerably

Response: Changed as suggested.