Reviewer’s report

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

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Reviewer: jean Gaudart

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I. Generalities:
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The presented work aimed to find a threshold of parasite density associated with fever.

As the author know, the literature on the subject is already significant. However, the authors present an interesting approach, using different statistical models and simulations to estimate parameters.

Nevertheless, there are many points to clarify, particularly the different models.

II. Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached):
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1/ the aim of this work was to find a threshold of parasite predicting fever. Fever is defined as axillary temperature >= 37.5°C. How this fever has been defined? it is not clear that this threshold temperature is adequate to define a fever. The choice of this threshold will modify the parasite threshold.

2/ in the “Method” section, subsection “Parasite threshold models formulation”, sub-sub section “threshold model”:

2.1/ The definition of alpha seems to be wrong. Indeed, the probability of clinical malaria in individuals with parasite below tau is F(alpha), not alpha.

2.2/ the function F() is not defined.

2.3/ Statistical models 1 and 2 have to be rewritten. Indeed, it seems that these models are logistic models with a noisy parameter tau.

In the first model, the parasite density P is defined as a binary variable.

In the second model, the parasite density P is defined as a quantitative truncated variable.
Logit (gamma) = alpha + beta P
This formulation is preferable.
Note that if P = 0 then logit(gamma) = alpha.

2.4/ For parameter estimations and inferences, it is not necessary to translate the parasite density P; ie, use pi (where P is a quantitative truncated variable) instead of (pi-tau).

3/ in the “Method” section, subsection “Parasite threshold models formulation”, sub-sub section “estimation of threshold by regression”:
3.1/ Here are presented another cofactor (age). Please write models as logistic regressions (see 2.3). Furthermore, this logistic formulation will introduce a basic probability depending an age, which is a classical point.
3.2/ It is not clear why authors used means of age group instead of individual ages. Please clarify.
3.3/ Note that the function tau = theta0 + theta1*A + theta2*A^2 is still a linear function, over the parameters.

4/ in the “Method” section, subsection “Simulation studies”:
4.1/ “the simulated samples were multiplied by 40”. Please argue.
4.2/ there are confusing notations: between pi and gammal as well as xi and pi.

5/ in the “Result” and “Discussion” sections:
5.1/ the numbering of the models is very confused: why 8 models? Only 6 are defined?
5.2/ As the model 2 used a quantitative truncated variable, and then used more information than model 1 (with the same number of parameters), information criteria will be obviously better for model 2 than model 1.

III. Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct) :

1/ in the “Result” section, page 9 line 24: “prevalence of of fever”

IV. Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore) :

1/ In order to compare different diagnostic method, authors should use the Diagnostic Odd Ratio (DOR)
2/ why did not you used the ROC curves?

Level of interest: An article of limited interest
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests