Reviewer's report

Title: Quantitative assessment of behavioural interactions between humans and mosquitoes: Application to measuring the protective effectiveness of insecticidal nets in Tanzania

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Reviewer: Kim A Lindblade

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General

Killeen et al. have written an interesting article presenting a model to estimate the effective protection from mosquito bites provided by ITNs. The authors report two objectives for the model: the first is to compare biting patterns before and after ITNs were made available through social marketing programs to determine whether changes in the time or location of bites are responsible for a lack of impact of ITNs on community-level transmission, and the second is to evaluate new vector control strategies rapidly and cost-effectively. The former objective seems clear and the model and data support its utility (although I have some questions below). While there were significant differences between the two time points presented here with regard to the peak biting time and mean biting density, the protective effectiveness of ITNs in reducing exposure to mosquito bites was similar.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The second objective of the model suggested by the authors is to rapidly evaluate new vector control strategies. I can understand how this method would assist in evaluating protective interventions that are specifically associated with certain times of day (such as topical repellents, IRS and insecticide-treated clothing) but I am unclear as to how this method be appropriate for larval control or other interventions that would presumably reduce overall biting density. I would think that the traditional methods of comparing biting or indoor resting densities between areas where the intervention has been applied and where it hasn’t would provide the same information.

2. The authors have conflated the terms “coverage” and “adherence” and this causes the reader some confusion when it is reported that “coverage” of nets is approximately 75% of the population in the area, but the model assumes that “coverage” (actually adherence or deployment) is equivalent to the proportion of people sleeping at that time. These terms should be separated and defined.

3. I have some confusion regarding equations 2 and 3. In equation 2, the risk is equal to the sum of the hourly hazard (biting rate) discounted by 1 minus the coverage (proportion sleeping) times the protective efficacy. Equation 3 has the hourly hazard calculated as a sum of the products of the outdoor and indoor biting rates multiplied by the proportion of people outdoors and indoor sleeping, respectively. Doesn’t equation 2 discount outdoor biting by the protective efficacy of nets? Isn’t R really:

   \[ R = \sum Ot (1-St) + \sum It St (1- Ct P) \]

As the model currently stands, the risk for net users during hours when not everyone is asleep is underestimated because their outdoor exposure is also discounted by net efficacy. This falsely increases the PE slightly.

4. If ITNs confer a community-effect by reducing the overall density of mosquitoes, the model will result in a reduced PE. This can be shown by reducing both indoor and outdoor biting rates by the same proportion. The resulting PE is lower. Therefore, this model may underestimate protective effectiveness if there is sufficiently high coverage with insecticidal nets to achieve a community effect. This should be discussed as a limitation of the model.

5. Please explain how the result that mosquitoes would encounter a potentially fatal ITN on 42% of all attempts to feed upon humans was calculated (just before discussion).

6. In the discussion, it is said that the approach described in the paper also elucidates the impact of ITNs on
community-level transmission. It is not clear to me how the method achieved this. Please elaborate.

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. Page numbers would have been helpful for comments.

2. In the Results section of the abstract, it is said that ITNs consistently conferred >70% protection against exposure to malaria transmission, regardless of net coverage. This is a bit confusing because net coverage per se was not entered in the model; the authors could please clarify what is meant by this phrase.

3. After the section titled, Estimating the personal protection provided to users by bednets, there are numerous errors and careful copy editing should be done. Line 2 of the first paragraph has â€˜specificallyâ€™ written twice. The 6th line has the phrase, â€œ...the has terms hazard,â€ that doesnâ€™t make sense. â€˜Pseudo-equationâ€™ should be plural or have a â€œtheâ€ before classical, and it appears that there is a â€œtoâ€ missing before imply. In the next lines, it says that â€œhazard (H) of malaria transmission, measured as entomological inoculation rate measured by outdoor human landing catchesâ€ does not seem correct. Further on, H is defined loosely as biting activity without consideration for infection rates of mosquitoes. Second, it is measured both indoors and outdoors.

4. Equation 5 should have the subscript b added to the RR.

5. Just before equation 7 the sentence, â€œ(Psleep) can thus be calculated by the risk incurred during these hours by the total risk.â€ Shouldnâ€™t that be divided by the total risk?

6. Figure 1 has 14 time intervals on the x axis but only 13 time period labels. Figure 3 is correct with 13 time intervals and 13 labels.

Discretionary Revisions (which the author can choose to ignore)

1. I would suggest that the data (Ot, St and It) used to calculate the estimates of PE, Psleep, etc., be provided in the form of a table. This will allow readers to follow the equations and ensure they are understanding the model.

2. The paper uses a narrow interpretation of net effectiveness. Effectiveness is apparently defined as the reduction in exposure to mosquito bites afforded by fully insecticidal bednets when deployed and used properly. Effectiveness is generally more broadly defined as the typical impact on reduction in exposure to mosquitoes and will be affected by adherence and net efficacy (which is affected by the amount of insecticide on the net). The definition used by the authors is fine for the purposes of comparing the effect of nocturnal biting patterns on ITN effectiveness over time, but it is not appropriate for conclusions such as â€œITNs remain highly effectiveâ€ when changes in only one factor (biting pattern) have been assessed. I would suggest that the authors define their meaning of effectiveness and clarify that it does not take into consideration changes in adherence over time and the efficacy of non-insecticidal nets.

3. The 80% efficacy figure comes from experimental hut studies â€œas the nets in Kilombero are largely untreated nets, what is a more reasonable figure for efficacy of untreated nets?

4. I am unclear as to why the village of Namwawala has been singled out in the Methods â€œStudy area section as it does not appear elsewhere in the methods.

5. In the Results section, Figure 1 for 1997 is described as, â€œbiting activity continued and increased all the way up until dawn when activity surged again as previously described.â€ I would not describe the graph in that way as biting rates appear to have steadily decreased after the early evening peak until around 5 am when there was the surge.

Which journal?: Not appropriate for BMC Medicine: an article whose findings are important to those with closely related interests and more suited to BMC Infectious Diseases
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.