Reviewer's report

Title: Modeling the public health impact of malaria vaccines for developers and policymakers

Version: 4 Date: 16 December 2012

Reviewer: Hope L Johnson

Reviewer's report:

Minor Essential Revisions
The authors have made very good improvements to the manuscript. In general the comments to follow are focused on: a) ensuring the language and concepts described are more concise and comprehensible for the non-vaccine specialist readership of this journal; and b) to further clarify the function and limitations of the model and how the conclusions from the demonstration analysis should be interpreted. Detailed comments are provided below.

1. Abstract:

1.1 Background:

1.1.1 Need to clarify what types of “model-based estimates” are needed and what types of “decisions” they will inform.

1.1.2 Need to clarify the “complexity”, “results” and “non-specialists” referred to.

1.1.3 Re-state the objective to demonstrate the functionality of the MVM which includes dimensions (provide examples) critical for developers and policymakers. Use of language such as “tailored to the needs of developers and policymakers” is not sufficiently comprehensible for non-vaccine readers.

1.2 Methods:

1.2.1 Replace terminology of “half-life” here with “assumed duration of protection” as this concept is not described here and may not be intuitive for non-vaccine readers.

1.2.2 The method of “adjusting” historical vaccine implementation rates requires elaboration.

1.3 Conclusions:

1.3.1 The value of the model for decision-makers will hinge on performance which has not yet been evaluated. Suggest revising terminology to something like “upon demonstrated performance, the functionality of the MVM could potentially provide valuable information to assist both vaccine developers and policymakers in decisions to invest in malaria vaccines.”

1.3.2 In the Background section of the manuscript the authors also indicate that another objective is to communicate lessons learned and implications for other models but this is not evident in the abstract and could be mentioned in the conclusions.
2. Main text: In general, it would strengthen the article for the authors to go through and make sure the concepts, etc. would be understandable by the general BMC Infectious Diseases audience which may include disease experts not as well versed in issues with decisions for investments in vaccines. Additionally, many points could be made more concise and with greater degree of specificity. For example, in the Background section multiple paragraphs refer to “decisions” to be made by the intended audience but it is not until the 7th paragraph where the types of decisions are explicitly described and this is important for the audience of this journal which includes non-vaccine specialists. Also, there are a large number of acronyms used throughout which may be difficult for the reader to keep track of therefore I suggest to limit use of acronyms to just those that are most frequently used in the manuscript (e.g. use Applied Strategies in place of AS; possibly consider referring to the group as developers, rather than repeatedly mentioning each of the different groups).

2.1 Background:

2.1.1 I appreciate the authors are responding to reviewer comments but the Background section requires more of a focused discussion of the context and objectives of the manuscript. This section could be reduced to 3-4 paragraphs including: a) need for this type of information specific to the objective of this manuscript (e.g. condensed and more concise version of paragraphs 1, 2, last two sentences of paragraph 7, paragraph 4), b) description of other relevant modelling initiatives as context (i.e. paragraph 3), c) malaria-specific models and objective for this paper (i.e. concise version of paragraphs 5 & 6). The details of the use of models could, for example, be reduced to one sentence and the description of “decisions” should be specific in mention of the types of decisions (as provided from last 2 sentences in paragraph 7).

2.1.2 Paragraph 3, sentence 1: restate as “have recently estimated the impact of interventions worldwide”.

2.1.3 Paragraphs 6-7: Only mention the history and evolution of the model as relevant to rationalize the current functionality of the model. A detailed history is not needed as it is appreciated that any model and analysis has an evolution process and many of the readers may not likely be familiar with the original version. Statements such as “increase access to the model’s simulations by vaccine developers and policy” is not clear. I may have missed this but my understanding was that the simulations inform inputs into the MVM and that the user does not have access to change the simulations per se. Please also use consistent terminology when referring to the versions of the model (the text switches between reporting version numbers and original vs. current and first vs. second).

2.1.4 Paragraph 7, sentence 4: the description of “aggregate financing needs” is not clear.

2.1.5 Paragraph 8, sentence 3: Suggest removing: “This demonstration scenario draws on” and revising to state that the scenario modelled was the strategic goal established in 2006.

2.1.6 Paragraph 8, sentences 4-5: move to discussion section and describe how
the results of the hypothetical scenario may change given the latest empirical
evidence for some of the inputs (already in discussion but statement needs
further clarification).

2.1.7 Paragraph 8, sentences 6-7: Suggest to restate to something like “Here we
present the results of a hypothetical scenario modelling the 2006 strategic goal of
a highly efficacious malaria vaccine to demonstrate the functionality of the MVM
and use this example to provide considerations for future development of models
to inform investment decisions targeting both vaccine developers and
policymakers.”

2.2 Methods: Please ensure the corresponding tables are identified in the text. If
for example Table 4 is never referred to in the text then it is probably not needed.

2.2.1 Overview of model structure, sentence 5: Please provide some examples of
the key parameters referred to “(e.g. vaccine efficacy, duration of protective
immunity, etc.).”

2.2.2 Software and interface: Is the user only allowed to enter information country
by country in the interface or could they perform an analysis for a number of
countries simultaneously? Please specify this in this section then add mention of
this as a strength or limitation in the Discussion section.

2.2.3 Supply and demand forecast, Reference data: Please indicate more clearly
which data are regularly updated as part of the MVM updates (e.g. when you
access the MVM the user knows the population structure is the most up-to-date)
and which need to be updated by the user.

2.2.4 Supply and demand forecast, Module summary and demonstration
scenario, paragraph 3, sentence 5: Please provide further clarification of
statements in this sentence.

2.2.5 Supply and demand forecast, Module summary and demonstration
scenario, paragraph 3, sentence 6: Please further clarify. Is the point indicating
that the modelled scenario assumed maximum level of immunization coverage
(as measured by DTP3) in the first year of vaccine introduction which may be an
over-estimate since it typically takes time to achieve maximum coverage?

2.2.6 Public health impact estimates, paragraph 1, sentence 2: Please clarify
what type of data was used in this module to inform simulation of the age
structure of the population (just states that it was based on Ifakara, Tanzania-but
what data from this site?). Would this likely produce a disconnect with the age
structure inputs used in the Supply and demand module? If so then this should
be mentioned in the Discussion section.

2.2.7 Public health impact estimates, Reference data, Disease burden, sentence
2: Please move this sentence to the discussion and revise the language as the
model is not assumed to “track trends” but rather the point is that there are
changes that occur over time (e.g. development, etc.) that impact child mortality,
including malaria, and that the resulting outputs of the model are not adjusted for
these trends.

2.2.8 Implementation cost and financing requirements, Module summary and
demonstration scenario, paragraph 1: Suggest removing the reference to the
original MVM as the user is likely unfamiliar with the original version and disaggregated costs would be of general interest.

2.2.9 Implementation cost and financing requirements, Module summary and demonstration scenario, paragraph 2: Please provide additional clarification of the “viewpoints” referred to as the rationale for the 5% discounting used as it is not apparent and 3% is most widely used.

2.3 Results:

2.3.1 Supply and demand module, sentence 2: Suggest revising “532 M doses would be used” to “532 M doses would be required”.

2.3.2 Public health impact module, sentence 1: Suggest revising to something like “The estimated number of doses of vaccine required from the supply and demand module were then used as inputs in the public health impact module.”

2.3.3 Sensitivity analysis, sentence 2: Suggest revising to something like “Reducing the vaccine efficacy to 75% decreased the estimated number of uncomplicated cases averted over 10 years by 14%.” Then refer to Table 7, where I suggest you add the results from the sensitivity analyses so the reader can assess the impact across scenarios. This will avoid the need to cite all the numbers in this paragraph.

2.4 Discussion:

2.4.1 Paragraph 1, sentence 1: This sentence overstates the results and needs to be revised. The robustness and reliability of the outputs were not evaluated as this would require an evaluation of the performance of the model and this analysis only demonstrated functionality. Suggest removing this entire sentence.

2.4.2 Paragraph 1, sentence 2: Suggest restating “costs associated with a vaccine” to “costs associated with a hypothetical vaccine”.

2.4.3 Paragraph 1, sentence 3: Suggest restating “it will be important to compare the model results” to “it will be important to compare both the functionality and performance across malaria vaccine models”.

2.4.4 Paragraph 1, sentence 4: Either elaborate or remove it as it is not apparent why models cannot be compared now particularly given the fact that there is now empirical data and the models could be run to see how well they simulate the observed results. The lack of performance evaluation should be mentioned as a either limitation of this analysis or the next steps.

2.4.5 Paragraph 2, sentence 3: Please revise this sentence to be more clear and to correct grammatical errors.

2.4.6 Paragraph 2, sentences 4-5: Please revise this sentence as it might be implied as stated that the RTS,S results indicate a likely further reduction in clinical episode whereas the point is most likely that the estimated public health impact using results from RTS,S is likely to be half the impact estimated in the demonstration scenario with a hypothetical vaccine. Please also revise sentence 5 to be more clear on why additional modelling is needed.

2.4.7 Model design, paragraph 1, sentence 1: Please clarify what is meant by “field data” as this could be the data entry field or empirical data collected from
field studies.

2.4.8 Model design, paragraph 1, last sentence: Please remove this sentence. The readers are likely only familiar with the MVM version 2.0 (also please use consistent terminology when referencing versions of the model).

2.4.9 Model design, paragraph 2: Please only state what is currently used and rationale as needed to inform development of other models. Change “negative consideration” to “limitation” and further elaborate this point.

2.4.10 Model design, paragraph 2: Please provide examples of the extended “other uses” referred to.

2.4.11 Also should provide a statement on how readers may access the model. Need to provide clarification of what types of modifications can be made to the model as is and which will require additional simulations run by Swiss TPH. Strengths/limitations in terms of reader ability to access and modify the model should be more explicit in the Discussion section.

2.4.12 Uses and outputs: The section could be reduced to 1 paragraph.

2.4.13 Parameters, paragraph 3, sentence 1: Suggest to revise “a suite of possible interventions” to “multiple interventions”.

2.4.14 Parameters, paragraph 3, last sentence: Please revise this sentence (e.g. do not start the sentence with “$5”), remove the parentheses, and remove the last portion of the sentence.

2.4.15 Parameters, paragraph 4, sentences 1-3: Please remove the first sentence, and revise the second and third sentences to something like: “The purpose was to demonstrate the functionality of the model and timing of implementation by countries and time to maximum coverage are important drivers of public health impact.”

2.4.16 Parameters, paragraph 4, sentence 4: Please revise this sentence to more clearly state the point.

2.5 Conclusion:

2.5.1 Sentence 5: Remove sentence 5 as it overstates the findings from this analysis. Policymakers cannot be reassured if we do not understand the performance of the model.

2.5.2 Sentence 6: Could possibly be restated to reiterate the message that this model can be used to inform decisions for investment in malaria vaccines.

3. Tables/Figures:

3.1 All acronyms in the Titles/descriptions should be spelled out (e.g. PE in Figure 3 description).

3.2 Figure 2 description: Suggest replacing “that began implementation each year” to “to introduce each year”. Suggest removing the last sentence.

3.3 If there are multiple input values for a given parameter make each as a separate row within that parameter (e.g. separate number of doses and year available as separate rows within the Manufacturing capacity parameter in Table
1). Add row and column borders to Table 2.

3.4 Use consistent method for identifying parameters where there are categorical responses (e.g. Table 2, Number of doses per regimen should be “Select one: 3 vs. 4 doses”). This helps the reader to understand more quickly what is programmed and what can be directly altered for data entry.

3.6 Table 4. If not cited in the main text then remove. Not apparent how to interpret/use the information in this table.

3.7 Table 7. Suggest adding the results from all the modelled scenarios (demonstration and sensitivity analyses).

3.8 Supplemental Document A is a great addition to the manuscript.

Discretionary Revisions

1. May consider adding additional labelling to the figures denoting “numbers of doses”, “number of adopting countries”, etc. although this may not be possible if these are outputs from the software not allowing for changing the labels.

Level of interest: An article whose findings are important to those with closely related research interests

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

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests