Author’s response to reviews

Title: Malaria paediatric hospitalization between 1999 and 2008 across Kenya

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Version: 2 Date: 28 October 2009

Author’s response to reviews: see over
28th October 2009

Mick Aulakh, M.Sc.
Assistant Editor, BMC Medicine

Dear Mr Aulakh,

Re: Malaria hospitalization between 1999 and 2008 across Kenya (MS: 9322078829904378)

Thank you for the opportunity to reply to the reviewers; we found their comments insightful and useful in revising the manuscript. Our responses are set out in this letter below and we have made the changes required or otherwise explained reasons for not doing so. We have also made some alterations to the manuscript which are identified in a marked up copy attached as additional information, together with a revised version also attached.

We very much hope we have provided a satisfactory response such that the article is acceptable for publication in the Journal.

Yours sincerely

Dr Emelda Okiro

Reviewer's report 1

Title: Malaria hospitalization between 1999 and 2008 across Kenya
Version: 1 Date: 15 September 2009
Reviewer: Peter Byass

Reviewer's report:
I was very interested to read this exceptionally fascinating, but complex, paper. I am not aware of any other work that takes a national (Kenya) long term (10 year) view of paediatric malaria while also taking into account background factors such as catchment populations of health facilities, meteorological data, etc.

I think it is realistic to suppose that the majority of readers will see this as a "black box" approach, from which interesting findings emerge. In my opinion, you have achieved a generally good balance in your Methods section between describing your approach, but not going into so much technical detail as to make it incomprehensible. Nevertheless there is still some degree of jargon with which the majority of readers might be unfamiliar - for example "convex hull polygon", "discontinuous EA polygons were smoothed", "spatial-temporal Bayesian generalised linear geo-statistical model", "longer-term trend signals", and so on. I think it would be worthwhile trying to re-review your text from an outsider's perspective and insert a few further clarifications for the less-specialist reader.

Except for the term "longer-term trend signals", we have made every effort to further simplify, explain and clarify the different terminologies used in the manuscript or otherwise removed technical terminology where used. I can't think of a simpler way to explain the underlying real trend in the data other than what is already stated in the text. Additional information with significantly more detail on how we have defined the catchment is also provided as supplementary information. Details on the geo-statistical models are also elaborately explained in the publication by Noor et al. BMB Infectious Disease which is now in press.
The reference to "Noor et al. submitted" is also obviously crucial to the methods used this paper - hopefully that can be available by the time this paper is published.

This paper has been accepted for publication in the BMC Infectious disease journal and is now in Press.

In the manuscript copy that I have, Figure 2 extends over several pages but even so is too small to read properly! I am not sure how that can be resolved, or how a journal might handle that in a published version, but it needs some further thought.

We have tried to present the figure in the most sensible way. However we presume that this will be tackled by the journals’ publications team. We will therefore wait for further communication from them on how best to scale this figure.

Which journal?: Appropriate or potentially appropriate for BMC Medicine: an article of outstanding merit and interest in its field

What next?: Accept for publication in BMC Medicine after minor essential Revisions

Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Reviewer’s report 2

Title: Malaria hospitalization between 1999 and 2008 across Kenya
Version: 1 Date: 21 September 2009
Reviewer: Patricia Graves

Reviewer’s report:
This manuscript describes important and novel information on incidence of paediatric admissions for malaria in Kenya in a sample of sites over time. The results are valuable especially for showing that there is not a consistent decline in admissions across the country in the last ten years. The increased gathering and use of these kinds of population-adjusted clinical data is to be strongly encouraged. The collection of data from registers and definition of hospital catchment areas using actual data on patient’s homes is a thorough approach to estimating incidence, although hard to replicate on a routine basis. Appropriate imputation and adjustment for rainfall and for all cause admissions to account for changes in utilization lend validity to the data on malaria specific admissions and the trends over time.

- Major Compulsory Revisions
1. I find that the attempt to impose the predictions of transmission intensity from the prevalence model (described under “defining parasite prevalence within the catchment area” on page 6) detracts from the presentation of this paper’s important findings on incidence and trends. Those estimates of infection risk derived from the prevalence model perhaps represent potential transmission or vulnerability in the absence of control measures, but in this paper you are presenting rich empirical monthly data over a lengthy time period that should speak for itself. The data could even be used (especially if you had more detailed data on control measures applied) to validate the prevalence model. The admissions data may be as useful as, or even better than, the prevalence model as an indicator of actual (rather than potential) transmission intensity. It seems preferable to me to use the incidence data here to inform the decision about whether the areas around each hospital should be described as low, medium or high intensity transmission, and whether that has changed over time. Therefore please downplay the prevalence model predictions and speculations throughout the paper. This would include:
a) rewriting the first two paragraphs of discussion to clearly distinguish the incidence intensities and
trends found in this study from the confusing information interspersed there from the prevalence
model predictions.

b) removing or qualifying all references in text to sites as being of “low transmission intensity” (para
2 results page 8); “exceptionally low transmission areas” (para 1 discussion page 10); “moderate to
low transmission intensity” and “predominantly high transmission” (page 11) etc., unless they are
derived from the estimates of incidence in this study.

c) editing abstract results and conclusions as I am not convinced that different patterns of decline
related to ‘transmission intensity’ have been demonstrated and in discussion it is only regarded as a
‘suggestion’ (middle of page 13). Some of the highest incidence sites (using estimates from these
data, not other models) show a decrease.

We acknowledge the deficiencies identified by the reviewer. Even though we do not necessarily
agree with the reviewer’s assessment of our use of references to predictions from the
prevalence model, we accept that because we do not have empirical infection prevalence data over
time from all sites at the same temporal resolution as that for the clinical incidence data, we haven’t
proven the relationship between changing transmission and disease incidence in this paper. We do
allude to this in the discussion but to satisfy the reviewer we have downplayed all direct reference to
the transmission hypothesis in the manuscript. We have removed the reviewers suggested
deletions. We remain convinced that the data alone as a set of descriptive observations does add to
the debate on whether there has been a universal decline in malaria in Africa but will further explore
the transmission intensity hypothesis in separate analyses on subsets of data where we can
assemble longitudinal data on infection prevalence, intervention coverage and other covariates –
which were not possible for the series presented here.

- Minor Essential Revisions
The author can be trusted to make these. For example, missing labels on figures, the wrong use of a
term, spelling mistakes.

1. Please order the 17 hospital sites consistently throughout. That includes the supplementary
material. For example, Table 1 in the main manuscript starts with Busia, Bungoma, Homabay.....
(the latter spelled as two words in text and other tables). Tables in Supplementary info are in the
same order. However Figure 1 starts in a different order with Bungoma, Busia... The maps in
supplementary info 1 are in the order Bondo, Kisumu, Homa Bay, Siaya, Busia, Bungoma. This is
very confusing to the reader trying to put the pieces together so please make them consistent and
describe them in same order in text (e.g. page 4).

Thank you for identifying the mistake. The spelling of Homa Bay has been corrected to reflect
the right spelling. We have also changed the order across all text, tables, figures and
supplementary information to be consistent across the whole manuscript.

2. In paragraph 2 of results please describe the groups of hospitals using the same categories as in
the tables and maps i.e. “Western/Lakeside”, “Highlands” etc.

We appreciate the reviewer’s suggestion and have made the necessary changes to the
manuscript. Wherever feasible we have endeavoured to use the same categories in the text as
those used in the Table and map

3. Figure legend to Fig 2 is not clear at all. I had to refer to supp 2 tables to work out what the
different coloured lines in left panels referred to. Please expand.

The figure legend has now been expanded to provide additional details on the figures on the left
panel of Figure 2
4. The description of defining health facility catchment population on page 5 is repeated in the Supp 1, but that has more details, suggesting that the summary in text is not quite correct (doesn’t talk about the radius for example but only the hull polygon). Please give a consistent description in one place or the other.

The manuscript has been modified to allow for further clarification and also to achieve consistency with the more elaborate description given in the SI 1.

- Discretionary Revisions
1. It would be interesting to more directly compare the admission incidence estimates described here with predictions from the prevalence model, rather than trying to impose categories of transmission intensity from the prevalence model onto the sites. Because of change in incidences over time I suggest doing the comparison at the beginning and end of the time period.

We are exploring this hypothesis separately with better data on infection prevalence transitions and in selected sites included here where this data is available. We will now publish this separately and more elaborately

2. I would be interested in more discussion of the painstakingly derived absolute incidence estimates – how they relate to other countries for example, and the differences in these incidence estimates between the sites and possible reasons for that. The incidence of admissions for malaria at some of the Arid/Semi Arid sites (Supp info 2 table 2) are as high or higher than the Western/Lakeside sites, for example. Regarding changes over time, can you add any information on differences between the sites in when ITN coverage was scaled up or drug policy changed?

We appreciate the reviewers’ suggestion. However to the best of our knowledge we are not aware of other studies that have carefully defined populations as risk of hospitalizations in the same way we have done here. We believe these to be the best data relating to defining catchment and estimating incidence therefore a cross-country comparison isn’t as easy as it may appear at face value. Most hospital based studies either do not report catchment denominators or make some arbitrary guess.

3. While actual rainfall data is used, sometimes the stations are located relatively far from the hospitals or had missing data. Presentation of the trends over time in rain would be interesting. Use of satellite derived rainfall estimates (averaged over the catchment areas) would add to the analysis.

We only used rainfall as a covariate for seasonal and temporal variation of malaria admissions. Our primary objectives weren’t to examine the relationships between seasonal presentation of malaria and rainfall. The series of admission data and rainfall data from the nearest metrological station can be provided to those who may be interested in exploring this further – we’d be happy to share with the reviewer if she were interested in exploring this in more detail.

Which journal?: Appropriate or potentially appropriate for BMC Medicine: an article of outstanding merit and interest in its field

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Reviewer’s report

Title: Malaria hospitalization between 1999 and 2008 across Kenya
Version: 1 Date: 15 October 2009
Reviewer: Lawrence Ndekeneni Kazembe
Reviewer's report:
General Comments
This study considered the pattern of malaria admissions in Kenya for a period of about 10 years. Because of limitations of data, the authors used data from 17 representative health facilities in ecologically divergent areas across Kenya. The authors used autoregressive models to adjust explain the changing pattern in malaria admissions. The study has several limitations and am glad to note that many of these limitations have been acknowledged in the discussion. Its an interesting paper among those of related field.

The paper, in the introduction, did acknowledge and highlight the fact that most studies attributed the changing pattern in malaria morbidity to a number of factors. As such, I was expecting to see a model that does related malaria hospitalization data related to such factors. This I find to be a major gap in the paper. It remained therefore mostly descriptive epidemiologically, probably this is the first step, and future research will consider why malaria admissions have been changing.

We appreciate the reviewers' comments. However in this particular paper we sought only to describe the temporal patterns in the data. Assembling the coverage of interventions, access to care and other intermediary covariates within the catchments servng these hospitals is non-trivial and we would need to dig carefully into all available sources of varied information to triangulate parsimonius estimates of temporal changes in intervention coverage. This is something again we intend to explore within a sub-set of hospitals included here where these data may be available across the entire time series.

Minor comments
Abstract
1. The paper should consider including some confidence intervals or range for the admission rates cited and the reduction percentage.

The confidence intervals are included in the left panel graph of Figure 2 but they are extremely narrow so may have been missed by the reviewer. Additionally, in the supplementary Information 2 we have provided the values for the confidence intervals for each site.

Introduction
2. page 4, top paragraph, last line, there is mention of 100 of 120. Can they justify this figure.

We accept this is slightly subjective but there was a very skewed distribution most hospitals did not report for at least 50% of months and then this jumped to those where it was circa >80% we therefore elected to use this as the cut off – albeit arbitrary it allowed us to maximize the inclusion of those with majority data for the time series.

Which journal?: Appropriate or potentially appropriate for BMC Medicine: an article of importance in its field

What next?: Accept for publication in BMC Medicine after discretionary revisions

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.