Author's response to reviews

Title: The usefulness of school-based syndromic surveillance for detecting malaria epidemics: experiences from a pilot project in Ethiopia

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Author's response to reviews: see over
Response to BMC Public Health comments on MS 1677620913166731: “School-based syndromic surveillance for detecting malaria epidemics: experiences from Ethiopia”

Dear Editor,

We are grateful for the two reviewers’ comments.

It has been difficult to address all of the comments raised by the reviewers, since their feedback differed markedly – one recommending acceptance of the manuscript with no changes, and the other making many comments and recommending rejection.

While we strived to edit the manuscript in line with all the reviewers’ comments, we did not agree with all of the comments and suggested revisions made by reviewer 1 – where disagreement did occur, we provided our reasoning for rebuttal.

Reviewer 1 – Olivier Maillard

1. This article presents results of a prospective study of a school based syndromic surveillance focused on absenteeism indicators for detecting malaria epidemics in the community. Unfortunately, no malaria epidemics occurred during the study and results were thus inconsistent. I am quite upset about this study particularly its methods. As illness is not the major factor for school absenteeism, it is actually difficult to make the assumption that school attendance could be an indicator of malaria burden at community level especially in a low transmission place. There is also a lack of sensitivity and specificity as malaria may not represent all the diseases even with fever. Only 50% of children who reported fever as a reason for absence from school attended a health facility. Moreover, the study location is not exactly well defined in the SNNPR region (altitude, malaria epidemiological profile, school and health facility density compared to the whole country).

Response

We acknowledge the concerns of the reviewer. We would like to re-state the hypothesis that led to the development of this study – that while a large proportion of Plasmodium infections in low transmission settings such as Ethiopia are low density and asymptomatic, during an epidemic it is expected that population rates of symptomatic malaria would increase due to increase in the total number of Plasmodium infections. This was the hypothesis that we sought to investigate and is clearly stated on page 4, line 22.

We agree that the syndromic surveillance approach presented in this paper may have low specificity for malaria, due to multiple factors contributing to fever and school absenteeism. However, the absenteeism-based syndromic surveillance is proposed as a crude mechanism to improve the responsiveness of community-level surveillance systems to potential epidemic events in this resource limited setting – malaria is a priority disease in Ethiopia with epidemic potential, but this system could also capture other epidemics. This is extensively discussed on page 16, line 20.

It is not surprising that only 50% of children reporting fever as a reason for absence attended a health facility for further diagnosis and treatment. This is consistent with the 2011 Malaria Indicator Survey where
in SNNP, 46.3% of children under five years with fever were taken for diagnosis or treatment from any type of provider.

Additional description of the study sites has been included in the methods section (page 6, line 13).

2. Some limitations need to be mentioned as the little number of school and pupils included without presentation of the sample size calculation, the feasibility of reporting accurate school attendance indicators by schools, local thresholds ...

Response
We agree with the reviewer’s concerns and have expanded the limitations section of the discussion, which now specifically mentions the lack of sample size (page 15, line 17):

“Identification of valid indicators for piloting was limited by inclusion of only six sites in Phase 1 and the low malaria transmission experienced in SNNPRS in 2012. The study was also limited by the inability to provide a formal sample size calculation for the comparisons we sought to undertake, due to lack of data describing changes in these indicators during normal and abnormal transmission seasons.”

3. In Oromia study, more than 20,000 pupils from 197 schools have been included. The range age was also larger from 5 to 18 yo !

Response
This comment appears to refer to a different study conducted in Oromia Regional State [reference #47], which had an entirely different aim: using school surveys to develop a predictive risk map for Oromia. Consequently, the sample size for that particular study was determined in order to generate population-representative indicators for each of the defined ecological zones. For the present study in SNNP Region we wanted to explore temporal variations in indicators at school and community levels – therefore, only small number of sites were included; however, these were sampled multiple times during the study period.

Regarding the age range of 5-18 years in Oromia, this range was used in order to retain maximum data from pupils who were sampled at schools, but the proportion of children aged five, six, 17 or 18 was small (0.9%). The age range was restricted to 7-16 years in the SNNP Region study, in line with the Regional Education Bureau guidance on recommended school enrolment age.

Major Compulsory Revisions
4. Authors have first to shorten their article, particularly the method section (as it is said school surveys followed a standard methodology previously described and cited in references) and the discussion. A sample size calculation should be presented, as for the threshold chosen depending on each school attendance history

Response
Following the reviewer’s comment, we edited both methods and discussion sections.

As described on page 16, line 23, specific thresholds were not defined for schools – therefore, this calculation is not presented. The lack of formative research on likely indicator values during malaria epidemics precluded a sample size calculation. However, the lack of sample size is presented as a limitation in the discussion section (page 15, line 18).
5. I wonder if the article title is really accurate for 2 reasons: first no significant results are reported for detecting malaria epidemics but for non-enrolment, second assumptions made and methods used are not clear. As Phase 1 did not show any relevant findings that neither school attendance, nor absenteeism and febrile illness could be good indicators for malaria epidemics in the community, it is unclear how Phase 2 has been conducted. A school based “syndromic” surveillance to be accurate does not require diagnosis. Moreover absenteeism is not actually a health indicator and the authors would rather talk about school based surveillance. Then, as presented in Table 1, targeted diseases are usually communicable diseases such as influenza (a seasonal surveillance can thus be settled), outbreaks generally speaking (high attack rate compared to other age group and likely to spread disease to relatives), emerging infectious diseases ....

Therefore malaria is not so a good example of disease especially when illness is not the first reason of absenteeism. Furthermore, as enrolment is stately irregular and insufficient, a school based surveillance system for monitoring community health and epidemics is not a good system particularly when non-enrolment is a confounding factor for the targeted disease.

**Response**

*In light of the suggestions made by the reviewer, the title of the manuscript has been adapted to reflect the pilot nature of the study. The revised title is:*

“The usefulness of school-based syndromic surveillance for detecting malaria epidemics: experiences from a pilot project in Ethiopia”

6. In fact, these findings could have been provided by simple observations or after Phase 1. Concerning the other results based on school-based syndromic surveillance, they already have been published in this setting and lack of school enrolment make difficult an assumption of the results at community level. As a conclusion, this study assesses results already made and published in this setting. Many limitations could have been predicted with simple investigation. I suggest to axe the paper on school based surveillance and the limitations of enrolment in the local context. It was attempted to study/validate this system during malaria season but some other limitations occurred.

**Response**

*We disagree with the reviewer that this study was already done or that the result have already been published. As explained in our response to comment #3 above, the study that the reviewer seems to be referring to is a completely different study, in a different geographical location, with different study objectives.*

*We acknowledge that this study has methodological limitations, and cannot lead to strong conclusions to recommend this alternative school-based surveillance approach. However, in the iterative approach of research, we strongly believe that the methodological approach, process and findings from this study will be of value for future attempts developing infectious disease surveillance approaches in resource-limited settings.*

*Furthermore, we disagree with the reviewer that this paper presents no additional information on the use of syndromic or surrogate health indicators in these settings, since --as described in the manuscript’s introduction section-- the vast majority of the published literature relates to high-income countries and*
influenza. The use of absenteeism or syndromic indicators to identify malaria epidemics has been neither conclusively proven nor disproven to be a valid, feasible or acceptable approach in the literature.

Minor Essential Revisions

7. P4L7 : only one reference (reference 14 from 1994 in Kenya) is used to assess the rationale that school absenteeism is a recognised consequence of malaria epidemics in the highlands of East Africa

Response
Ethiopia is fortunate to have not experienced any severe malaria epidemics comparable to that of 1994 in recent years, and as a result there are few publications which specifically describe rates of febrile illness in Ethiopia during a malaria epidemic. While there was an epidemic in 2012 in Amhara Region of Ethiopia, these data have not been published and are not available for secondary analysis to explore associations between all-case febrile illness and confirmed malaria incidence during an epidemic.

8. P4L13 : delays in data reporting, incomplete or inaccurate data also exist in a school based system

Response
It is reasonable to expect that limitations which affect reporting of data from health facilities, such as resources, motivation and feedback, may also be limitations in school data reporting. However, as stated in the discussion (page 16, line 15 onwards), the authors view this approach as being a mechanism for local decision making and action – whereby school staff who observe unusual increases in absenteeism (according to their perception, not necessarily a formal threshold) should alert the local health extension worker to review their malaria diagnosis data for evidence of any increase in burden. The concept is not to establish a parallel reporting system to that of the health extension workers, but simply provide additional intelligence regarding health of the local population.

9. P4L17 : please provide a date of access for reference 23

Response
The bibliography has been re-formatted to the journal style, and now includes access dates for all references.

10. P4L18 : reference 24 article is based on the comparison of RDT prevalence in school and community population, not on school surrogate and syndromic indicators for predicting malaria burden in the community.

Response
It is correct that Stevenson et al. compare Plasmodium prevalence determined by RDT between school and community surveys, not other syndromic or surrogate indicators. Nevertheless, we feel that this paper is relevant evidence of the possible representativeness of school-level data of the wider community-level malaria epidemiology. The sentence has been edited (page 4, line 18) to clarify that the paper refers to a specific malariometric indicator.

11. P5L6 : why using a box 1 in the introduction section?
Response
The information in the box was intended to provide additional background on the previous applications of syndromic surveillance, which may be particularly relevant for readers from low-income countries or the malaria sector, among whom this approach may be less well-known.

12. P8L5 : Duration of Phase 2 is unclear. Till January 2013 in the text or till the end of the transmission season (December 2012 on Figure 1)

Response
Data collection continued until the end of the school semester, which falls before Ethiopian Orthodox Christmas, in the first week of January. Therefore a few days of data from January were included. The text has been edited accordingly (page 8, line 2).

13. P9L2 : how was chosen a convenience sample of schools ? why 5 schools from cluster A and 2 schools from cluster B ?

Response
The schools from which attendance registers were collected for validation were a convenience sample due to logistical challenges in re-visiting some schools repeatedly in order to gather all required registers. Schools in cluster A were prioritized for collection of attendance registers in order to maximize the amount of attendance data available for subsequent analysis. Considering the request to reduce the length of the paper, this additional detail has not been added to the manuscript.

14. P10L2 : the authors could have applied an Hosmer and Lemeshow test to check the fitness of the final model.

Response
The Hosmer and Lemeshow test is not widely used for assessing the goodness of fit of mixed multi-level models. Limitations of the Hosmer and Lemeshow test have been described by Hosmer et al. (1997) Stat Med. 16:965-980.

15. P10L8 : did the risk the same along the study period and over the SNNPRS region for calculating mean absenteeism?

Response
As described in the results section (page 12, line 11), absenteeism was similar between classes within the same school, but absenteeism significantly increased over the study period due to drop-out of students during the semester. Weekly absenteeism did vary between schools, as seen in Figure 3.

16. P10L22 : written consent were compulsory to include children in school surveys but only from the head to include the whole household members even if a verbal assent was sought for them ??

Response
We are unclear on the question being asked by the reviewer. Written consent was required from a parent or guardian for school children to be included in the school surveys. Written consent was also required from the head of household for inclusion of all individuals in that household in the household survey. In addition, verbal assent was sought from all participants in both the school and household surveys – individual children and household members were therefore able to refuse to take part (if, for example, they were scared to have a finger-prick blood sample) after written consent had been granted.

Following the reviewer’s comment, we edited the ethical consideration section in the revised manuscript for clarity (page 10, line 6 onwards).

17. P11L1 : treatment by primaquine with checking of G6PD deficiency was not available in the country?

Response
While provision of primaquine for P. vivax radical cure is included in the malaria national treatment guidelines, at the time of the study primaquine was not routinely available in health facilities. The primaquine treatment policy had not been operationalized due to lack of individual G6PD testing services at health facilities other than referral hospitals, and insufficient evidence of G6PD deficiency levels in the Ethiopian population to justify primaquine treatment without G6PD testing. A G6PD mapping study is underway in Ethiopia and it is expected that the primaquine treatment policy will be reviewed and may be implemented in the near future.

Since the national treatment guidelines are referenced and available to the readers for download, and in the interest of avoiding further lengthening the manuscript, we decided against including this additional information on lack of primaquine treatment in the manuscript.

18. P11L11 : Is it the mean prevalence or median one as the range is mentioned ?

Response
It is the mean prevalence, as stated in the manuscript (page 10, line 25). The maximum and minimum prevalence by school is also presented to give an understanding of the level of variation in this indicator across the sites.

19. P12L10 : what kind of symptoms could be checked at school level by the teachers ?

Response
In the symptom questionnaire, teachers were only asking the children if they had one of 10 symptoms, they did not conduct any testing or validation of the reported symptom. Additional detail on the symptom questionnaire has been added to the relevant section in the methods (page 8, line 15).

20. P14L1 : Oromia study seems not so different and methodology was the same as authors said

Response
See also response to comment #3. The Oromia study was designed to generate a predictive risk map, rather than being a recommended ongoing real-time surveillance approach, or an epidemic early warning system. Therefore we believe that the highlighted sentence is valid for the study in SNNP Region, referring
to Phase 2 of the study whereby the syndromic and surrogate indicators were collected from schools throughout the major transmission season.

21. P15L6: obviously, children that are not enrolled at school are more likely to have malaria during farming activities so this part of the population (only 54% are reported to be enrolled) may be more representative of the malaria burden

Response
We are not aware of any rigorous evidence that children who are not enrolled in school are at higher risk of malaria, or individuals engaged in farming activities (the majority of the population) are at greater risk. While we had hoped to provide evidence to describe risk of malaria for enrolled and non-enrolled children, the small number of confirmed Plasmodium infections meant that there was insufficient power to test this hypothesis. However, it is plausible that there are common risk factors for non-enrolment and increased risk of malaria, such as lower household socio-economic status.

The sentence specified by the reviewer (page 14, line 11) has been edited in the revised manuscript to “Considering that universal enrolment and attendance at primary school has yet to be achieved in Ethiopia, it is likely that the sensitivity of a school based syndromic surveillance system was reduced, since the whole community will not be captured at a school-level platform.”

22. P15L26: the goal of school based surveillance is to provide a sooner alert and response system than hospital/dispensary surveillance. If absence are reported once a week and of unknown origin, it is a serious limitation

Response
The aim of the school-based surveillance system is to provide a supplementary mechanism to generate alerts of unusual health events in the community, considering the limitations of routine facility-based surveillance. The importance of innovations in community-level malaria surveillance was highlighted in a recent paper by Tanner et al., now included in the introduction (page 4, line 15). The school data and alerts are not reported to central staff, but discussed with community health workers in order to initiate community-level responses (page 16, line 14).

23. P16L8-11: in the method section?

Response
The indicated sentences have been removed, considering the recommendation to shorten the manuscript.

24. P16L17: this could be of interest if dropout is more likely to be due to illness/malaria!

Response
In this low malaria transmission setting, there are few cases of severe malaria which could lead to long-term disability resulting in withdrawal from school. It is also expected that there would be few chronic malaria cases which could lead to drop out. The evidence presented in the manuscript (references 44 & 52) describe the findings from in-depth qualitative and quantitative assessment of reasons for drop out from primary education in Ethiopia.
Response
The school teachers and director, with their local knowledge of seasonal farming activities and average dropout rates, would be the ones to determine subjectively what a ‘normal’ absenteeism level is for their school. We were reluctant to define a specific threshold for absenteeism, since levels were observed to vary widely between schools, and it would not be feasible to assign school-specific, fixed thresholds based on previous years’ data if this approach were to be scaled up. We also believe that this flexibility is actually a benefit rather than limitation of the system, since it enables the teachers to combine evidence from attendance registers with their knowledge of the local environment and population.

Response
This has been corrected.

Response
This has been corrected.

Reviewer 2 – Louise Randall
This study was described in excellent detail. Although the study was unable to ultimately test the crucial hypothesis due to a lack of malaria transmission peak, the study was able to describe the study group in greater detail and to examine the potential positive and negative contributors to the successful use of a syndromic surveillance system to detect malaria in the community.

Major Compulsory Revisions
None

Minor Essential Revisions
None

Discretionary Revisions
None