Author's response to reviews

Title: Cost of dengue and other febrile illnesses to households in rural Cambodia: A prospective community-based case-control study

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Author's response to reviews: see over
Dear Sir/Madam,

Thank you very much for the review of our manuscript No MS:1948190552427719 [Cost of dengue and other febrile illnesses to households in rural Cambodia: A prospective community-based case-control study]. We found the reviews to be very helpful, and have made a number of changes, which we think clarify the issues raised by the reviewers.

Below are our responses to the reviewers’ specific comments:

**Reviewer's report**

**Title:** Cost of dengue and other febrile illnesses to households in rural Cambodia: A prospective community-based case-control study

**Version:** 1  **Date:** 10 January 2009

**Reviewer:** Pankaj Garg

**Reviewer's report:**

The authors need to be complemented for carrying out this work on cost of dengue and other febrile illness. The findings reiterate the fact that dengue viral and other febrile illnesses continue to ravage resource poor settings and households compared to the average daily incomes. The findings are relevant not only for Cambodia but for much of South East Asia as well as South Asia; regions complexed with poverty, unique social and cultural circumstances on one hand and grossly inadequate public health infrastructure on the other.

I have following Minor discretionary comments to offer:

• The most striking part of the findings is that non severe dengue does not add to an additional burden as compared to other febrile illness; it is the severe dengue requiring hospitalization with its anticipated complications which is a cause substantial burden. However, this needs to be interpreted with caution considering the small study sample size which could easily result in significant small difference between dengue and other febrile illness to go unnoticed. It would have been worth gold to attempt to involve the entire 89 laboratory confirmed dengue cases for interview.

**Answer:** I totally agree with the reviewer that including all the dengue infected patients would have been more valuable. Unfortunately the study was ethically approved by September 2008 which was too late to interview dengue and non dengue cases detected during the early phase of
the epidemic period without encountering major recall biases. As the reviewer pointed it out below, we chose to minimize this bias while considering a lower number of cases and controls.

• Secondly the reasons of substantial costs incurred by the outpatients in many of these settings could be due to inappropriate prescriptions of antibiotics, etc; in the absence of appropriate training of health care providers at primary and secondary care providers especially in the private health sector. Thus appropriate training of health care providers is a method for reducing financial burden due to dengue to poor.

Answer: Although we did not collect in this study further information about medical procedures and prescriptions, we believe that the major reason that may explain why costs to outpatients are substantial is related to the abusive use of IV infusions and therapeutic injections as described in Vong et al BMC 2004. The private sector is unregulated allowing lay health practitioners to practice and the general public to buy medicines without any prescriptions. As far as we are concerned this situation requires a discussion that is beyond the scope of this paper.

• The authors conclusions of that higher social economic class results in greater hospitalization is valid, as is a also noted by us during our management of major dengue epidemic of September to November 2006 in northern India.

Answer: we thank the reviewer for this interesting information from India

• The implications of the authors findings are not only for the development of the vaccines but also for the national vector control programs such as cost –effectiveness of the fumigation (aedes control) programs etc.

Answer: the reviewer is correct that efforts need to increase in terms of vector control interventions. However many recent reviews in the literature stressed out the fact that vector controls only work when done intensively and properly. In addition, as described by Ooi EE et al EID 2003, despite an effective vector control program, Singapore still faces huge seasonal outbreaks due to permanent importation of the virus each year in the context of low immunity of the population to dengue viruses. Therefore, we wanted to underscore the need for a dengue vaccine to sustain the reduction of the burden of dengue worldwide.

We edited one sentence in the last paragraph of the paper to clarify: Dengue is an important cause of febrile illness in Asia and the Americas. To sustain the reduction of the overall burden of dengue, it is recognized that dengue vaccines are needed; hence several vaccine candidates are currently in development [16]. To assess the cost-effectiveness of the potential use of a dengue vaccine but also other control measures, country-specific cost-of-illness data are needed for hospitalized and non-hospitalized cases cared for in the public and private sector.

• The most challenging issue for any cost analysis related to dengue is to find out the exact proportions of children requiring hospitalization, platelet transfusions, need of intensive care, etc. Because these are the variables which pose substantial burden not only to the households but also to the health systems of the nation.

Answer: We again agree with the reviewer the parameters he mentioned above would have been helpful for an accurate analysis of the cost, particularly when dealing with a small number of cases and controls. Unfortunately we did not collect this information.
• The study has been well conducted, methods well described, language use and statistical analysis are accurate. Discussion contains the relevant limitations of the study. My only minor concern is that the interviews were conducted one to two months after the illness which has the potential to lead to recall bias. However, I realize it might be a feasibility issue and authors have accepted this in the limitations of the study.

Answer: We concur with the reviewer’s comments and we acknowledged this crucial limitation

• It would be extremely useful for other researchers to include the questionnaire developed and used by the authors in their study as an additional file in the manuscript.

Answer: we would be happy to provide the journal with a copy of the questionnaire

Level of interest: An article of importance in its field
Quality of written English: Acceptable
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'

Reviewer's report
Title: Cost of dengue and other febrile illnesses to households in rural Cambodia: A prospective community-based case-control study
Version: 1 Date: 30 January 2009
Reviewer: Sokrin Khun

Reviewer's report:
I think this is an excellent piece of work of research and worth publishing. The authors have designed clear methodology and conducted great data collection and analysis. The findings are supportive to similar studies in Cambodia and elsewhere.

I have some comments regarding this work:
1. The authors should clearly state what types of interviews they used to interview the parents/legal guardians

Answer: we edited the sentence to clarify as follows the interview process and on the type of questionnaire we used:

Parents or legal guardians of cases and controls were interviewed approximately 1-2 months after recovery from the illness by two trained interviewers after obtaining written informed consent. All data were collected during face to face interviews using a standardized closed-ended questionnaire. The collected variables included demographic information, disease duration and symptoms, perception of health status, health seeking behaviours, care received by the child, indirect and direct costs for parents and other household members, financing of disease-related costs, and housing and food-related indicators (for example, weekly expenditures on food and number of meat-containing meals per week, based on figures from the week prior to interview).

2. The authors should clearly state how they analyze qualitative data

Answer: Unfortunately we did not collect any qualitative data. All the questions were closed ended. The main purpose of the study was to estimate the range of costs of a dengue case in
Cambodia accounting for hospitalization and cost related comparison with other fever illnesses. This is crucial for the assessment of the cost-effectiveness of a potential dengue vaccine.

3. The authors should use some qualitative data in their findings

Answer: please see answers above in questions 1 and 2.

4. The authors interestingly stated dengue cases tended to occur less often in households with a high educational status of the father? Why?

Answer: We agree this was an interesting anthropological aspect of the finding. In many settings health care handling of children are more frequently associated with the mothers’ education level. Unfortunately the number of the questions was limited to this respect and we did not attempt to explore further this gender difference.

5. The authors should expand on the amount of money that the Equity Fund covers for medical costs and the travel for each admitted patient

Answer: at the request of the reviewer we changed the fourth sentence of page 8 describing how the health equity funds in place in the Kampong Cham hospital operates:

*Health equity funds have been implemented in Cambodia to increase access for the poor to quality health service by exempting poor patients from paying hospital fees. In the case of the Kampong Cham hospital, other costs such as travel were also reimbursed to the poorest patients.*

6. The authors mentioned the importance of dengue vaccine development in the conclusion section. I think these sentences should be placed elsewhere.

Answer: we respectfully disagree with the reviewer. It is well recognized that vector controls only work when done intensively and properly. In addition, as described by Ooi EE et al EID 2003, despite an effective vector control program, Singapore still faces huge seasonal outbreaks due to permanent importation of the virus each year in the context of low immunity of the population to dengue viruses. Therefore, we wanted to underscore the need for a dengue vaccine to sustain the reduction of the burden of dengue worldwide.

We however modified this sentence in the conclusion paragraph to clarify as follows:

*Dengue is an important cause of febrile illness in Asia and the Americas. To sustain the reduction of the overall burden of dengue, it is recognized that dengue vaccines are needed; hence several vaccine candidates are currently in development [16]. To assess the cost-effectiveness of the potential use of a dengue vaccine but also other control measures, country-specific cost-of-illness data are needed for hospitalized and non-hospitalized cases cared for in the public and private sector.*

The authors should give their conclusive comments regarding the ability to pay for dengue, the solutions for user-fee exemptions and the Equity Fund.

Answer: we added one sentence in the limitation paragraph (second phrase of page 16) to underscore the fact that would the equity funds not exist in the study hospital; the financial burden related to hospitalized dengue cases could have been worse. We also added another
reference which described the various impacts of the health equity funds on the hospital access for the poor in Cambodia.

In addition, costs of a dengue episode may vary broadly from one health facility to another depending on how well the health equity funds operate - User-fees exemption for the poor shown in some Cambodian hospitals could worsen inequity [8,16]. Anecdotal reports made us believe that the health equity funds in Kampong Cham hospital has helped increase hospital access for the poor.

We believe that the discussions on the potential solutions or alternatives for the health equity funds system are beyond the scope this paper.

Once again thank you for the review of the manuscript,

Best regards,

Sirenda Vong