Author’s response to reviews

Title: Sharing experiences: Towards an evidence based model of dengue surveillance and outbreak response in Latin America and Asia

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Version: 2 Date: 11 May 2013

Author’s response to reviews: see over
Author's response to reviews

Title: Sharing experiences: Towards an evidence based model of dengue surveillance and outbreak response in Latin America and Asia

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Version: 2  Date: 9th May 2013
Author's response to reviews: see over
Editorial request:
1. Please give the full names and affiliations of the committees that approved the study, and add them to the revised manuscript. If the list is lengthy you may choose to add the information as an additional file.

Response: This has now been done. The manuscript now reads (page 5):

“Ethical approval was received from WHO Regional Offices (Ethical Review Boards at the Pan American Health Organisation (PAHO), South-East Asian Regional Office (SEARO) and the Western Pacific Regional Office (WPRO)) which was accepted by the study countries except for Peru where an additional ethical approval was obtained from the Institutional Review Board at Cayetano Heredia University.”
Reviewer's report

**Title:** Sharing experiences: Towards an evidence based model of dengue surveillance and outbreak response in Latin America and Asia  
**Version: 1 Date:** 11 April 2013

Reviewer: Olaf Horstick

**Reviewer's report:**  
Major Compulsory Revisions

Methods:
1. The data analysis, how the different elements were done and especially, how the data were subsequently analysed and combined is not described at all. This needs addressing and applies to all sections of the methods, but especially, how the expert consensus was organised.

**Response:** There is now a more detailed description of the methodology regarding the data collection instruments, interviewers and participants in the international meeting. The manuscript now reads (page 5-6, last paragraph in Methods section):

“The field work was done within a 5-month period (October 2011 to March 2012). The interviewers produced a comprehensive report which included a detailed analysis of the dengue epidemiology in their country, the completed data collection forms and the completed matrix with the summary of findings of each item in the questionnaire/topic guide “Evaluating dengue surveillance and response”. The information package was sent to the central team at WHO-TDR for compilation and preliminary comparative analysis. A 24 page synopsis of findings for both Latin American and Asian countries was produced. It was circulated among interviewers, Ministry of Health staff in the participating countries and WHO focal points for verification and complementation. Thereafter in June 2012 a three-day international expert workshop was organised by WHO-TDR involving all interviewers and two representatives from Ministries of Health of each country. The 45 participants were tasked to a) further validate the collected information; b) interpret and regionalise country findings and c) discuss recommendations. Expert consensus was gained through mediation by the Chairperson. The following section provides the results of a synoptic analysis of the 10 study countries.”

The methodology to derive the results for each section is also more clearly stated. The manuscript now reads (page 6):

“Comparative results of the 10 study countries included the description of the surveillance system (purpose, stakeholders and operation –based on interviews and document analysis), mechanisms of outbreak detection (timeliness, validity, validation approaches, quality assurance of data –based on interviews), country experiences with the last outbreak (based on interviews, and document analysis) and expert opinions about prospects and limitations (based on interviews) [3]. The information was summarised in the above mentioned data matrix and further analysed during the expert meeting. The
presentation of results in the text below follows a more functional order. An overview of findings is presented in Table 1.”

2. The ethics statement is not quite clear: was it that only Peru asked locally for an ethics approval and the other countries stated they did not require this? Or is it that Peru required an approval and the other countries were not asked? Please clarify

Response: Now better explained. The manuscript now reads (page 5):

“Ethical approval was received from WHO Regional Offices (Ethical Review Boards at the Pan American Health Organisation (PAHO), South-East Asian Regional Office (SEARO) and the Western Pacific Regional Office (WPRO)) which was accepted by the study countries except for Peru where an additional ethical approval was obtained from the Institutional Review Board at Cayetano Heredia University.”

3. Also, it is not clear how confidentiality was guaranteed to the participants. Please include a statement about this,...

Response: Now better explained. The manuscript now reads (page 5):

“Verbal, and in some cases, written consent was obtained from respondents. The interviewees were assured of the anonymisation of their responses and interviews took place in closed rooms with no other persons being present. The completed forms were kept in separate files and no individual names of the respondents were recorded.”

Discussion:

4. There is not much of a discussion, really, discussing the findings and putting these in to context. The discussion is a presentation of the results of the expert consensus. No “scientific” discussion of the findings has been attempted. This needs addressing.

Response: From the findings of the study, key areas were identified for improvement and are presented in the Discussion section. This rationale is now more explicitly stated, the findings more directly considered and recommendations linked to show their relevance. The manuscript now reads (pages 12-13):

“Based on the data presented in the previous section, the WHO-TDR expert meeting with country representatives identified best practices, reasons for failures and research needs. The discussion below focuses on key areas identified for improvement.

Need for distinguishing between “expected increase in cases” (i.e. seasonal peak) and “unexpected increase in cases” (i.e. an outbreak)

Our findings show that most countries did not distinguish between a seasonal rise in dengue cases, usually during the rainy season (see figure 1), and the unexpected increase in cases above a defined threshold, usually called an outbreak [2,13]; the number of reported cases exceeding expected levels is referred to as “aberrations” [14]. The need for dengue control and clinical care systems to respond differently to each of these scenarios was identified. The expected increase of dengue vectors and
subsequently of cases during the “dengue season” requires routine measures be stepped up at a relatively predicable point each year. The annual need for increased vector control staff should correspond to the weeks when the vector density increases and preparations should be made for adequate staffing levels, equipment and supply (including chemicals and/or biological agents, IEC materials and other elements of social mobilisation). Likewise, clinical services should define in their annual plans the additional staff, equipment, reagents and treatment units needed and whether clinical refresher courses are required. The dengue outbreak as an “unexpected increase of cases” requires additional efforts that are described below.

Need for an agreed outbreak definition

The data on country experiences shows a wide range of definitions used for defining dengue outbreaks, sometimes leading to confusion for stakeholders and delayed emergency outbreak responses. Discussions at the expert meeting identified the importance of a generally agreed outbreak definition. Many countries use a version of the “endemic channel” for visualising the expected case levels, based on the weekly (or monthly) average number of cases over the preceding 5 years. Above this is a line that represents +2SD; others use the median and the 3rd quartile (Fig.1).”

Given the paucity of existing literature (highlighted in our Background section), the recommendations were often generated through expert opinion at the meeting. Instances of this are more explicitly stated throughout the Discussion section. (Changes made in the manuscript throughout the Discussions section). Key findings have now been summarised in a new figure (Figure 4, page 16 and 19).

5. Limitations are not really discussed, some potential biases are mentioned, but not how strategies have been applied to reduce these, etc...
Response: The section “prospects and limitations of the study” at the beginning of the Discussion has now been re-designed and treatment strategies of the limitations described. The manuscript now reads (page 12):

“This study details a novel attempt to use a standard methodology across 10 Latin American and Asian nations to characterise country experiences of dengue surveillance, outbreak detection and response. As with all qualitative data, subjective bias may have been introduced through the opinions and perceptions of individual respondents; variability in responses was noted between country interviewees in the following areas: reporting delays, timeliness of outbreak detection and response and assessment of effectiveness of interventions. However, the use of complementary data collection methodologies, combined with several rounds of verification with country representatives at the WHO-TDR expert meeting ensured the triangulation of information collected from various sources and facilitated a high level of internal validity. Whilst any attempt to fully characterise the global situation of dengue surveillance and outbreak detection/response would require a stratified random sampling of countries, the detailed data gathered and presented here from a diversity of countries in both Latin America and Asia provides useful information towards the development of an evidence-based model contingency plan for dengue outbreaks.”

General:
6. The article requires major editing by an English native speaker, also
concentrating on the use of either American English or British English. Some items are addressed under Minor Essential Revisions

Response: Done, several minor changes throughout manuscript.

Minor Essential Revisions
Abstract
7. Abstract, second paragraph,
First sentence: Please put the country lists in alphabetical order
Response: Done

8. Last sentence: Please include the complete name of TDR, or delete and put WHO/TDR (consistently in the document please)
Response: Done as WHO/TDR

9. Abstract, third paragraph:
First sentence in brackets (In all Latin American,... ): you probably mean (In all participating Latin American,..)
Response: Corrected as suggested

10. Last sentence: I guess you mean “hospitals participating in the study”,...
Response: Corrected as suggested

Introduction
11. Introduction, third paragraph:
First sentence: studies on what? Please specify: “comparative studies on the practices of dengue surveillance”
Response: Corrected as suggested

Methods
12. Methods, first paragraph:
(Runge Ranzinger,... ), maybe better (Runge Ranzinger et al., unpublished data) Response: Corrected as suggested

13. Methods:
Please search for „lab technician“ and replace with „laboratory technician“
Response: Corrected

14. Methods: country list, please put in alphabetical order (in all lists in the document)
Response: Done

15. Methods: TDR/WHO? Or is it WHO/TDR: please use consistently in the article
Response: done as WHO-TDR
Results:
16. “All Latin American countries attempted to carry out laboratory confirmation of all dengue suspected cases, mainly with IgM and IgG ELISA and increasingly with NS-1; only during outbreaks were a small fraction of suspected cases tested: at least 10% in Brazil and 30% in Mexico.

Sounds contradictory, are suspected cases tested or not – please clarify

Response: All participating have the rule to test all suspected cases...but this is in reality not being done in 100% of cases. To clarify this, the sentence in the manuscript (page 7) now reads:

“All Latin American countries attempted to carry out laboratory confirmation of all dengue suspected cases, mainly with IgM and IgG ELISA and increasingly with NS-1; however during outbreaks a small fraction of suspected cases were tested: at least 10% in Brazil and 30% in Mexico.”

17. “The mode of data transmission within the surveillance system was mainly electronic in Brazil, Dominican Republic, most parts of Mexico and Colombia, Malaysia (“e-dengue”), Maldives and parts of Sri Lanka. Paper forms, transmitted by fax or reports by telephone were used in the Dominican Republic, most”

Not clear how it is done in the Dominican Republic – seems to be contradictory

Response: Now better explained. The sentence in the manuscript (page 7) now reads:

“The mode of data transmission within the surveillance system was mainly electronic in Brazil, Dominican Republic, most parts of Mexico and Colombia, Malaysia (“e-dengue”), Maldives and parts of Sri Lanka and Vietnam. Paper forms, usually transmitted by fax or sometimes read out over the telephone, were used in remote areas of the Dominican Republic, most parts of Peru, Indonesia, Vietnam (partially electronic) and Sri Lanka.”

18. Results, organisation of dengue vector surveillance

Please replace “communes” with “communities” – throughout the document Response: Vietnam uses the term “commune” which is a geographical unit composed of several communities. The manuscript (page 8) now indicates this specific use of this term with inverted commas: “sentinel communes”

19. Same paragraph as the “communes”, not clear what you mean by “levels presented in section “epidemic preparedness”).”

What do you mean by levels?

Response: deleted for the purpose of clarity. The manuscript now reads (page 8):

“In all countries the standard larval indices (HI, CI, BI) were used but specific indicators were used for outbreak alert (BI in Sri Lanka, HI and BI in Vietnam and Indonesia, HI in Peru).”

Discussion

20. First paragraph: not quite clear what is meant by “statistical analysis” –
nothing presented in the results, I guess,...

Response: Now deleted. The manuscript now reads (page 12):

“This study details a novel attempt to use a standard methodology across 10 Latin American and Asian nations to characterise country experiences of dengue surveillance, outbreak detection and response. As with all qualitative data, subjective bias may have been introduced through the opinions and perceptions of individual respondents; variability in responses was noted between country interviewees in the following areas: reporting delays, timeliness of outbreak detection and response and assessment of effectiveness of interventions. However, the use of complementary data collection methodologies, combined with several rounds of verification with country representatives at the WHO-TDR expert meeting ensured the triangulation of information collected from various sources and facilitated a high level of internal validity. Whilst any attempt to fully characterise the global situation of dengue surveillance and outbreak detection/response would require a stratified random sampling of countries, the detailed data gathered and presented here from a diversity of countries in both Latin America and Asia provides useful information towards the development of an evidence-based model contingency plan for dengue outbreaks.”

Tables and figures:
21. Table 2: would be good to give in a footnote an explanatory scale of the points given, seem to be varying between 1 – 4 crosses,...
Response: done. See manuscript (page 21): “++++ very strong; +++ strong; ++fairly strong; + weak”

Discretionary Revisions
22. “Warning sign”: not sure if not better to say: indicators used for early outbreak detection,... the word signs (and symptoms) is confusing here, since also used in the context of clinical warning signs in dengue cases (The latter also occurs in the results section)
Response: Now “alert signals” is consistently used

23. Introduction, second paragraph:
Last sentence: reference 7 is a systematic review not a literature review
Response: Corrected

24. As a general comment the figures are not very good when it comes to quality,....
Response: To be discussed with the editor

Level of interest: An article of importance in its field
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 delcare that I have no competing interests
Reviewer's report

Title: Sharing experiences: Towards an evidence based model of dengue surveillance and outbreak response in Latin America and Asia

Version: 1 Date: 22 April 2013
Reviewer: Raman Velayudhan

Reviewer's report:
MINOR ESSENTIAL REVISION

a) In Background section:- Ist para - dengue increases usually after the wet season (not during wet season)
Response: corrected

b) Please reduce the background section and highlight the purpose of the document.
Response: The Background has been shortened and the bullet-pointed section has been incorporated into the text. The manuscript now reads (page 3):

“Early detection of outbreaks poses a challenge, since no universally accepted operational definition of an outbreak exists and methods for distinguishing between seasonal fluctuations and true outbreaks are not generally applied. Candidate indicators for predicting a dengue outbreak, or for early outbreak detection through “syndromic surveillance” in order to trigger an early response, have been proposed [3]. However, our earlier literature review found that there were no systematic analyses or validations of these putative indicators or of their operational reliability and cost-effectiveness [4]. The published evidence-base is equally poor when it comes to defining what constitutes an effective and efficient outbreak response: remarkably, there are no proven methods recommendable for epidemic vector control [5,6] or for clinical-health systems management when there is a surge in cases. In a systematic literature review about the few documented experiences with outbreak response some criteria were highlighted [7] in relation to a) management of outbreak response (multidisciplinary response teams, Incorporation of public organisations, written information for mass media, monitoring and evaluation of all control activities), b) management of vector control (‘search and destroy’ teams, communities involvement, geographical coverage of activities, enhanced surveillance, education of households) and c) management of health services (staff training-including laboratory staff), mosquito nets in hospitals, establishing case report conferences, adequate supplies for laboratory and case management).

Following the efforts by Gubler et al. [8] to sketch the surveillance efforts in a number of dengue endemic countries, there was a first attempt to define best practices in dengue surveillance in Latin America and Asia through expert meetings [9]. This resulted in a number of useful general recommendations: dengue should be notifiable, regional disease classification applied, electronic reporting developed, laboratory networks initiated, reporting focussed at the essentials, additional studies done and early prediction of outbreaks achieved.”

The purpose of the document is more clearly stated in a separate paragraph (page 3):

“To the best of our knowledge however, comparative studies on dengue surveillance and outbreak response using the same methodologies across participant countries have not yet been published. To get a more comprehensive view of existing surveillance systems and early outbreak detection ability, we analysed the contingency plans from 11 countries, updated the systematic literature review on dengue
surveillance (publications in preparation) and report here on the analysis of dengue surveillance, outbreak detection and response in 10 countries in Asia and Latin America. The purpose is to contribute to the development of a new evidence-based model for dengue surveillance and outbreak response, adaptable to individual country requirements and capacities, combining the best of existing strategies with a framework for the acquisition of evidence for novel approaches and tools. On the basis of the findings presented in this paper a model contingency plan will be developed, adapted to country needs and prospectively tested in different settings.”

c) An organogram of an optimal situation of disease surveillance and vector surveillance should be included.

Response: This will be done in the model contingency plan to be developed on the basis of this paper and other documents

Page 7: under vector surveillance - 1% temephos should be 1% temephos WG.

Response: corrected

Page 14 Research recommendations should include studies on the possible increase in larval densities prior to possible outbreaks. how many weeks before the outbreak does larval density increase occur.? can this be a good predictive indicator?

Response: Research recommendations included as suggested. The manuscript now reads (page 15):

“Research recommendations for outbreak detection and alert signals

The research needs presented in Table 2 were complemented by the following more detailed recommendations:

a) Retrospective and prospective analysis of different thresholds for outbreak detection (eg. 2 SD above mean; 1 SD; 50% above mean) and calculation of the sensitivity and specificity of these thresholds for subsequent outbreaks.

b) Long term representative sentinel based vector surveillance to assess the association of vector indices with clinical cases and the usefulness of alert signals based on virus surveillance, vector surveillance, climate data and others.

c) Prospective comparison of monthly incidence by province with virus surveillance data to see whether virus introduction/shift is followed by outbreaks (determine positive predictive value of such events) and with what approximate time lag.”

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

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: Sharing experiences: Towards an evidence based model of dengue surveillance and outbreak response in Latin America and Asia

Version: 1 Date: 24 April 2013

Reviewer: Isabel Rodriguez-Barraquer

Reviewer’s report:

The paper by Badureen et al. presents a review of practices, experiences, strengths and limitations of dengue surveillance, outbreak preparedness, detection and response in 10 countries across Latin America and Asia. While the question is relevant and the data collection seems to have been extensive and rigorous, the paper needs major revisions in terms of data presentation/summarizing of findings and discussion. As it stands, the manuscript seems more like a “working paper” from an expert meeting than a synthesis of the findings, and is therefore difficult to read and not very informative.

Major compulsory revisions

Introduction and methods
1. These sections are generally fine. Perhaps it would be good to provide more detailed information about the areas where the interviews were conducted. Also, please be consistent with how the areas are presented. (e.g. in some instances “national level” is in parenthesis and in others it is not, the administrative level of Iquitos, Tarapoto and Moyobamba is not reported, etc.)

Response:
This section has been improved and now reads as follows (page 5 of manuscript):

“The country interviewers completed the data collection in the following areas:


Colombia: Bogota (National Institute of Health, National level), Departamento Valle del Cauca (State level)

Dominican Republic: Santo Domingo (National level); Santiago, Valverde, San Juan, Azua, and Hato Mayor (Provincial level), Laguna Salada, Esperanza y Cienfuegos (Municipality level)

Mexico: Mexico City, Ministry of Health (National level), Yukatan and Guerrero (State level)

Peru: Lima, Ministry of Health (National level), Loreto and San Martin (State or Regional level), interviews in hospitals of Iquitos (Loreto), Tarapoto and Moyobamba (San Martin; local level)
Indonesia: Jakarta (National, Provincial and District level); Yogyakarta (Provincial level), Bantul (District level).

Malaysia: Kuala Lumpur, Ministry of Health, Federal Territory of Putrajaya (National level), Selangor, Penang (State level); Klang, Hulu Langat, Gombak, Petaling, Banting, Kuala Selangor (District level)

Maldives: Male, Ministry of Health (National level), Hulumale, Thinadoo, Addu (Regional and District level).

Sri Lanka: Colombo, Ministry of Health, Medical Research Institute (National level), Colombo and Gampaha district (District level), hospital interviews in three hospitals in Colombo and Gampaha District (local level)

Vietnam: Ha Noi, Ministry of Health and National Hospital of Infectious Diseases (National level); Ho Chi Minh City (Hospital for Tropical Diseases, District 8 hospital, Pasteur Institute, University of Medicine and Pharmacy, Preventive Medicine Centre of Ho Chi Minh City); Dong Thap province (Provincial Hospital Dong Thap; Preventive Medicine Centre and Volunteer Group for Dengue)

Results
2. I believe this section needs lots of work and synthesizing. Some tables (or perhaps even figures) would perhaps be useful to compare the most relevant aspects of the systems across countries and region. Table 1 is not very informative because, while it itemizes some of the findings, it does not really allow for comparison and does not contain additional information (as compared to the text).

Response: The excessive information has been further reduced and the bullet points have been re-grouped to make reading easier. The text has been arranged into more coherent and manageable sub-sections. (Changes made throughout the Results section). The methodology used for each section is also more clearly stated. The manuscript now reads (page 6):

“Comparative results of the 10 study countries included the description of the surveillance system (purpose, stakeholders and operation –based on interviews and document analysis), mechanisms of outbreak detection (timeliness, validity, validation approaches, quality assurance of data –based on interviews), country experiences with the last outbreak (based on interviews, and document analysis) and expert opinions about prospects and limitations (based on interviews) [3]. The information was summarised in the above mentioned data matrix and further analysed during the expert meeting. The presentation of results in the text below follows a more functional order. An overview of findings is presented in Table 1.”

Table 1 provides an overview of the main findings. The main idea is not to show that some countries are worse than others, but to identify shortcomings wherever they appear and
identify areas for improvement. (As we got positive feedback from other reviewers on this table, we made only some minor changes).

One major finding of this comparative study was that, in the absence of a guide on how to develop surveillance systems and organise early detection and response to outbreaks, countries tend to develop their own systems with quite a lot of errors.

We have now added a new figure (figure 4, pages 16 and 19) in the conclusions section which highlights the essential elements of surveillance and preparedness systems that we were able to identify.

3. In addition, paragraphs are too long, include too much information on different aspects and are very difficult to follow. Perhaps it would be better to focus the results on fewer items considered to be the most relevant, and concentrate on those.

Response: The long paragraphs have now been shortened. Each heading in the results section is broken down using new sub-titles for better categorisation of information and improved readability. Some text has been shortened. (Changes made throughout the Results section)

4. The list of definition of dengue outbreaks is confusing as several countries seem to have several definitions. Perhaps it would be good to be explicit about the administrative levels that originated these definitions? Very difficult to read.

Response: The text has been modified to more explicitly state that indeed several countries have a number of sometimes contradictory definitions, leading to confusion for stakeholders. The number of bullet points has been shortened and data better grouped together to improve readability. The manuscript now reads (page 9):

“What constitutes an outbreak?

Definitions of a dengue outbreak showed marked differences and in a number of countries several, often incompatible definitions were in use. Only in 6 out of 10 countries was a fairly consistent definition applied:

a) Case numbers 2 Standard Deviations (SD) above the mean of the preceding five years shown in endemic channels (Colombia, Dominican Republic, Peru (partially), Vietnam -national level). In Brazil and Malaysia the “moving average” (mean or median) was used, i.e. the “4-weekly average” above the mean of “three 4-weekly averages” in the five preceding years

b) >300 cases per 100,000 population at local level (Brazil); > 10 cases per week in a local area (Sri Lanka). Case number within a “commune” within 2 weeks: 2-20 cases = mild outbreak; 20-100 cases=moderate outbreak; >100 cases = severe outbreak (Vietnam).

c) Two or more connected dengue cases at local level (Mexico, Malaysia, Sri Lanka partially)
d) Continuous increase of dengue cases for 2 periods (hours, days, weeks) or double the number of cases within a month compared to the previous year, or 50% increase in case fatality rate, (Indonesia)

e) No outbreak definition (Maldives); no clear outbreak definition but larval indices as trigger for response: BI <6= routine response; BI= 5-20= house-to-house checks; BI> 20 = fogging (Sri Lanka)

Discussion
5. The discussion seems to present the recommendations, based on the data, from a WHO-expert meeting. However, the link with the data is not at all clear, and the information provided under each recommendation is not always relevant or well supported by references.

Response: The link to the data is now more directly shown and recommendations linked to show their relevance. The manuscript now reads (pages 12-13):

“Based on the data presented in the previous section, the WHO-TDR expert meeting with country representatives identified best practices, reasons for failures and research needs. The discussion below focuses on key areas identified for improvement.

Need for distinguishing between “expected increase in cases” (i.e. seasonal peak) and “unexpected increase in cases” (i.e. an outbreak)

Our findings show that most countries did not distinguish between a seasonal rise in dengue cases, usually during the rainy season (see figure 1), and the unexpected increase in cases above a defined threshold, usually called an outbreak [2,13]; the number of reported cases exceeding expected levels is referred to as “aberrations” [14]. The need for dengue control and clinical care systems to respond differently to each of these scenarios was identified. The expected increase of dengue vectors and subsequently of cases during the “dengue season” requires routine measures be stepped up at a relatively predictable point each year. The annual need for increased vector control staff should correspond to the weeks when the vector density increases and preparations should be made for adequate staffing levels, equipment and supply (including chemicals and/or biological agents, IEC materials and other elements of social mobilisation). Likewise, clinical services should define in their annual plans the additional staff, equipment, reagents and treatment units needed and whether clinical refresher courses are required. The dengue outbreak as an “unexpected increase of cases” requires additional efforts that are described below.

Need for an agreed outbreak definition

The data on country experiences shows a wide range of definitions used for defining dengue outbreaks, sometimes leading to confusion for stakeholders and delayed emergency outbreak responses. Discussions at the expert meeting identified the importance of a generally agreed outbreak definition. Many countries use a version of the “endemic channel” for visualising the expected case levels, based
on the weekly (or monthly) average number of cases over the preceding 5 years. Above this is a line that represents +2SD; others use the median and the 3rd quartile (Fig.1).”

The recommendations have also been made more concise. Given the paucity of existing literature (highlighted in our Background section), the recommendations were often generated through expert opinion at the meeting. Instances of this are more explicitly stated throughout the Discussion section. (Changes made in the manuscript throughout the Discussions section).

6. Other than providing examples, I do not understand the need for figures 1, 2 and 3 (that seem to be country examples?). Maybe only one would be enough.
Response: A number of participants in the expert meeting as well as readers of the manuscript do not understand the concept of the endemic channel, the different stages of an outbreak, the use of the alert zone etc. Therefore we found the graphical presentation useful together with a country example. In fact, dengue outbreaks in other settings had a very similar pattern. The key message conveyed by each figure is now detailed in more detailed figure legends (page 19):

“Figure 1. Illustration of the seasonal variation of a vector borne disease like dengue. An example of an ‘endemic channel’ is shown here. The ‘expected increase in cases’ usually coincides with, or follows, the rainy season. The shaded area corresponds to an ‘alarm zone’ where case numbers reach levels above the mean (or median) of a preceding time period (for example 5 years). The ‘epidemic zone’ is entered when case numbers reach levels above 2 standard deviations (or the third quartile).

Figure 2. An example of an outbreak curve of case numbers from the Dominican Republic is shown here. The number of new cases crosses the “historical” +2SD line from week 1 to 17 several times before, in week 18, the case numbers definitively rise.

Figure 3. Illustration of the different phases of a dengue outbreak and different levels of response. An example of an outbreak curve from Colombia in 2009 is shown here. An ‘outbreak alert’ is identified early through a combination of ‘alert signals’, and triggers an ‘initial response’. The evolution into ‘early’ and ‘full outbreaks’ are detected early using standard definitions and trigger appropriately staged ‘early’ and ‘emergency responses’.

Fig. 4 Essential elements of a surveillance and preparedness system to ensure an early, staged outbreak response.”

7. There are big inconsistencies in the way in which each recommendation is presented and discussed (e.g. only one includes research recommendations, others present lists of response components that are not very well defined, etc).
Response: The recommendations are now presented in a more consistent way. Each section highlights a key limitation (eg outbreak detection) identified from our results, followed by a summary of the expert meeting discussions and recommendations (changes made to the manuscript throughout the discussion section). Research recommendations are now better highlighted in separate sections- the manuscript now reads (page 15):

“Research recommendations for outbreak detection and alert signals

The research needs presented in Table 2 were complemented by the following more detailed recommendations:

d) Retrospective and prospective analysis of different thresholds for outbreak detection (eg. 2 SD above mean; 1 SD; 50% above mean) and calculation of the sensitivity and specificity of these thresholds for subsequent outbreaks.

e) Long term representative sentinel based vector surveillance to assess the association of vector indices with clinical cases and the usefulness of alert signals based on virus surveillance, vector surveillance, climate data and others.

f) Prospective comparison of monthly incidence by province with virus surveillance data to see whether virus introduction/shift is followed by outbreaks (determine positive predictive value of such events) and with what approximate time lag.”

And page 16:

“Research recommendation for a staged outbreak response

The staged outbreak response suggested here will need to be tested prospectively for its feasibility, effectiveness in mitigating dengue outbreaks, cost-effectiveness (i.e. cost in relation to number of expected dengue cases avoided) and acceptance by all relevant stakeholders.”

The list of response components were based on expert opinions extensively discussed during the WHO meeting. Their rationale is more clearly defined, as is their presentation- bullet points have been removed and they are grouped together in coherent subsections (changes made to the manuscript throughout the discussion section).

Minor essential revisions

p.14 – What do you mean by increase in dengue seropositivity? In acute phase samples? In the population?
Response: In samples sent to laboratories (usually in sentinel hospitals). The level of such an increase in seropositivity will need to be further defined.
The manuscript now reads (page 14): “Increase in dengue sero-positivity (level of increase to be defined)”
Level of interest: An article of limited interest
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: declare that I have no competing interests
Reviewer's report

Title: Sharing experiences: Towards an evidence based model of dengue surveillance and outbreak response in Latin America and Asia

Version: 1 Date: 4 April 2013

Reviewer: supat chamnanchanunt

Reviewer's report:

Abstract: What kind of syndrome did you use to define?

Clinical (mainly with warning signs)

p.3 What is the criteria to define as big or small countries in each region?

Response: Examples now given in the text. The manuscript now reads (page 3):

“In order to get representative information on dengue endemic countries, five countries in Latin America (Brazil, Colombia, Dominican Republic, Mexico, Peru) and five countries in Asia (Indonesia, Malaysia, Maldives, Sri Lanka, Vietnam) were selected, based on the following criteria: a) representation of large (e.g. Brazil, Indonesia), intermediate (e.g. Peru, Vietnam) and small countries (e.g. Dominican Republic, Maldives) in each region;...”

p.3 What is the reason to exclude three countries?

Response: In order not to do a second very similar evaluation. Manuscript (page 3):

“Three countries were excluded as they had been analysed previously in a WHO-TDR supported study: Thailand, Cambodia and Bolivia (Runge-Ranzinger et al. unpublished data).”

p.7 What is the definition of laboratory confirmation?

Response: Manuscript now reads (page 7):

“In contrast, in Asian countries the laboratory confirmation of dengue –generally using IgM/IgG ELISA- was done on a small sample of patients (usually less than 10% of patients), though laboratories used the same tests as in Latin America.”

p.6 Is it the 2009 revised WHO dengue case classification?

Response: Yes, now clarified. Manuscript now reads (page 6):

“All Latin American countries and some Asian countries (Vietnam, partly Malaysia and Indonesia) used the revised WHO dengue case classification (dengue/severe dengue [5]) for clinical case management (in Brazil with modifications) and for reporting.”

p.8 Please make a discussion with expertise field for this topic

Response: Please see discussion section (now extensively edited)

p.12 If you can define how many weeks should be perform after spreading dengue cases? This will be a good expectation.
Response: We are unclear as to what the reviewer would like clarified/changed here. However, we would direct him to the changes made in the discussion section regarding the ‘staged outbreak response’ (pages 14-16) and the following statement on page 12: “The annual need for increased vector control staff should correspond to the weeks when the vector density increases”