Author's response to reviews

Title: New tools for dengue vector management: Insecticide treated materials and targeted interventions on productive breeding-sites in Guatemala

Authors:

Nidia Rizzo (nrizado@ces.uvg.edu.gt)
Rodrigo Gramajo (rodrigogramajo@gmail.com)
Maria Cabrera-Escobar (mangiecabrera@gmail.com)
Byron Arana (aranab@who.int)
Axel Kroeger (kroegera@who.int)
Pablo Manrique-Saide (msaide@uady.mx)
Max Petzold (max.petzold@nhv.se)

Version: 2 Date: 16 August 2012

Author's response to reviews: see over
Dear Editor
BMC Public Health

Please find attached a the revised manuscript MS: 9712271596982942

New tools for dengue vector management: Insecticide treated materials and targeted interventions on productive breeding-sites in Guatemala

with the modifications and suggestions from the reviewers and the editorial requirements indicated.

We have included in the following pages a point-by-point response in that order.

With best wishes
(On behalf of the authors)

Dr. Pablo Manrique-Saide
Zoology Department
Universidad Autonoma de Yucatan
REVIEWER 1

Reviewer's report
Title: New tools for dengue vector management: Insecticide treated material and targeted interventions on productive breeding-sites in Guatemala
Version: 1 , Date: 15 June 2012, Reviewer: Roberto Romi

Reviewer's report:
This paper reports a good example of a well-planned, extensive field trial on dengue vector management. The trial was carried out throughout a period of 18 months, that encompasses two dry seasons alternate to a wet one. It was aimed to evaluate the impact of two different kind of approaches (one with and one without use of larvicides), aimed to reduce vector density. Although the results of the study indicate one time more that use of the insecticides for an effective control of dengue vectors in urban environment is essential, the study is original and worthy of publication in BMC Public Health ". Nevertheless, despite the great effort carried out by the Authors, the text is often written in a confusing manner, resulting in a paper of difficult reading. However, it is my opinion that the MS need a careful (major) revision before publication. I hope that the notes reported above may help the Authors in that “not easy” revision, giving also them some more starting point for discussion.

1. Vector breeding-sites baseline. Data are no clear (example: 1.6% 0r 52% were those positive?). I think that these data should be reported as a table. I suggest to use the same table for displaying the variation in number, rate f positivity of the breeding sites and PPI by cluster and by season.

Response: We have simplified the text and made it clearer now. The following table was finally not inserted in the manuscript as the main messages are now clearer in the results section and discussion.

<table>
<thead>
<tr>
<th></th>
<th>Dry season, baseline</th>
<th>1st follow up; wet season (after 1st intervention)</th>
<th>2nd follow up (after 2nd intervention)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. water containers</td>
<td>8558</td>
<td>8965</td>
<td>9120</td>
</tr>
<tr>
<td>% containers outdoor</td>
<td>79.2%</td>
<td>85.1%</td>
<td>85.3%</td>
</tr>
<tr>
<td>Total no. of pupae</td>
<td>1783 (646 in control)</td>
<td>8885 (4375 in control)</td>
<td>4054(3022 in control)</td>
</tr>
</tbody>
</table>

2. Avoid to cite more than an Index (PPI) in order to avoid confusion

Response: We use PPI and total pupal counts as the primary outcome indices (now better described in the text and the classical Stegomyia indices as additional information.

3. Temephos. Operative p.a. concentrations, kind of formulate, method and number of treatments should be reported.
Response: Now included

4. Although very interesting, bioassays carried out by two different Institutions on PermaNet curtains obtained with different procedures gave dissimilar data that cannot be compared. Because unfortunately the good data from the CRISP, Mexico, obtained with the "operative" method (3 min exp) are limited to the 9th month, I suggest to report only the results of the HPLC analysis carried out in Liverpool (which cover all the study period, showing the persistence of the p.a), without the results of the bioassays carried out with the WHO method (1 h exp.) in order to avoid confusion.

Response: We have now made clearer that the same methods and exposure times were used by the two institutes. We have also mentioned that the results are principally the same. By using two different labs we can be quite sure that the bioassay results are correct (at least until month 9).

5. The number and localization of dengue case occurred in the study period in the whole study area should be reported and discussed.

Response: Number of confirmed dengue cases now included in description of the study site. Location was not recorded but it is now mentioned that cases could have been infected anywhere in town.

6. The different results of the two kind of intervention (no difference whit the control for the first and 1/3 of reduction of the breeding sites for the second) and their meaning in terms of of risk assessment should be stressed in the discussion.

Response: Now the discussion has been extended and possible confounding factors have been listed.

7. References; Trop Med Int Health 15:619-631 and 13:56-57 are reported twice in the list. The paper submitted to PLOS-NTD cannot be cited. A reference (by the Health Authority of Poptun) reporting the cases of dengue cited in the discussion should be added to the list.

Response: Unpublished document from the National Health Laboratory, is now mentioned in the text.

8. Tables and figures Table 4 become useless. (HPLC values may be reported in the text only) Fig 1 should be completed with a scale and with a more detailed legend. Fig 2 should be reported as a table, the present form being typical of a technical report rather than of a scientific publication..Figure 4 is redundant. data are sufficiently reported in the text.

Response: Tab 4 represent the Liverpool results. We clarified the label. Fig. 1 is now completed. Fig. 2 is changed as suggested. Fig.4 was deleted as suggested.
Title: New tools for dengue vector management: Insecticide treated materials and targeted interventions on productive breeding-sites in Guatemala

Version: 1 Date: 3 July 2012, Reviewer: Rajpal Singh R.S. Yadav

Reviewer's report: Major Compulsory Revisions

1. Title of the paper.
   Drop the word “New” from the title “New tools for dengue vector management .....”. Use of treated materials for vector management is no more new now.
   Response: Title has been changed according to suggestion.

2. Introduction
   Third paragraph: Provide clear information on what insecticide treated material were used. The sentence “....deployed as window/outdoor curtains (IT curtains) and 200L drum IT covers and targeting of productive breeding sites” is better rephrased such as “.... deployed as window and external door curtains and covers of 200L drums, and targeting and elimination of productive breeding sites of Aedes aegypti ...”. Also mention here the year(s) of the study.
   Response: All changes included as suggested. Years of the study at the end of the introduction.

   The study site, first paragraph, line 7: Is drinking water supplied by a pipeline? I believe households store water for their use, hence it is worthwhile to mention about water storage practices of the community and type of containers/drums used for this purpose.
   Response: Included as suggested.
   Design of the cluster randomized trial including sample size, line 3: clarify if the “buffer zones” were open spaces or houses.
   Response: Now clarified that these were untreated houses.
   The first intervention to be tested: ITMs as insecticide treated curtains and 200L drum Covers. This sub-title refers to use of 'ITMs as insecticide treated curtains' although they are made out of long-lasting insecticidal netting. Earlier the authors used the term “IT covers”; here they use 200L drum covers. To be consistent and clear, explain these devices once in detail in the beginning and then use simple terms such as treated curtains and treated drum covers, respectively.
   Response: Terminology changed as suggested.
Line 1: The sentence “A total of 3,079 PermaNet® 2.0 curtains (100 % polyester treated with deltamethrin 55 mg/m2 ± 25%) ....” is not clear. Did Vestergaard-Fransdsen supply readymade curtains and covers using the same materials that is used to manufacturer PermaNet 2.0 long-lasting insecticidal nets? If so, clarify this and rephrase the description as: "....PermaNet® 2.0 (deltamethrin coated on polyester netting at 55 ± 13.75 mg/m2)". The ±25% variation in chemical contents of a net constitutes a standard product specification for long-lasting nets and should be specified only if the manufacturer certified to this or if baseline chemical content of a sample of netting was determined.

Response: Now changed

Were the curtains and covers made of 75 or 100 denier netting?

Response: 75 denier, now mentioned

Line 4: Is “dumuria” a brand name? Is it treated too? If yes, at the same dose that of curtains?

Response: Dumuria is the place in India where this textile is manufactured. It has double strength and is treated in the same way as the curtains.

Line 10: How frequently the National services treated water containers in six clusters with temephos, and what dose was used?

Response: Now included (temephos 1%, target dose 1ppm)

The second intervention to be tested: ITMs and targeted intervention in productive containers. Description of the interventions applied is not properly written in this section. Improve the language.

Response: Now re-written.

Line 2: Since long-lasting nettings have a useful life of at least three years, why did they replace the old curtains? Were they lost, damaged or discarded by the households? What were the old curtains replaced with?

Response: a) 10 to 20% of nets were damaged. Therefore we replaced them all with the same Permanet 2 materials in order to create the same conditions. B) at the time of the second intervention we had not yet the chemical and bioassay results. Curtains and drum covers are exposed to sunshine and we were not sure for how long the LNs are active

Bioassays for determining bioavailability of the insecticide, paragraph 1, line 11: Reference to Abbott 1925 is missing under the "References" section. In line 11, it is mentioned that bioassays were carried out in Mexico and Liverpool. Were they repeated or was the work shared?

Response: Abbot now quoted in the references. Bioassays in Liverpool and Mexico done independently and on different samples.

Chemical analysis of netting materials. In intervention trials with treated nets or materials, it is important to determine the baseline chemical content of such materials to ensure that it
conforms to the manufacturer's specifications of the product. It is not clear if the chemical analysis was done at baseline? It is stated that "Other samples were analyzed at Vestergaard-Frandsen laboratories in Hanoi, Vietnam". What were those "Other samples"? I am not sure if a standard analytical method was used in this case. Can you give reference to such analytical tests? WHO specifications for PermaNet 2.0 describe standard analytical tests to determine deltamethrin content in deltamethrin long-lasting (coated) nets (available at: http://www.who.int/whopes/quality/newspecif/en/).

Response: This part has now been shortened in the text as we relied mainly on the Liverpool and Mexico results who used standard methodologies.

Ethical aspects. Line 2: Make it clear that informed consent was obtained from heads of all participating households and not from all participants. Right?

Response: Corrected in the text

4. Results.

Characteristics of the study population, Line 1: The information contained in Figure 2 can be included in footnote to Table 1. In that case, delete Figure 2.

Response: Done as suggested

Line 4: Move the information on house characteristics to the section “The study site”.

Response: Moved as suggested

The first intervention (ITMs) during the dry season and its acceptance, paragraphs 1 and 2: Authors have used the term “ITs”. What is this?

Response: IT= insecticide treated. Now deleted throughout the text.

Vector breeding 6 weeks after the first intervention during the wet season, paragraph 1, last line: Table 3 should be Table 2.

Response: Corrected

The second intervention (IT curtains plus targeted interventions on productive containers) during the wet season and its acceptance: This is a long sub-heading. Moreover, treated covers were also put on the drums, which the sub-heading does not reflect. Avoid using the term ITs, which makes no sense.

Response: Corrected as suggested

There is no mention in the Results section of why old treated curtains were replaced with new ones (?) at month 17, i.e. at the beginning of the second intervention phase. What proportion of them had been found damaged or missing/removed at that time?

Response: Now the information has been included

In 3 each of clusters where temephos was used, did it make any additional impact on pupal and Stegomyia indices.

Response: Now included in the discussion as a confounding variable.
In the dry season, how discarded car tyres had pupae? Was it during the wet season immediately after the dry season? “Temephos in water tanks with >200L” should be “Temephos in water drums with >200L in 6 of 10 clusters”. Instead of using the term bioavailability, use “bio-efficacy of treated curtains and covers”. Clearly mention that impact was measured six weeks after the implementation of second intervention (17 months after baseline).

Response: Changed as suggested. Instead of “bioavailability” we put “insecticide residual activity” taken from the WHO-WHOPES publication in 2006.

Chemical analysis of ITs
Authors have interpreted that the deltamethrin content of treated curtain and covers showed satisfactory results. In case of PermaNet 2.0, the acceptable deltamethrin content should be 55 ± 13.75 mg/m2 i.e within the range of 41.25–68.75 mg/m2. Results of chemical analysis show that samples of curtain and covers tested at various timelines had very a low to a very high chemical content (when taking into account standard deviation of the mean content). Thus, many of them had deltamethrin content beyond the acceptable safety limits. Higher chemical content may pose risk to the users and overestimate performance, while lower doses make the product poor performing under operational conditions. Authors should clearly bring out this limitation in the discussion to better inform the readers and emphasize the need for use of good quality treated materials, which should be ascertained at the baseline or procurement stage.

Response: We have deleted the few chemical tests of Dumuria textile in Vestergaard labs as this part does not have contact with the water, the textile is much thicker and stronger than the netting material and the tests were done with a different methodology. We use the Liverpool tests in Tab 4 which show a range of 54 to 64 mg/m2. The variation may be due to exposure to sunshine or shade which is also reflected in the results from Mexico and mentioned now in the discussion.

Cost analysis of the intervention, line 4: The authors have used the term ITNs for curtains and water container covers. Use the terms consistently rather than ITM, ITs, IT curtains, IT covers, etc. Fig. 5 is actually Fig. 4. Table 5 gives all the details of costing, hence Fig 4 is unnecessary. I did not find reference to Table 5 in the text.

Response: Corrections done according to suggestions.

5. Discussion
Bioassays and chemical analysis, line 4: PermaNet 2.0 nettings are manufactured by a coating technology, therefore migration of deltamethrin content from within the fibres under sunlight exposure is not the most likely reason of increase in deltamethrin content. The variation in chemical content was most probably due to variation in chemical content of the treated curtains and covers supplied.
Response: Now mentioned in the discussion.

6. Abstract

   Methods: mention year of the study, avoid use of abbreviated terms IT or ITM; rephrase 'coverage of windows/outdoors' to 'coverage of windows and exterior doorways with curtains treated with deltamethrin at 55mg/m2 and of 200L drums with similar treated material’; rephrase “larvicide’ to “larviciding with temephos” and change 'residual quantity of the insecticide’ to “insecticidal content’.

   Response: Done

Minor Essential Revisions

   Methods, The study site, first paragraph, line 6: correct ‘story’ to ‘storey’.
   Methods, Design of the cluster randomized trial including sample size, Line 4: correct “meters” to ‘metres’.
   Methods, Analysis of coverage and people’s acceptance, paragraph 1, line 5: Expand the term KAPs.

   Response: All changes included as suggested

   Results, Vector breeding at baseline during the dry season, paragraph 2, line 4: Suffix HI, CI and BI after their respective terms in this paragraph.

   Response: Done

   Discussion, Cost, line 3: Correct ‘stationary’ to ‘stationery’

   References: Esu et al (2010) and Vanlerberghe et al. (2011) are not quoted in the text.

   Response: Corrected
ADDITIONAL EDITORIAL REQUIREMENTS:

(1) Title page: Please include the email addresses of all authors in the title page. A title page should contain; Title, Author list, Affiliations (department names, institution name, street name, city, zip code, country), email addresses. The author list and email addresses must be identical in the manuscript file and on the submission system, and it must be clear which affiliation pertains to each author.

Response: Done

(2) Abstract: Please rename the 'Context and objectives' to 'Background.'

Response: Done

(3) Competing interests: Manuscripts should include a Competing interests section. This should be placed after the Conclusions/Abbreviations.

Response: Done

(4) Authors' Contribution: Please include an Authors' Contributions section after Competing interests.

Response: Done