Author’s response to reviews

Title: A systematic review of the economic impact of rapid diagnostic tests for dengue

Authors:

Jacqueline Kyungah Lim (kajlim@gmail.com)
Neal Alexander (Neal.Alexander@lshtm.ac.uk)
Gian Luca Di Tanna (g.ditanna@qmul.ac.uk)

Version: 1 Date: 03 Nov 2017

Author’s response to reviews:

Thank you for communicating with us on the review outcomes. Please find enclosed our revised manuscript (BHSR-D-17-00676) entitled, “A systematic review of the economic impact of rapid diagnostic tests for dengue”, Lim, et al. This work was revised according to comments and feedback of the reviewers. We appreciate comments from the reviewer and provide response and clarification as below. Editor Comments:Yen Wei Lim (Reviewer 1): In response to reviewer 1’s comments, we revised the manuscript to make it more clear about our findings. Also, the search was extended to cover the period since the initial search. This found two studies (two articles and one abstract) found. In order to comprehensively describe findings obtained from the search which combined dengue and RDT with cost/economic, we decided to keep the search focus broad. Thus with the purpose of the search to document evidence of economic impact of dengue RDT use, including individual patients’ cost-saving by Mitra et al. as well as cost-effectiveness of RDT by Lubell et al. it is from the point of view of cost-effectiveness of RDT or from the perspective of financial impact of RDT in reducing the cost-of-illness of dengue (early diagnosis possibly leading to cost-saving). In the discussion, we try to distinguish two conclusions to be drawn from those two studies.. Minor: Item no. CommentsResponse1Methods: Please include the exclusion criteria as well for the search methodology. This was included in the methods section2Results: Please elaborate more on the articles reviewed (Hang et al., Phuong et al. & Blacksell et al.) and try to link them to the discussion part. The review was re-done with expanded search terms, following suggestions of reviewer #2, and additional searches led to more specific outcomes. Also, we covered extended period (March 2015 to September 2017) which were not included in the previous search and we found more relevant articles that were published in 2016. With new articles, the previously reviewed articles were removed. Following comments from reviewer 2, we decided to re-do the search by adding economic as a key search term and narrowing the search with inclusion of “dengue and RDT” instead of just “dengue”. Thus, there were some changes in the search outcomes. For the articles selected, we tried to elaborate more on the articles selected for data extraction. 3Discussion: Suggest to restructure the flow by discussing the cost of disease burden of dengue first and then continued with how the early detection test may reduce the dengue burden. In the new search, we found two studies that reported on economic impact of RDT use for dengue. In accordance with the main study findings, we kept the flow in the discussion where we discuss further on the articles and review outcomes and then discussing cost of dengue burden and
how it would be important to have future studies on this topic to determine economic impact associated with use RDT for early diagnosis of dengue.4Reference: Please add the date access for web-source reference. This is now reflected in the references list. 5Sentence 161: the word "combo" looks informal. This has been revised. 6Sentence 161: please spell out the abbreviation of "NS1" in the first appearance of manuscript. This has been revised. 7Sentence 204: Duplication of "that". This sentence was removed in the revision. 8Sentence 205 - 207: Rephrase the sentence. This has been revised. 9Sentence 295: Please add a full-stop (".") after "regions" . This has been revised. Annelies Wilder-Smith (Reviewer 2) Item no. Comments Response 1It is important to investigate and report on the economic impact of Rapid diagnostic assays for dengue surveillance, control and clinical management. I hence commend this paper. However, the research question is not clearly spelled out, and the introduction is convoluted with text not directly relevant to the economic impact of diagnostics, such as describing the Phase 3 vaccine trial. It is also unclear whether the authors only want to study RDT's or all dengue diagnostic assays (because in the introduction they describe all diagnostic assays). We have further clarified and defined the research question. This literature review is to document any evidence of economic impact of dengue RDT use, whether from the point of view of cost-effectiveness of RDT or from the perspective of financial impact of RDT in reducing the cost-of-illness of dengue (early diagnosis possibly leading to cost-saving). We tried to make introduction more relevant to dengue diagnostics, more focused on the RDTs. 2The conclusions hence do not add much novelty to the current knowledge, e.g. the conclusions basically just state there are no studies showing an economic impact. How do the authors define "an economic impact"? The first sentence in the discussion says: "The hypothesis behind this review was that prompt detection of dengue in the early phase of illness using RDT leading to economic benefit in terms of patients' cost of illness." - this hypothesis needs to be better introduced in the introduction to allow for a better logical flow of the manuscript. The value of a systematic review is driven by the research question, which is currently unclear in the manuscript. The authors need to rewrite the paper by giving it more structure, focus and clarity. The current interpretation of the paper is too nonspecific, diffuse and does not add novelty. We conducted additional searches (adding "economic" to "cost" as a search term and narrowed the search by replacing the general term 'dengue' to 'rapid diagnostic assays for dengue') and the conclusions were changed (i.e. it no longer states that there are no studies showing an economic impact). Much of the paper is restructured and rewritten to be more clear, focused, and with additional information from new articles added. The first sentence in the discussion is also shown in the introduction to set the tone of the review. 3E.g. the paper could be structured into: Introduction: First paragraph: Current burden of disease and shortcomings in dengue diagnostics. Second paragraph: RDTs - what are they? List the NS1 and duo assays. How sensitive and specific? What is known about the cost of RDTs? Third paragraph: Why are RDTs important? E.g. separate the importance in the context of surveillance and control (a more public health perspective) and clinical management (an individual perspective). Why could early information on the diagnosis have an economic impact? (e.g. refer to the hypothesis in the first sentence of the discussion, which should be part of the introduction, and then discussed in the discussion) Fourth paragraph: the objective of the systematic review. The manuscript has been revised following the reviewer’s suggestions. 4Methods: The authors emphasize the 'economic impact' of RDTs, both in their introduction as well as in the discussion. However, they limit their search terms to "cost" only. "Cost" is usually related to cost of illness, cost of the diagnostic assay, out of pocket costs, etc. - but may not refer to economic impact. I am hence not surprised that the authors did not find anything on economic impact. I would suggest to add "economic" to "cost" as a search term. If the