Author's response to reviews

Title: The burden of pertussis in low and middle-income countries since the inception of the Expanded Programme on Immunization (EPI) in 1974: a systematic review protocol

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To the Editor

Thank you for allowing us to resubmit our revised manuscript, titled “The burden of pertussis in low and middle-income countries since the inception of the Expanded Programme on Immunization (EPI) in 1974: a systematic review protocol” to the Systematic Reviews journal. Below are our responses to the review comments. The amendments themselves are contained in the numbered-line accompanying manuscript.

Please note that we have added a section to the manuscript containing a list of abbreviations as requested (Lines 270-276). All changes made have been highlighted in yellow.

Reviewer's report: General:

This review is important because it will show gaps in data availability of data or otherwise on the epidemiology of pertussis in LMIC. There may be silent resurgences, which go largely unnoticed and is increasing the prevalence of childhood mortality.

Major Compulsory Revisions: Types of Studies:

Comment 1:

The systematic review will include "cross sectional, cohort and surveillance studies". The authors will need to provide more information on how these different types of studies will be managed especially in quality assessment, risk of bias and analysis. Are there methods to assess their qualities as separate study type as well as analysis or will they be pooled and assessed with same criteria and standards?

Response to comment 1:

The quality assessment tool that we propose to be use will enable us to conduct quality assessment of all the mentioned study designs as previously done by Wasserman S et al., Systematic Reviews 2013 (reference number 18).

Only studies that show homogeneity (detail provided in the data synthesis section, line 224-225) will be pooled together. However this step (pooling the studies) will be conducted after the studies have been selected through the inclusion criteria specified. To address this comment, we have added the following statement:

“This assessment criterion is comprehensive and sufficient for the different types of study designs that will be selected for inclusions (Lines 212-213).”
Comment 2a:

Data Synthesis, paragraph 1 - Authors should provide more details on methods of analysis and how different types of data will be dealt with. Some of the secondary outcomes cannot be reported as "incidences and/or prevalence". How will other continuous or categorical data be analyzed? It may be necessary to provide information on how the authors intend to deal with the limitations in determining incidence/prevalence from cohort studies.

Response to comment 2a:

Our primary outcome is the prevalence or and incidence data. Therefore, studies for which prevalence or incidence cannot be determined (i.e. no determinable numerator in the form of clearly defined cases or no obvious denominator representing the population base that gave rise to the cases) will fail the inclusion criteria.

We have added the following statement on the analysis of the continuous and categorical data where applicable:

“Proportions as percentages will be used to depict vaccination status, case fatality rate and HIV prevalence while deaths per 100 000 population will be used to represent mortality rate (Lines 234-235).”

We anticipate some limitations with cohort studies such as loss to follow up. The interpretations of the results from such studies will be guided by the quality assessment that will be subjected to all the studies.

Reviewer comment 3

Data Synthesis, paragraph 3 - Sub-group analysis will be done based on the income level of the countries as low, lower and upper middle income countries. Please provide a specific criteria for placing countries in each of the categories or a citation to point readers to the source where this classification is defined.

Response to comment 3:

The criteria set down by the World Bank will be used to classify countries by income level. An amendment containing the relevant references has been added to the manuscript (Lines 227-229). The statement reads thus:

“Subgroup analysis will be conducted based on the income level of the country as defined by criteria set down by the World Bank using the World Bank Atlas method (Low, Lower and Upper middle income countries).[21, 22]"
References added (Lines 343-347):


Minor Essential Revisions:

Discretionary Revisions:

Comment 4:

Data Synthesis, paragraph 3 - Authors may consider a sub-group analysis to include hospital based vs population based survey as pooling results from both populations may mask the differentials in incidence/prevalence usually experienced from these research populations.

Response to comment 4:

We agree with the suggestion. We have amended the manuscript to reflect this addition as follows:

Other variables that will be considered for subgroup analysis are: age group, HIV status (if indicated), HIV prevalence in the study country at the time of the study, diagnostic criteria, period in which the study took place, vaccination coverage as well as the location of the study (hospital versus population based). (Lines 231-232).

We would like to thank the reviewer for very insightful comments.

As indicated in the initial submission, the study has received no external funding and the authors have no conflict of interest to declare.

Thanking you anticipation.

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