Author’s response to reviews

Title: Knowledge, attitudes and practices on adolescent vaccination among parents, teachers and adolescents in Africa: A systematic review protocol

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Author’s response to reviews: see over
Dear Editor:

Ref: MS: 6524571041340070 -Response to reviewer comments

Thank you for reviewing our manuscript. The manuscript has benefited from the peer review process and we are very thankful.

We trust the revised manuscript will receive a positive consideration to be published in your journal.

Below, we have provided a point-by-point response to the reviewer comments.

Best regards,

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Response to reviewer comments

Reviewer 1: Alexander Tsirtsavadze

Reviewer 1, comment 1: Will the authors register the protocol with the PROSPERO? Once registered, please include a statement with the registration number in the beginning of Methods section.

Response to reviewer 1, comment 1: Yes, we have registered the protocol with PROSPERO. In our revised manuscript, we have stated about the registration of this protocol in the abstract and at the beginning of methods section, page 8:

“This review protocol is registered with the PROSPERO International Prospective Register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO), registration number CRD42014010395”[35].

Reviewer 1, comment 2: Introduction; Page 6, 1st paragraph. The authors state that adolescent immunisation programmes are non-existent or have a suboptimal coverage in African countries. Will the authors back up these statement by providing relevant literature citations/references?

Response to reviewer 1, comment 2: We have added a reference link (http://www.vhpbo.org/files/html/Meetings_and_publications/Presentations/LJUS22Shapiro.pdf) to back up this statement in our revised manuscript, page 4:

“However, routine adolescent immunisation programmes are non-existent in most African countries [7].”

Reviewer 1, comment 3: Objective; Page 7. I would suggest dividing the review objective into two parts:

a) To assess the knowledge, attitudes and practices (KAP) on adolescent vaccination among parents, teachers and adolescents in Africa

b) To assess/evaluate the effect of KAP on adolescent vaccines’ uptake in Africa

Response to reviewer 1, comment 3: We agree with the suggestion. We have divided the objective in the revised manuscript, page 7:

a) To assess the knowledge, attitudes and practices (KAP) on adolescent vaccination among parents, teachers and adolescents in Africa

b) To assess the effect of KAP on adolescent vaccines’ uptake in Africa

Reviewer 1, comment 4: Methodology; Pages 8-12. This section needs some re-organization of its sub-sections. Specifically, the sub-sections should be in the following order:

- Study eligibility criteria (inclusion/exclusion criteria by study design, population, intervention, study outcomes, setting, publication type: full text/abstract, language, publication status)
- Search strategy
• Study selection
• Data extraction
• Study quality (e.g., risk of bias, reporting quality) assessment
• Data analysis and synthesis

Response to reviewer 1, comment 4: In our revised manuscript, we have re-organised the method section. We have yellow highlighted the re-organised section (pages 8-12) in the attached revised manuscript.

Reviewer 1 comment 5: Methods; Page 8.

• ‘Study eligibility’, ‘Search strategy’, Study selection’, ‘Data extraction’, ‘Assessment of Study quality’ and ‘Data analysis/synthesis’ should be the same level subheadings, whereas inclusion/exclusion criteria by study design, population, etc. need to be lower level subheadings because they all fall under ‘Study eligibility criteria’ section

• Study quality (e.g., risk of bias, reporting quality) assessment
• Data analysis and synthesis

Response to reviewer 1, comment 5: The method section of the revised manuscript is re-organized as suggested. We have reduced the font size of the following subheadings “study design, study participants, intervention and outcomes” to font size 11. These changes are highlighted in yellow in the attached revised manuscript”.

Reviewer 1 comment 6: Methods; Page 8. Please, change ‘Study selection criteria’ and ‘Type of studies’ to ‘Study eligibility criteria’ and ‘Study design’ respectively

Response to reviewer 1, comment 6: We have effected these suggested changes to “Study eligibility criteria” and “Study design” respectively in the revised manuscript.

Reviewer 1 comment 7: Method. The merits/description of qualitative research seems out of place in the ‘Study design’ section (1st paragraph on page 8) and could be moved to Discussion section

Response to reviewer 1, comment 7: In our revised manuscript, this section has been moved to discussion, page 14.

Reviewer 1 comment 8: Methods; Page 9. Type of intervention – not applicable: if one of the aims of the review is the assessment of the effect of KAP on adolescent vaccines’ uptake in Africa would not ‘KAP’ be an intervention and ‘uptake of vaccines’ an outcome?

Response to reviewer 1 comment 8: For our primary objective, knowledge, attitudes and practices (KAP) is not an intervention, rather, an outcome. However, for our secondary objective we agree with the reviewer that KAP is an intervention. We do not anticipate many studies that evaluate KAP as an intervention and vaccines uptake as an outcome. However, the few studies that will be selected and enable us to address the secondary objective, we will treat KAP as an intervention. To address
this comment, we have added the following information on page 8 of the revised manuscript:

**Type of intervention**

- Knowledge, attitudes and practices (KAP) for interventional studies
- No intervention applicable for all the other eligible studies in this review.

Reviewer 1 comment 9: Methods; Page 9. Primary outcomes; Will the authors measure uptake of vaccines?”

Response to reviewer 1, comment 9: Yes. In our revised objectives and outcomes (secondary outcome) on page 9 we have now stated we will measure the vaccine uptake:

**Secondary outcome**

Vaccination coverage (i.e. proportion of adolescents who have received the recommended doses of the vaccine in a study)

Reviewer 1 comment 10: Search strategy on the systematic reviews; Page 10. Please delete ‘on the systematic reviews’ from the above sub-section heading; should read ‘Search strategy’

Response to reviewer 1, comment 10: This method section, page 9 has been deleted as suggested and reads as follows in the revised manuscript: “Search strategy”

Reviewer 1 comment 11: Search strategy. Indicate years/dates for which the databases and other sources will be sought

Response to reviewer 1, comment 11: We have addressed this comment, page 10 under search strategy sub-heading:

“We will search both published and unpublished articles with no language restrictions from 1950 to 31 August 2014.”

Reviewer 1 comment 12: Search strategy. Will the authors search unpublished studies (i.e., grey lit)? explicit statement and justification for not doing it would be useful

Response to reviewer 1, comment 12: Yes, we will include studies in grey literature. In the revised manuscript, we have addressed this comment as shown on page 10.

Reviewer 1 comment 13: Study selection; Page 10. Will the authors screen their studies using a pre-defined and piloted screening form containing their eligibility criteria?

Response to reviewer 1, comment 13: Yes. The first page on data extraction form will evaluate study eligibility (appendix 2, page 26). In addition, we have stated the details of the screening process for selected studies in the methods section under data extraction subheading, page 11 in our revised manuscript:

“Data will be extracted from selected studies independently by two authors using standardised data-extraction forms (appendix 2). Disagreements on study selection and data extraction will be resolved by consensus between the two review authors, failing which a third author will arbitrate. Prior to use, the extraction form will be piloted on at least four studies identified randomly from the list of included studies.”

Reviewer 1 comment 14: Study selection; Page 10. Will the authors provide the study flow chart (graphical depiction of study screening, eligibility, and exclusion processes)?

Response to reviewer 1, comment 14: Yes and we have stated that in the methods section under study selection, page 11 of the revised manuscript:

“A PRISMA flow chart will be used to summarize the search and selection of studies for the review”.

Reviewer 1 comment 15: Data extraction Data synthesis; Page 11. Please, delete ‘Data synthesis’ after ‘Data extraction’

Response to reviewer 1, comment 15: We have deleted the text as suggested by the reviewer to read: “Data extraction”

Reviewer 1 comment 16: Will the data be extracted by two independent extractors? How the conflicts will be resolved?

Response to reviewer 1, comment 16: Yes, data will be extracted by two independent reviewers and a third independent author will be consulted when the two data extractors disagree. In the revised manuscript, we have clarified this data extraction process in the methods section, page 11:

“Data will be extracted from selected studies independently by two authors using standardised data-extraction forms (appendix 2). Disagreements on study selection and data extraction will be resolved by consensus between the two review authors, failing which a third author will arbitrate. Prior to use, the extraction form will be piloted on at least four studies identified randomly from the list of included studies.”

Reviewer 1 comment 17: I cannot find Appendix 2 at the end of the manuscript, will the authors add it?

Response to reviewer 1, comment 17: We have added appendix 2, which is on page 26 of the revised manuscript.
Reviewer 1 comment 18: Data extraction section needs more detail. For example, will the authors specify what type of data (e.g., study and population characteristics, outcomes, etc…) will be extracted from included studies?

Response to reviewer 1, comment 18: We have added more details as suggested by the reviewer under the data extraction subheading on page 11 of the revised manuscript:

The data extraction will include the following eligibility criteria:

1. Setting of the study (city and country).
2. Study design- randomised control trials (RCTs), controlled before-and-after studies (CBAs), interrupted time series designs (ITS), cohort studies, case-control studies, cross-sectional studies, focus group discussions, in-depth interviews, direct observation, case studies, and ethnography and action research.
3. Type of participants- adolescents, caregivers and teachers.
4. Types of outcomes measured- knowledge, attitudes and practices.

Reviewer 1 comment 19: How the authors will handle missing data?

Response to reviewer 1, comment 19: We will write to the corresponding authors in studies with missing data. If we do not get a response or are unable to contact the corresponding author, we will evaluate and discuss the possible effects of such missing data on the review.

In the revised manuscript, we have added a subheading of dealing with missing data on page 12:

“If necessary, we will contact the corresponding authors of included studies to give us any missing data. We will describe missing data for each included study and discuss the extent to which the missing data could alter our results.”

Reviewer 1 comment 20: How the authors will handle missing data? Data analysis and synthesis; Page 11. This section is little bit vague and needs more detail. Specifically, provide what methods will be used to synthesize the results (mixed, quantitative, etc…). If there is any quantitative data, how this will be handled? What will be the summary (statistical parameters) of association and variability measures for each individual study? Is there any subgroup/sensitivity analysis planned in order to explore clinical and methodological sources of heterogeneity? I am not sure if publication bias is applicable to this review, but it would be useful if the authors provide a statement to this effect. This type of bias may be relevant if non-English language publications are excluded.

Response to reviewer 1, comment 20: On dealing with missed data, we have addressed this comment: please refer to “Response to reviewer 1, comment 19”.

The data analysis and synthesis section has been revised to give clarity. We have separated the analysis and synthesis of qualitative and quantitative data in the revised manuscript as shown on page 12-13:

“Qualitative data analysis and synthesis"
Qualitative synthesis for this review will be based on thematic synthesis of qualitative research. By examining the findings of each included study, key descriptive themes such as demographics, study design and findings of the studies on levels of knowledge, types of attitudes and practices on adolescent vaccination will be independently coded by two authors. Once all of the included studies has been examined and coded, the resulting themes and sub-themes will be discussed within the study team to examine their relationship to the research questions. The qualitative synthesis will then proceed by using the ‘descriptive themes’ to develop ‘analytical themes’, which will be interpreted in reference to the research objective.

Quantitative data analysis and synthesis

We will express the result of each study as a risk ratio with its corresponding 95% confidence intervals for dichotomous data, or mean difference with its standard deviation for continuous data. We will group studies that compare broadly similar types of outcome to get feasible results on an overall estimate of effect. Log relative risks and standard errors of the log relative risk will be calculated for intervention studies. The log relative risks for intervention studies will be analysed together using the generic inverse variance method in Cochrane Review Manager. Random effects meta-analysis will be preferred due to anticipated heterogeneity in study results. If we encounter variation in reported outcome measures between studies, we will not pool the results but summarize the findings in a narrative format. Sub-group analyses may be conducted if possible, taking into account but not limited to: age of target population, vaccine given, setting of the studies, and country income status.”

Section on subgroup analysis on page 13 have been added and it states

“Sub-group analyses may be conducted if possible, taking into account but not limited to: age of target population, vaccine given, setting of the studies, and country income status.”

Reviewer 1 comment 21: The authors mentioned ‘strength of evidence’. If they plan to only assess the quality of included studies (without grading overall quality using GRADE system), I suggest to delete this term.

Response to reviewer 1, comment 21: We plan to do grading on the quality of evidence and this statement is revised in data analysis and synthesis section on page 13 of the revised manuscript.

“Both qualitative and quantitative findings will be interpreted taking into account the methodological quality of the studies and the strength of evidence. The basic principles of the GRADE approach will be applied to the synthesis of both quantitative and qualitative evidence [38].”

Reviewer 1 comment 22: Discussion; Page 12. Will the authors highlight strengths/limitations in identified evidence (e.g., amount, validity, applicability, etc...)?, Will the authors highlight strengths/limitations of their review (any limitations in the review methods)?

Response to reviewer 1, comment 22: We have highlighted the strengths and limitations in the discussion section on page 14 of the revised manuscript:
To our knowledge, this is the first study that will attempt to use both quantitative and qualitative methods to assess and synthesise knowledge, attitudes and practices (KAP) on adolescent vaccination among parents, teachers and adolescents in Africa.

The combination of qualitative and quantitative evidence in this study will make it more relevant and robust.

A potential limitation of our study is high heterogeneity of studies and therefore not possible to conduct a meta-analysis.

Reviewer 1 comment 23: Discussion; Page 12. Will the authors highlight future research and policy implications of this review?

Response to reviewer 1, comment 23: Yes. We have highlighted the potential implications of this review on page 14 of the revised manuscript:

“We anticipate our findings will be utilised to improve adolescent vaccination coverage in Africa through development of new policies on adolescent vaccination programmes.”

Reviewer 2: Kumanan Wilson

Reviewer 2 comment 1: Clarify how intervention and baseline studies will be examined. The methods are generally well presented with a few exceptions. As an overall objective I was unclear as to whether the review would just look at baseline attitudes or the impact of interventions on changing attitudes. These are substantially different subject matter areas and if the review is going to examine both of them they should be treated separately. The former is likely best examined through qualitative and cross-sectional studies while the latter through intervention studies and may lend itself to synthesis.

Response to reviewer 2, comment 1: Largely our focus is on the assessment of baseline KAP. This is our primary objective and we will utilize cross sectional studies.

In rare cases we may find KAP interventional studies and we plan to evaluate if indeed improved KAP may improve the vaccines uptake among adolescents, this is our secondary objective and interventional studies will be used to address this objective. We have modified our methods section as follows:

Primary objective
a) To assess the knowledge, attitudes and practices (KAP) of adolescent vaccination among parents, teachers and adolescents in Africa

Secondary objective
b) To assess the effect of KAP on adolescent vaccines’ uptake in Africa”

Primary outcomes
Knowledge, attitudes and practices of adolescent vaccination among teachers, adolescents and parents

Secondary outcomes

Vaccination coverage (i.e. proportion of adolescents who have received the recommended doses of the vaccine in a study)

Reviewer 2 comment 2: Consider grey literature to be included in search strategy. The search strategy should seek to identify studies from the grey literature. NGO's and international organizations (WHO, UNICEF) in particular may have examined this question and published the results in reports.

Response to reviewer 2, comment 2: We agree with the suggestion. In our revised manuscript, we will search for grey literature as stated on page 10. The grey literature website has been added to the search strategy:


Reviewer 2 comment 3: Have separate and more detailed discussion of data synthesis for quantitative and qualitative components. I have concern with how the quantitative and qualitative methodology is mixed together. In particular, wrt data synthesis, I would prefer if they were explicitly separated.

Response to reviewer 2, comment 3: The section on data analysis and synthesis, page 12 has been explained in details. The section has been subdivided into two sections of qualitative and qualitative analysis as suggested by reviewer two:

“Qualitative data analysis and synthesis

Qualitative synthesis for this review will be based on thematic synthesis of qualitative research. By examining the findings of each included study, key descriptive themes such as demographics, study design and findings of the studies on levels of knowledge, types of attitudes and practices on adolescent vaccination will be independently coded by two authors. Once all of the included studies has been examined and coded, the resulting themes and sub-themes will be discussed within the study team to examine their relationship to the research questions. The qualitative synthesis will then proceed by using the ‘descriptive themes’ to develop ‘analytical themes’, which will be interpreted in reference to the research objective.

Quantitative data analysis and synthesis

We will express the result of each study as a risk ratio with its corresponding 95% confidence intervals for dichotomous data, or mean difference with its standard deviation for continuous data. We will group studies that compare broadly similar types of outcome to get feasible results on an overall estimate of effect. Log relative risks and standard errors of the log relative risk will be calculated for intervention
studies. The log relative risks for intervention studies will be analysed together using the generic inverse variance method in Cochrane Review Manager. Random effects meta-analysis will be preferred due to anticipated heterogeneity in study results. If we encounter variation in reported outcome measures between studies, we will not pool the results but summarize the findings in a narrative format. Sub-group analyses may be conducted if possible, taking into account but not limited to: age of target population, vaccine given, setting of the studies, and country income status.”

Reviewer 2 comment 4: Include Appendix 2. I could not find appendix 2 which had the data extraction form.

Response to reviewer 2, comment 4: In our revised manuscript, we have added appendix 2 which is on page 26.

Reviewer 2 comment 5: More detail could be provided on how the qualitative data synthesis will take place. The authors may want to consider the following: http://www.ncbi.nlm.nih.gov/pubmed/16223649.

Response to reviewer 2, comment 5: Thank you for this useful reference that has given us a good idea on structuring our methods. The methods section on data analysis and synthesis (qualitative analysis) has been revised as shown on page12:

“Qualitative data analysis and synthesis

Qualitative synthesis for this review will be based on thematic synthesis of qualitative research. By examining the findings of each included study, key descriptive themes such as demographics, study design and findings of the studies on levels of knowledge, types of attitudes and practices on adolescent vaccination will be independently coded by two authors. Once all of the included studies has been examined and coded, the resulting themes and sub-themes will be discussed within the study team to examine their relationship to the research questions. The qualitative synthesis will then proceed by using the ‘descriptive themes’ to develop ‘analytical themes’, which will be interpreted in reference to the research objective.

Reviewer 2 comment 6: Consider subgroup analyses. Will any form of subgroup analysis or sensitivity analysis be conducted? Even if the results are presented narratively differences in KAP amongst subgroups could be examined. This would be particularly important geographically given the differences between countries in Africa. For example subgroup analyses based on GDP categories could be conducted.

Response to reviewer 2, comment 6: We agree with the suggestion and have now added a subgroup analysis section on 13 indicating the variables that will be considered for this type of analysis:

“Sub-group analyses may be conducted if possible, taking into account but not limited to: age of target population, vaccine given, setting of the studies, and country income status.”

Editorial requests:
1) Please include your PROSPERO registration number at the end of your abstract. Alternatively, if you have not registered with PROSPERO then please mention this in your Methods section.

Response to Editorial request 1: The protocol is registered with PROSPERO and we have added the information on the registration of the protocol in the abstract and the methods section, page 8: “This review protocol has been published in the PROSPERO International Prospective Register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO), registration number CRD42014010395.”

2) Please include a list of abbreviations used in the manuscript and their meanings

Response to Editorial request 2: This new section has been included and it states, page 15:

**Definition of key terms:**
Knowledge refers to the understanding of any related topic on adolescent vaccines. Attitude refers to the feelings towards adolescent vaccines, as well as any preconceived ideas that one may have towards vaccination. Practice refers to the ways in which one demonstrates the knowledge and attitude (and any other influences) through actions.