

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Impact of Point-of-Care Diagnostics on Maternal Outcomes in HIV-Infected Women: Systematic Review and Meta-Analysis Protocol
<b>AUTHORS</b>	Mashamba-Thompson, Tivani; Sartorius, Benn; Thabane, Lehana; Drain, Paul; Shi, Cynthia

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Vivian A Welch Bruyere Research Institute, Bruyere Continuing Care and University of Ottawa, Ottawa, Canada
<b>REVIEW RETURNED</b>	24-Apr-2015

<b>GENERAL COMMENTS</b>	<p>Questions:</p> <p>There is no mention in the background about the presence of HIV counseling with the point of care diagnostic test. However, the presence of counseling may influence the uptake of ART and links to successful care. Would it be useful to consider the presence or absence of counselling as explaining heterogeneity in subgroup or sensitivity analysis?</p> <p>In Table 1, maternal morbidity and child morbidity are not listed, however these are listed later in the list of inclusion criteria- should they be in Table 1 as secondary outcomes?</p> <p>Will the search process involve peer review of the electronic search strategy by an information scientist, as recommended by the Peer Review of Electronic Search Strategy (PRESS) guidelines?</p> <p>There appear to be some parentheses missing in this paragraph- eg missing ‘(’ before “reduced maternal mortality)</p> <p>“(hiv infected women) OR hiv positive women) AND point of care diagnostics) OR point of care testing) OR rapid testing) OR laboratory testing) OR laboratory diagnostics) AND reduced maternal mortality) OR (prevention of maternal and child transmission)) OR successful linkage to continuity of hiv care) OR initiation of antiretroviral treatment”)</p> <p>Should it be “prevention of mother TO child transmission in bullet below:</p>
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	<p>Evidence about POC diagnostics and laboratory based or non-POC diagnostic interventions' impact on prevention of maternal and child transmission;</p> <p>Risk of bias: suggest naming the Cochrane risk of bias tool rather than calling this the "standard criteria", since there are many available tools for assessing methodological quality</p> <p>Unit of analysis issues: How will the authors handle potential unit of analysis issues in cluster randomized trials, where women are randomized by clusters, but analyzed at the individual level.</p> <p>Add a space in the heterogeneity section in "amongtrials "</p> <p>Add a space to "asystematic" in discussion</p> <p>In discussion, the authors state that they will include qualitative data and costs data, but this is not clear from their Table 1 (PICOS) or their inclusion criteria. Could this be clarified?</p>
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<b>REVIEWER</b>	Judy Levison, MD, MPH Baylor College of Medicine USA
<b>REVIEW RETURNED</b>	08-Aug-2015

<b>GENERAL COMMENTS</b>	I am unclear on the following: This is a proposal for a study (not a completed study) and therefore not ready for publication. The proposal is well thought out, and I expect the findings to add important information to the literature. The authors could enhance the study by also reviewing the impact of POC on partner testing.
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### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name Vivian A Welch

Institution and Country Bruyere Research Institute, Bruyere Continuing Care and University of Ottawa, Ottawa, Canada

Comment: Please state any competing interests or state 'None declared': None declared

Response: The above statement has been included in the manuscript

Please leave your comments for the authors below

Congratulations on a well written protocol on an important question.

Comment: I find the research question is unclear because the research questions do not mention maternal morbidity, child morbidity or cost which are then mentioned later on in the paper. I suggest modifying this to make these questions, PICOS and inclusion criteria consistent.

Response: The research questions have been modified in line with the PICOS and inclusion criteria.

Comment: Regarding the methods and statistics, these are well documented, except I did not find a section on how you will handle potential unit of analysis issues in cluster randomized trials, for example using a variance inflation factor, and if so, how you will obtain an ICC for this analysis.

Response:

The outcome ICC and adjustment for cluster correlation can be assessed using a clustered ANOVA method with bootstrapped 95% confidence intervals (CI). This can be implemented in Stata (1). Furthermore, a random-effects meta-regression will also be employed to account for the clustering effect. Again this can be implemented in Stata. Restricted maximum likelihood estimation will be used ('metareg') (2).

Comment: Regarding potential study limitations, you justify the inclusion of English-language only trials because of funding for translation, but you do not discuss the extent to which you think this is a limitation for your study. Is there evidence of how many non-English trials are likely to be published on this topic?

Response: This is a significant limitation as excluded eligible studies that are published in other languages other than English. To date, our database search results has demonstrated that there is a limited number of randomised control trials on this topic. Therefore, the authors have agreed to include non-randomised controlled trials and observational studies to help answer the research question. The protocol has been amended in line with these additions. This information had been added in the discussion and limitation section of the manuscript.

Reviewer: 2

Reviewer Name Judy Levison, MD, MPH  
Institution and Country Baylor College of Medicine  
USA

Comment: Please state any competing interests or state 'None declared': None

Response:

Please leave your comments for the authors below

Comment: I am unclear on the following: This is a proposal for a study (not a completed study) and therefore not ready for publication. The proposal is well thought out, and I expect the findings to add important information to the literature. The authors could enhance the study by also reviewing the impact of POC on partner testing.

Response: Partner testing has been added as one of the outcomes of the study and a new search will be undertaken to ensure retrieval of articles that reports partner testing as an outcome of point-of-care testing intervention on HIV infected women.

Response to attached document

Thank you for the opportunity to review this well-written protocol on an important question- the effect of point of care diagnostics for women with HIV on maternal morbidity, mother to child transmission of HIV.

Questions:

Question 1: There is no mention in the background about the presence of HIV counselling with the point of care diagnostic test. However, the presence of counselling may influence the uptake of ART and links to successful care. Would it be useful to consider the presence or absence of counselling as explaining heterogeneity in subgroup or sensitivity analysis?

Response: The reviewer's advice has been accepted and presence or absence of counselling will be considered during subgroup or sensitivity analysis. Literature on the importance of incorporating counselling in POC diagnostic services has been added to the background section.

Question 2: In Table 1, maternal morbidity and child morbidity are not listed, however these are listed later in the list of inclusion criteria- should they be in Table 1 as secondary outcomes?

Response: Table 1 has been updated to show maternal morbidity and child morbidity in line with the inclusion criteria.

Question 3: Will the search process involve peer review of the electronic search strategy by an

information scientist, as recommended by the Peer Review of Electronic Search Strategy (PRESS) guidelines?

Response: We currently have no access to an information scientist and this is a PhD study with very limited funds. A thorough electronic search strategy process is being undertaken by reviewers and authors experienced with systematic reviews/meta-analyses.

Question 4: There appear to be some parentheses missing in this paragraph- eg missing ‘(“ before “reduced maternal mortality)

(“(hiv infected women) OR hiv positive women) AND point of care diagnostics) OR point of care testing) OR rapid testing) OR laboratory testing) OR laboratory diagnostics) AND reduced maternal mortality) OR (prevention of maternal and child transmission)) OR successful linkage to continuity of hiv care) OR initiation of antiretroviral treatment”)

Should it be “prevention of mother TO child transmission in bullet below:

Evidence about POC diagnostics and laboratory based or non-POC diagnostic interventions’ impact on prevention of maternal and child transmission;

Response: Paragraph has been updated

Question 5: Risk of bias: suggest naming the Cochrane risk of bias tool rather than calling this the “standard criteria”, since there are many available tools for assessing methodological quality

Response: The sentence has been updated and the risk bias has been named as above

Question 6: Unit of analysis issues: How will the authors handle potential unit of analysis issues in cluster randomized trials, where women are randomized by clusters, but analyzed at the individual level.

Response:

The outcome ICC and adjustment for cluster correlation can be assessed using a clustered ANOVA method with bootstrapped 95% confidence intervals (CI). This can be implemented in Stata (1).

Furthermore, a random-effects meta-regression will also be employed to account for the clustering effect. Again this can be implemented in Stata. Restricted maximum likelihood estimation will be used (‘metareg’) (2).

Question 7: Add a space in the heterogeneity section in “amongtrials “

Response: A space has been added

Question 8: Add a space to “asystematic” in discussion

Response: A space has been added

Question 9: In discussion, the authors state that they will include qualitative data and costs data, but this is not clear from their Table 1 (PICOS) or their inclusion criteria. Could this be clarified?

Response: In order to gain a more quantitative view of the impact of POC diagnostics on the target group, evidence from qualitative studies and cost-effectiveness studies of POC diagnostics will be excluded not included. The typo had been rectified in the manuscript.

Reference

1. Donner A, Koval JJ. The estimation of intraclass correlation in the analysis of family data. *Biometrics*. 1980:19-25.

2. Rogers W. Regression standard errors in clustered samples. *Stata technical bulletin*. 1994;3(13).