Author's response to reviews

Title: Systematic review of public health research on prevention of mother-to-child transmission of HIV in India with focus on provision and utilization of cascade of PMTCT services

Authors:

Shrinivas Darak (shirishdarak@gmail.com)
Mayuri Panditrao (mayuri@berkeley.edu)
Ritu Parchure (rparchur@health.usf.edu)
Vinay Kulkarni (vinay@prayaspune.org)
Sanjeevani Kulkarni (sanjeevani@prayaspune.org)
Fanny Janssen (F.Janssen@rug.nl)

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Author's response to reviews: see over
Dear Dr Patrizio Pezzotti,

Thank you for the opportunity granted to us to revise and resubmit our paper “Systematic review of public health research on prevention of mother-to-child transmission of HIV in India with focus on provision and utilization of cascade of PMTCT services” for possible publication in *BMC Public Health*.

Based on the comments by the two referees and your letter we felt strengthened in the potential of our paper. The comments to improve our paper were very valuable, and we strongly believe that by carefully addressing them the paper has improved considerably.

We paid close attention to the formatting changes in the text during revision of our manuscript. The text of the paper has been rearranged according to the checklist presented in the PRISMA statement. We have included relevant rubrics from the statement in the paper. Figure 1 gives details of the papers on PMTCT including categorization of papers considered for in-depth review as suggested in the statement. We have closely followed the formatting instructions regarding tables and figures. We would like to include both tables in the manuscript.

Please find below a point-by-point description of how we addressed the comments and suggestions made by the two referees.

We feel confident that our paper has substantially improved and that it has reached the high level for publication in *BMC Public Health*.

We look forward to hear your final decision, hoping that you will agree with us.

Yours truly,

Shrinivas Darak,
On behalf of all authors
Addressing the comments by the reviewers

Reviewer: Philippe Msellati

This article is a review of all articles published in the field of PMTCT of HIV in India in order to identify difficulties and success and also eventual gaps of research. This work is appropriate and seems to be complete. Maybe we should have expected at the end a synthesis identifying the best practices and how to implement them.

In the revised version of our paper we have included a summary at the end under the heading “conclusions” and highlight the points for further research and policy interventions. [Heading: Conclusions, 1st and 2nd paragraph, page 22-23]. One of the observations made from the review is lack of published literature on the best practices from program experiences. We identify this as one of the important lacunae in the existing PMTCT literature in India and suggest better analysis and reporting of program data on PMTCT services in India.

They are two minor essential revisions for me

1 The sentence "Approximately 3,070,000 infants worldwide were infected with HIV in 2009, and most of them were from developing countries " gives the feeling that these three millions of children were newly infected in 2009. First they are approximately 300 000 infected each year, and the total number of HIV infected children is estimated to be around 2,500 000.

   Indeed the number 3,070,000 in the manuscript was wrong and resulted from a typing error. We have corrected the error. The sentence has been changed into:

   “Globally, an estimated 370 000 children were newly infected with HIV in 2009, and most of them were from developing countries.” [Heading: Background, 2nd Paragraph, Page 4]

2 the reference Petitet et al is wrong about the name of the author. The real name is Hancart Petitet.

   The name in the reference has been corrected [reference no.35] in both the reference list and in Table 1
**Reviewer: Rodrigo Cerda**

1. This is a very useful summary of the literature on the cascade of HIV PMTCT services in India, an area that clearly merits attention. It has a thorough methodological approach, which provides a comprehensive resource and bibliography for researchers and policymakers interested in the topic. Given the overview of existing literature, the paper also adeptly points out areas that deserve further investigation.

*Thank you*

**Major Compulsory Revisions**

2. While the literature is catalogued well, the findings of the literature need to be presented more powerfully in the results to better fulfill the second stated objective of this paper: “to describe the findings of public health literature on PMTCT.” This paper would benefit from a more accessible synthesis of the literature as a whole rather than listing out findings from papers in the text. It could be useful to graphically and perhaps statistically summarize the percentage drop-outs at each step of the cascade in order to more clearly point out high-yield focus areas. The paper starts to do this in the supplementary material, particularly in the section of “Numeric summary of uptake of services.” Categories of the cascade could follow the experience of mothers in antenatal care, such as maternal access to ANC, counseling, testing, receipt of results, treatment, adherence, delivery, and linkage to care. An example of a cascade of antenatal PMTCT is presented in: Ciaranello AL et al. WHO 2010 guidelines for prevention of mother-to-child HIV transmission in Zimbabwe: modeling clinical outcomes in infants and mothers. PLoS One. 2011;6(6):e20224. Epub 2011 Jun 2. For example, after a discussion of low rates of initial testing, a synthesis of findings regarding outreach, barriers to access, and counseling and testing can be discussed as explanatory factors. Other categories described, such as Treatment of ARV’s, Obstetrics, and Infant feeding should also fit in the cascade the authors could add to this paper.

We agree that the paper would benefit from a more accessible synthesis of the literature as a whole, and we thankfully followed your suggestions for doing so.

In the results, under “Studies on experiences of implementing a PMTCT program” we currently highlight the findings on the uptake of services in the cascade. In order to do so we separated the numeric summary of the uptake of services from the main table (Table1) and included this as a separate table (see Table 2), the result of which we then describe in the text. Also, we estimated the percent drop outs among pregnant women from counselling to HIV testing (average drop out rate 14%) and of HIV infected women before receiving ARV (average drop out rate 54%). We pointed out the need to address the high drop outs of HIV infected women before receiving ARV as an important focus area. A graphical or even statistical summary of the percentage drop outs at each step of the cascade is not feasible since all the studies do not report data on all the components of the cascade. [Main heading: Results, Sub heading: Studies on experiences of implementing a PMTCT program, Sub-sub heading: Numeric summary of uptake of services in the PMTCT cascade, page 9-10]

The provided example of a cascade of PMTCT services presented by Ciaranello et al. (2011) is indeed very useful and relevant, and we adopted this categorization for our paper. The
categorization of the cascade presented in Figure 1 and described in the results section under the subheading of studies on individual components of the cascade of PMTCT services is in line with the categories mentioned by Ciaranello et al (2011). While adopting this categorization we rearranged the text accordingly and added a new paragraph on the additional category “Access to ANC” [Result, subheading-studies on individual components of the cascade, pages 12]

We have also revised the order of presenting our findings as suggested by the reviewer. While describing the findings from the literature on the experiences of implementing a PMTCT program we first discuss the low rates of uptake followed by synthesis of findings on barriers in accessing PMTCT services, outreach, cost effectiveness and integration of PMTCT with other services which is then followed by synthesis of findings on individual components on the cascade such as counselling and HIV testing, delivery care and repeat testing, ARV, infant feeding and linking women and children to postnatal care.

In addition, we improved the link between the text in the results and the tables by including reference numbers in front of the author’s name in the tables, and by including subsections while describing the studies on experiences of implementing a PMTCT program.

In the beginning of the discussion, we have included a synthesis of the findings in two paragraphs. While the first paragraph gives a synthesis of findings on the literature on experiences of implementing a PMTCT program the second paragraph provides synthesis of the findings from literature on individual components of the PMTCT cascade [Heading: Discussion, 2nd and 3rd paragraph, Page17-18].

We also rewrote the results and conclusions section of the abstract accordingly.

3. A discussion of the data itself should be included in the discussion section, and point out areas for policy interventions in addition to areas for research. Using a rubric such as the one suggested above would help to point policymakers to a need for either increasing the number of women accessing ANC, or increasing the provision of ARV’s to the particular testing facility, for example.

We agree with the reviewer regarding the need to include a discussion on the data itself and to point out the areas of policy intervention. We provided the summary of the data in the discussion section [Heading: Discussion, 2nd and 3rd paragraph, Page17-18] and discuss some of the important issues such as a loss to follow-up of women in the cascade and factors related to uptake of counselling and HIV testing in subsequent paragraphs [Heading: Discussion, 6th and 7th paragraph, Page20-21] Under “Conclusions” we currently point out the areas of policy intervention in addition to the areas of research [Heading: Conclusions, 1st and 2nd paragraph page 22-23].

Due to a lack of published literature on many components of the cascade of PMTCT, which itself is one of the important findings of the paper, we could not use the rubrics in the cascade for pointing out areas for policymakers. That is, we can only emphasize the need to increase the provision and uptake of ARV as we do not know from literature the uptake of other services in the cascade.
4. Furthermore, in areas where the published papers demonstrate a wide variability of uptake between them, there could be an opportunity to learn from the differences in each situation. This variability is recognized in the third paragraph of the discussion, though it is not clear if the particular differences between programs are not discussed because of scope considerations or because they are not stated in the papers. If they are not discussed, they are major methodological gaps, and if they are, then they should be compared to glean policy insights.

Variability in the uptake rate is indeed an interesting factor to compare and glean policy insights. In the section of discussion we have included a paragraph on variability of uptake of services and discuss papers that show high rates of uptake [Heading: Discussion, 5th paragraph, Page 19-20]. However, most papers did not discuss the details of the PMTCT programs and the factors associated with the variability. We have pointed out this lacuna and mentioned the need for proper analysis and representation of program data which could be an important source of experiential knowledge helpful in program implementation [Heading: Conclusion, 2nd paragraph page 23].

5. In the cost and cost effectiveness category, variation among estimates from different papers is again an interesting finding. Further discussion on reasons for that variation, such as economies of scale mentioned in several of the Dandona papers, would be a useful point to highlight. It is also interesting that all of the papers except one in this category appear to have the same author. This may point out the need to attract and train more scholars to this field in India in order to allow for a richer academic discourse.

While describing the findings of the cost effectiveness we currently highlight the fact that only two papers (Kumar et al. 2006; Dandona et al. 2008a) were related to cost effectiveness specifically of the PMTCT program whereas the other four studies, all from Dandona et al., were related to Voluntary Counseling and Testing (VCT) services and HIV prevention interventions which included PMTCT as one of the components. We provide the details of the first two studies and also discuss the variability in economic cost per mother-infant pair receiving Nevirapine as observed by Dandona et al. (2008a) among the 16 PPTCT centers they studied. [Heading: Results, Sub heading: Experiences of implementing PMTCT programs, Sub-sub heading: Cost effectiveness, Page 11]. In the discussion, while discussing the variability in rates of uptake of services we mention about the possible factor for variation in the cost effectiveness studies [Heading: Discussion, 5th paragraph, Page 19]. The variations in the cost across studies could be because of the comparison of different programs and services in these studies.

In the last paragraph of the discussion we also point out the fact that all except one paper on cost effectiveness appear to have the same author and thus the need to attract and train more scholars to this field in order to allow for a richer academic field [Heading: Discussion, last paragraph, page 22].

6. While in the penultimate paragraph the methods section mentions they did not exclude any study based on the methodological quality of the research, it is worthwhile to discuss the methodological quality of studies in the discussion. For example, in the third paragraph of the
Discussion section, the paper describes loss to follow up papers that have very high retention rates. A critical discussion of these papers, including for example sample size and follow-up methodology, would be a good addition to this paper.

We agree that discussion on methodological quality would be a good addition to the paper. In the revised manuscript we included two paragraphs on the discussion of data. While the first paragraph is about the general methodological quality of the papers and availability of data [Heading: Discussion, 4th paragraph, page 18-19] in the second paragraph we discuss about the data and methods of the papers that described high rate of uptake to get more insights about the possible factors associated with the variability [Heading: Discussion, 5th paragraph, page 19-20].

Minor Essential Revisions

7. In the background, second paragraph: The sentence “Further, only 54% of women … received ARV” seems like it should specify that 54% of women ELIGIBLE FOR ARV’S received them.

We have revised the text accordingly. [Heading: Background, 2nd paragraph page 4]

Now the sentence reads

“Further, in 2009, of the women in low- and middle-income countries eligible to receive antiretroviral medication to prevent the mother-to-child transmission of HIV only on average 53% (40 % and 79 %, respectively) received them.”

8. Background, 4th paragraph: “it is important that appropriate strategies bedevised which are evidence-based” could be revised to “it is important to devise appropriate evidence-based strategies” This is a very minor change, though the phrasing could be better.

We have revised the text accordingly. [Heading: Background, 5th paragraph page 6]

Discretionary Revisions


This is a relevant publication and inline with the focus of this review. However, we have not included this paper in the review as it was published after the date of conducting the review.