Author’s response to reviews

Title: Knowledge and provision of misoprostol among pharmacy workers in Senegal: a cross sectional study

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Author’s response to reviews:

Reviewer / Editor Comments:

Reviewer #1: This is a useful study of an important topic. Changes in pharmacy practice in relation to misoprostol in low-income countries could have large beneficial effects on maternal mortality and morbidity.

Would the authors please make it clearer in the Abstract and Methods section that this was a survey by face-to-face interview, not by self-administered questionnaire.

We have included this detail to the Abstract (line 65, page 3) and Methods sections (line 172, page 8).
Presumably the interviews were entirely structured and there was no facility for interviewees to make their own spontaneous comments.

The interviews were entirely structured, except for the ‘other’ response options and there was an opportunity at the end for interviewees to make any additional comments they wanted to raise, but these data are not presented. We clarified this in the Methods section (line 187, page 8).

At line 114 would the authors mention the law in Senegal i.e Criminal Code of 1939 and Basic Law of 1965.

We have referenced Article 35, Decree n0 76-147 of February 10, 1967 instituting the code of medical deontology here (reference 18, line 126, page 6)

At line 182 the authors mention a response rate of 100%. This is most unusual in surveys and should be explained. How come no pharmacy workers declined to participate? Was there a financial or other incentive to participate?

Participation was not incentivised – we have added this to the Ethics, consent and permissions section (line 389, page 17).

We have explained in the methods section that participation was endorsed by the Order of Pharmacists (line 169, page 8), and that interviewers were trained to explain the importance of the study and to ensure potential participants understood that their responses would be anonymised (line 178, page 8). We have inserted a comment on the high participation rate in the discussion section (line 392, page 17).

At line 290 the authors should mention conscientious objection to abortion and abortifacient medicines among pharmacists and use a citation.

We have added that objection to abortion may be a reason that pharmacists do not want to stock misoprostol and have inserted a reference (line 392, page 17).
Reviewer #2: minor changes as suggested in the review comments on the document itself

Line 68 - A pharmacy is supposed to stock for it to sell – or what does stock out mean in this context. Did they not purchase as they did not see the sales market?

It is common for there to be gaps in the drug supply chain which mean pharmacies are unable to purchase more of a product from their supplier. We have clarified this in the text
(line 75, page 3)

Line 77 – Or research

We have made this change on (line 85, page 4).

Line 110 – What is the reference?

We have inserted the following references (Ref 13 and 14, line 121, page 6).


doi:10.1016/j.ijigo.2014.03.028.

Line 166 - For what period of time was the respondent asked to provide the information? Eg the past 3 months or 6 months –and were the doing it all from recall or were they using the registers maintained in the facility if that was the case.
Respondents were asked about current practices. The specific question in the questionnaire was “What brands of misoprostol do you sell?” This has been clarified on (line 185, page 8).

Respondents were able to refer to records if they needed to however this wasn’t required, we have clarified this (186, page 8).

Misoprostol may be a slow-moving product which may make recall more difficult. This has been clarified on (line 402, page 17).

Line 186 Not sure what this means – need to further explain (private professional training).

This has been clarified (line 208, page 9) and in Table 1 p28.

Line 256: The study was conducted in Sept 2013 and being presented in 3 years later. Is there any relevant programmatic change such as trainings already occurred etc –maybe this needs to be mentioned in the discussion

We have mentioned in the discussion that in-service trainings for pharmacists and prescribers on misoprostol have started (line 361, p16).

Line 299: The query posted earlier about the recall time is important –eg if they were asked to recall the practice and details clients over a period of 6 or 12 months –then information may not be very accurate.

Please see answer to comment above about line 166.

Table 1: Pharmacy Characteristics (education level – one respondent reports having primary education). Is it possible for a person whose education level is primary school to be employed in a pharmacy to dispense medication?
Formally, the minimum requirement to be a vendor in a pharmacy is to have reached secondary school level however in practice there are people are trained on the job who have very low education levels.

Table 2: Pharmacy worker knowledge of misoprostol – knowledge of side effects: vertigo.

This may be as a result of translation issues – but is an issue of signs vs symptoms – was that meant to be dizziness? Also was there no response for shivering which is a very common

Thank you, yes this was a translation error, it has been corrected and now reads dizziness (Table 2, page 29). Shivering wasn’t a response category however we had an ‘other’ category and shivering was not reported here. The fever category specified fever/chills, it is possible that shivering may have been categorised under this option. We have edited Table 2, page 29 accordingly.

Reviewer #3: Thanks for sharing this interesting and important paper. I have a few suggestions of how to improve the paper that I hope will be helpful.

For the abstract - I noted in the background that you mention that public providers mostly access miso through privately owned pharmacies - I think maybe the sentence or part of the background should note that for the most part, meds are always accessed through privately owned pharmacies in Senegal. Something like - "Privately owned pharmacies are integral in supplying medicines to the general public...

We have edited the background to clarify this: ‘Private pharmacies (thereafter called “pharmacies”) are integral in supplying medications to the general public in Senegal. In the case of misoprostol, pharmacies are also the main supplier to public providers and therefore have a key role in increasing its availability.’ (Line 58, page 3).

I suggest reviewing all of the references - some examples:
ref 4 - this is from 2006, there are several updated pubs from WHO and others on maternal mortality / deaths attributed to unsafe abortion that you can include here ref 8 - can you add a published study here instead of a weblink. some ideas Derman et al, India study and/or Diop et al/Lancet Global 2016 Senegal study

Thank you for these very helpful suggestions.

Ref 4: We have added the following ref (ref 5, line 103, page 5) to the statement about maternal deaths attributed to unsafe abortion. We have kept the 2006 ref as it specifies early maternal deaths: Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Heal 2014;2:e323–33. doi:10.1016/S2214-109X(14)70227-X.

Ref 8: We have replaced the references in this sentence with the following (line 106, page 5):


We have also updated the maternal mortality ratio estimate for Senegal to the 2015 WHO estimate. (line 97, page 5).

We have also added recent research about the cost effectiveness of misoprostol for PPH at the community level in Senegal when compared to oxytocin (line 121, page 6):

….and found it to be more cost effective than oxytocin for PPH [15].
For the WHO EML, the dates of each listing is incorrect. Miso for PAC was included in the 2009 EML, miso for PPH prevention was 2011. Can you double check on labor induction. I can't remember what year that was but it would be good to confirm (online and found this for labor induction in the 18th version of the EML: a 25-microgram vaginal tablet, for use in induction of labour, on the Complementary list (added in 2005))

We checked the EML lists again and found that it was first included in 2005 but wasn’t named for any indication, in 2009 it was indicated for management of incomplete abortion and miscarriage and in 2011 for PPH and induction of labour. We have updated the text (line 109, page 5).

I suggest adding citations for the Senegal studies mentioned in lines 109-110 (Sloan et al, Diop et al)

For the studies mentioned - Recent research on misoprostol provision at the community level for PPH and PAC in Senegal has shown high levels of efficacy and acceptability – we have added the following two citations (Ref 13 and 14, line 212, p19):


Line 111, remove webpage and replace with Diop et al 2016 Lancet Global paper on this study

We have replaced this reference: Gynuity. Étude de deux stratégies pour la prévention des hémorragies du post-partum au niveau communautaire: misoprostol et ocytocine en Uniject.

With this one (line 123, page 6):


Lines 116 - 117, perhaps reword - it seems odd to begin with reference 12 (2015) and say this contributes to reference 14 (2002). I think you can have an more up-to-date reference to replace # 14


Line 120 - you can add Hyman et al Contraception 2013

We have made this change (Ref 21, line 132, page 6).

Line 126 - reference 16, suggest you add published papers mentioning this topic

We’ve added the following references here (line 139, page 6):


Line 121 - 122 - suggest you remove phrase "and it is not known whether the product is being used for this purpose" I don't think you need this in the sentence and I disagree that its not pretty much known that its used for this indication globally.

We have removed this phrase (line 134, page 6).

Methods: can you say more about where the suburbs were - how may K/how long to travel from central Dakar - so that reader can better understand the geographical representation of the study (might be worth mentioning how many pharmacies outside of Dakar in the discussion and what the potential challenges could be to having access to miso supplies and information in those as well)
We have given more detail on the location in the methods (line 165, page 7). Dakar is relatively small and even pharmacies located in the suburbs are likely to have good access to pharmaceutical supplies. We have noted that transport links are good in the discussion (line 396, page 17).

Line 193 - 194 - can you say what other conditions miso is registered for in Senegal. I thought it was only registered for PPH, PAC and ulcer - would be good for the reader to have the info on other conditions

The information is included in the background section. We reviewed the text to list all of the conditions. (line 114, page 5).

Line 205 - I thought that if miso is blister packed, you don't need to worry about moisture. It might be helpful to mention how miso is generally packaged and how Misoclear is packaged for sale in Senegal.

Misoprostol in Senegal (and elsewhere) is packaged in moisture resistant blister packaging, however it is recommended practice to store away from heat and minimise exposure to humidity. We have included this information (line 233, page 9).

Line 214 - one extra word to delete - either "about" or "on"

We have deleted this (line 243, page 11).

Line 230 - I think its important to clarify here (as you later mention in the discussion) that sales were overwhelmingly reported for - this reads a little differently but I think the key point is this is what people reported, not what actually may have happened.

We have edited this sentence. (Line 260, page 11)
In the section starting line 238, it would be helpful if you could include a summary sentence - you say 6/110 report selling miso to clients wanting to buy OTC, 52/110 didn't sell and then there is the para starting line 245 that seems to report the others. I think one concise sentence that summarizes all the data.

We revised the section to make it clearer (line 271, page 12).

In general, throughout the results section I think having the N and the % is helpful, especially with these small numbers. eg 8% of 52, is...

We have amended this throughout the document.

Line 258 - you might quickly check online to see if reference 20 is now published

We checked, but have not found a journal publication yet.

Line 266- you list two reasons here and 3 in line 236 - I know the third reason appears later in the discussion, but it reads a bit odd to be missing here.

The reasons are not listed together as in the discussion section, we related each to the appropriate discussion point. Line 266 (now line325) refers to selling the product. The 3rd reason is listed later in relation to objecting to stocking an abortifacient.

I am not convinced by your comment that lack of pharmacy stock of misoprostol is a challenge for reducing maternal mortality, per se. Do you have any other citations that show that having miso in pharmacies reduces MM that you could add here or examples from other settings? Similarly, on lines 293 - 294, what are the "life saving properties". I think you could clarify further what you mean here.
For the first point:

We have deleted the sentence about lack of misoprostol stock being a challenge for reducing maternal mortality and revised the text (line 369, page 16).

For the second point:

We have amended this sentence (line 387, page 16) and added the following reference:


Lines 301 - 303 - I think this is an important point and wonder if you can bolster the discussion of this topic using references from other studies conducted in abortion restricted settings.

challenges to collecting data on abortion in general

We revised this section and added three references (lines 405-409, page 17):


[37] Reiss K, Aung O, Aung MM, Ngo TD. Availability and Provision of Abortifacients among Pharmacies in a Restricted Southeast Asian City. Pharm Care Heal Syst 2014;S1-5.


You may want to add more detail to the sub titles on lines 224 and 238 to help with clarity in reading these sections
We have edited the sub-title (line 254, page 11) to clarify the reading and inserted a clarifying first line to the second section (line 271, page 12).

Editorial Feedback

1) Please confirm whether you have declared all potential conflicts of interest. Declaration of potential competing interest does not mean that the paper will not be published. It is matter of transparency. It has been brought to our attention that 'MSI registered Misoclear in Senegal and distributes the drug there'. For further guidance please see: http://www.biomedcentral.com/getpublished/editorial-policies#competing+interests

Thank you for highlighting this. We have explained Marie Stopes International and Marie Stopes Senegal’s involvement with Misoclear and have indicated which of the authors worked for these organisations (line 458, page 20).

2) Please ensure that a Declaration section with all the subheadings is added to the paper as detailed here: http://bmcpregnancychildbirth.biomedcentral.com/submission-guidelines/preparing-your-manuscript/research-article

The document has been revised to comply with the Declaration section template.

3) Please ensure that your paper is formatted according to the journal guidelines

We have formatted accordingly.
4) Please ensure that the paper, in particular the Background section is thoroughly checked as it has been brought to our attention that it contains potential incorrect or out of date references.

We have reviewed the paper and have updated references throughout the manuscript.

5) Please ensure that the discussion section is strengthened giving explanations as to the significance/ importance of the results and why these matter. You can also strengthen the discussion by making the discussion more country applicable and there can be more in-depth discussion of the potential role of pharmacist providers globally, and then particularly in countries with limited legal access to abortion and abortion medicines.

We have strengthened the discussion section. In particular, we have expanded on the role of pharmacies globally, including in relation to the emphasis currently put on task-shifting/task sharing. We have also highlighted and elaborated on the Senegalese context.