Author’s response to reviews

**Title:** Results from a study using misoprostol for management of incomplete abortion in Vietnamese hospitals: Implications for task shifting

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**Version:** 2  **Date:** 15 January 2013

**Author's response to reviews:** see over
January 15, 2013

Dear Editor,

We thank you for the reviews of our original research article Results from a study using misoprostol for management of incomplete abortion in Vietnamese hospitals” and for the opportunity to revise it for consideration of publication in BMC Pregnancy and Childbirth.

Reviewer’s report 1:

Major Compulsory Revisions:
The authors posed a question of “introducing misoprostol as first line care for the treatment of incomplete abortion in Vietnam”. The objectives could be more precisely described (task shifting from doctors to midwives?) and answered in conclusions.

We thank the reviewer for this comment and have attempted to modify the paper accordingly. (edits throughout)

Material and methods:
There is a major problem concerning the selection of patients.

1. This study included spontaneous and induced abortions and should have separated these groups in the results.

We believe this must be due to a confusion on the part of the reviewer. Although we did not specifically limit the enrollment to one group - eg spontaneous or induced - we suspect that the majority if not all participants were experiencing spontaneous abortion given the legal access to abortion and the easy access to care in Vietnam. That said, it is not uncommon in the literature to include both groups as the decision of who is spontaneous versus who is induced is in fact often arbitrary in itself, particularly in clandestine settings where women may be reluctant to identify as one versus the other. Further, many other studies have grouped these women together for enrollment purposes.

2. Material and methods-section does not include any information of the abortion before incomplete abortion was suspected. How about information of the gestation or treatments? How was the induced abortion treated, surgically or medically? All these have impact on the results.

We believe there may be some confusion in the manuscript so we have proofread it again and attempted to edit for clarity. No women with induced abortion were enrolled in this study. (see page 6 of tracked changes manuscript) Only women with diagnosed incomplete abortion (diagnosis criteria are noted in the methods section) were enrolled. (see page 6 of tracked changes manuscript)

3. The definition of incomplete abortion is partly based on clinical symptoms and partly on ultrasound findings. This leads to a very heterogeneous group of patients. I find the >8mm endometrial thickness a very strict criteria to residual tissue and there can be patients among the study population whose bleeding does not need any intervention (= not a true incomplete abortion).

The definition of incomplete abortion for enrollment was based on clinical symptoms and only ultrasound in some cases. We agree that > 8 mm endometrial thickness may appear arbitrary; however,
it is the local criteria used for this condition. We choose to follow the local guidelines in this respect. We also agree that many women diagnosed with “incomplete abortion” probably need no treatment, e.g. products will evacuate on their own. Unfortunately, expectant management is often not desired by either the woman or the provider in some instances. The option of misoprostol, at a minimum, reduces the proportion of other unnecessary procedures, e.g. aspiration, D&C, commonly used to remove RPOC.

4. The efficacy of the misoprostol-treatment was defined partly on clinical symptoms and partly based on ultrasound findings. This causes a bias. This study ends up selecting and treating a very heterogeneous group of patients and also defines the success of the treatment with different methods.

We disagree. For the most part, outcome assessment was managed as is standardly done. If outcome can be assessed clinically there is no reason to perform ultrasound. Furthermore, there were no differences in the outcomes assessed clinically or by ultrasound: complete uterine evacuation rate was high for all participants (96.2% with ultrasound and 97.6% without ultrasound).

Conclusions and discussion:
The conclusions are not supported by the results.

We disagree with this comment and have attempted to modify the paper to better describe the results and their impact to provide additional clarifications. (see changes throughout the results and discussion section)

This paper does not discuss the limitations of this study at all? (The role of selection bias? The heterogeneity of the study group?).

We thank the reviewer for this important comment. We have included a paragraph addressing limitations of the study in the discussion section of the paper. (see page 12 in the discussion section of tracked changes version of manuscript)

Was it likely that this study included patients whose “incomplete abortion” was a misjudged ultrasound finding and “the efficacy” of the treatment was something that an expectant management would have treated.

This is entirely possible in this study and also in any and all other studies addressing “incomplete abortion” since in many instances, expectant management can be used. However, as we stated above, expectant management is often not desired by either the woman or the provider in some instances. The option of misoprostol, at a minimum, reduces the proportion of other unnecessary procedures, e.g. aspiration, D&C, commonly used to remove RPOC.

Indeed, as was noted in the Cochrane Review comparing surgical and expectant management for miscarriage “Expectant management led to a higher risk of incomplete miscarriage, need for unplanned (or additional) surgical emptying of the uterus, bleeding and need for transfusion ... Given the lack of clear superiority of either approach, the woman’s preference should be important in decision making. Pharmacological (‘medical’) management has added choices for women and their clinicians and has been examined in other reviews.” (Nanda K, et al, Expectant care versus surgical treatment for miscarriage. Cochrane Database Syst Rev. 2012 Mar 14;3:CD003518.)
Minor Essential Revisions:
A figure of study flow could have helped understanding how the patients were selected.

We have added a figure showing study flow. We are not sure if this addresses how patients were selected, per se, but we have modified the methods section to try to provide further clarification in that section. (we have included a figure in the attached)

I find the lack or sparse use on references annoying (especially in the background section).

We have added additional references. There are now more than 20 references. We are happy to include more if considered useful. In the past, we’ve been asked to reduce references so we had initially tried to keep the number to a minimum. (see pages 20 – 23 in the tracked changes version of the manuscript)

Also the number of patients needed for this kind of study could have been calculated based on earlier evidence or the power of this study population calculated afterwards.

This study was not designed to have statistical power. The method is already proven and widely accepted. Rather, we sought to demonstrate with a relatively small number of women its application in this setting.

The authors could have discussed whether the treatment of incomplete abortion has any other impacts on the woman’s health if it is treated with misoprostol instead of surgical evacuation (intrauterine adhesions? placenta accreta etc..)

This is mentioned in the introduction section of the paper. (page 5)

Statistical review:

The number of patients needed could have been calculated before the onset of the study. Or the number of patients could have been calculated after the patients have been collected in order to know whether this number of patients was enough to show statistically significant results. However, there is no need to show this manuscript to an expert statistician.

This study was not designed to have statistical power. The method is already proven and widely accepted. Rather, we sought to demonstrate with a relatively small number of women its application in this setting.

Reviewer’s report 2:
1. Is the question posed original, important and well defined?
The use of misoprostol to reduce maternal mortality is a very important topic. The question of this study is not original as there have been many studies that look at the effectiveness of the use of misoprostol to treat incomplete abortion also in Vietnam and other similar low resource countries (also indicated in the study itself) (1, 2)

We agree. This study was developed at the request of the MoH of Vietnam to provide further evidence in that setting to help foster national level change in favor of expanding coverage of incomplete abortion using misoprostol. Furthermore, the regimen studied had not yet been studied in the country.
Other studies also show that expectant care of an incomplete abortion leads to a higher risk of incomplete miscarriage, need for unplanned (or additional) surgical emptying of the uterus, bleeding and need for transfusion than the use of surgery or misoprostol (3) It also has been researched already that misoprostol is a good alternative to surgical evacuation in low resource settings.

We agree. Furthermore, as mentioned above, expectant management is often not desired by either the woman or the provider in some instances. The option of misoprostol, at a minimum, reduces the proportion of other unnecessary procedures, e.g. aspiration, D&C, commonly used to remove RPOC.

2. Are the data sound and well controlled? yes
The researchers should explain who diagnosed the incomplete abortions. What kind of doctors, or trainees, and who evaluated the women and who provided the misoprostol. It would also be useful to know what is the rate of vacuum aspirations for incomplete abortions in Vietnam if these figures exist. To get an idea about the size of the problem. A better explanation of the working of the Vietnamese health system would also be useful and the main question would be if misoprostol provision would be allowed on commune level and whether there is need of a special permission for this or if this could be introduced without any further requirements. As now it was provided at district level hospital.

We have edited the text in the discussion to clarify what level of provider offered care in this study and what the potential for misoprostol care would be at other levels of the health care system with different levels of providers. We do not have data on the rate of vacuum aspirations carried out country-wide for this indication. Of note, we were able to provide misoprostol at district level for this study because it was in the context of a study, generally misoprostol is not permitted for incomplete abortion management at district level. We’ve included description of how incomplete abortion managed at district level in the discussion. (see pages 11 – 14)

3. Is the interpretation (discussion and conclusion) well balanced and supported by the data?
I do think that the discussion about the ectopic pregnancy is very important as it is a main concern of many doctors and this study shows that actually even in case an ultrasound is required an ectopic pregnancy can be missed easily, so it supports the argument that an ultrasound is not needed.
The conclusion however does not seem to be supported by this study as the misoprostol seems to be provided by physicians in district or university hospitals.
The conclusion is supported by the study in Nigeria where midlevel providers diagnosed the incomplete abortions, provided the misoprostol and evaluated the outcome, and also for MVA in other studies. (4, 5)

In this study, ultrasound was available and ectopic was still not seen at entry into study. From this we are trying to make point that ultrasound alone cannot detect ectopics, when done by any level of provider, but that clinical interview/exam still needed. We hope this is clear in the revised version of the manuscript. (see pages 11 – 14)

This study just shows that misoprostol is effective for use in incomplete abortion and very acceptable by Vietnamese women What seems very important in this study is to understand who and what was the status of the persons who diagnosed the incomplete abortion and who provided the misoprostol and who did the follow up, where these gynecologists, general physicians, nurses, midwives working
in the hospital? Who was doing the ultrasounds? The doctors or as in other countries special trained midlevel personnel?

As mentioned above, we edited the discussion to clarify what level of provider offered care in this study and what the potential for misoprostol care would be at other levels of the health care system with different levels of providers. Of note, we were able to provide misoprostol at district level for this study because it was in the context of a study, generally misoprostol is not permitted for incomplete abortion management at district level. We’ve included description of how incomplete abortion managed at district level in the discussion. (see pages 11 – 14)

The study seems to be written to show that the use of misoprostol is safe, effective and acceptable for use in incomplete abortion in Vietnam to make a very valid argument for the widespread use misoprostol on community level in Vietnam, where it is not yet used.

(1) Copyediting: After reading through your manuscript, we feel that the quality of written English needs to be improved before the manuscript can be considered further. We advise you to seek the assistance of a fluent English speaking colleague.

The paper was drafted by native English speakers. We have reviewed it and attempted to edit/improve it accordingly.