Author's response to reviews

Title: Factors associated with postpartum hemorrhage maternal death in referral hospitals in Senegal and Mali: a cross-sectional epidemiological survey.

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Author's response to reviews: see over
Dear Editor in chief,

Thank you for your review and comments.
Please find enclose our comments of the revised manuscript entitled: “Post-partum hemorrhage in referral hospitals in Senegal and Mali: Factors associated with maternal death” for re-submission to BMC Pregnancy & Childbirth.

Editorial requests:
1) We included email addresses of all authors on the page title.
2) Concerning the trial registration number, we would underline that our study is a cross-sectional study nested in the first year of the randomized controlled trial, QUARITE.
3) QUARITE has been registered on 2007 with ClinicalTrials.gov, number ISRCTN46950658. This trial, including the data collection in the pre-intervention period (material for the present study), has also been approved by the ethics committee of Sainte-Justine Hospital in Montreal, Canada, and by the national ethics committees in Senegal and in Mali.
4) We ensured our manuscript adheres to STROBE guidelines for reporting cross-sectional studies. We included a completed STROBE checklist as an additional file.

Elisabeth Butrick’s report:

Minor Essential Recommendations:

⇒ We included all following minor essential recommendations:

ABSTRACT:
line 31: recommend changing among to including
line 48: change clinician to clinicians
line 49: change More particularly to In particular; delete the word the before anemia

Background:
line 72: change are concentrated over %05 of maternal deaths to over 50% of maternal deaths are concentrated
line 75: change and are related to uterine atony in 80% of cases to and 80% of cases are related to uterine atony
line 80: add the word care after obstetric and change contribute to contributes
line 87: drop the word the and change more to More

MATERIAL AND METHODS:
Setting
line 99: change referral public hospitals to public referral hospitals
line 100: change were enrolled to participated (use of enrolled implies enrollment happened over 4 years whereas I think in fact all hospitals were enrolled in 2007 and participated over the 4 year period mentioned)
line 102-104: Delete the last sentence of this paragraph which begins with
Between pre- and post-intervention periods,... This is a result of the overall study and does not belong in the setting description and is not important to the reporting of these results as it is only an analysis of the deaths in the first year.

Population
line 124: change to the visually estimation to to visual estimation

Study variables
line 151: place a period after >35 years and begin the next line wit a new sentence beginning Aspects of pregnancy, labor and delivery include:
line 159: including does not need a capital I

Statistical analysis
line 181: change within hospital to within hospitals
line 190: change missing value to missing values

RESULTS
Components of PPH management
line 212: change Women to women

DISCUSSION
line 263: delete the word the before transfers, change the word selection to identification, and change the words before the to who require
line 270: change the words too less to insufficient
line 280: insert the word than after hospitals and delete the word the
line 283: add the words care providers after the word qualified

CONCLUSIONS
line 310: change clinician to clinicians
line 313: can decision to decision-making
line 315: change transport security to transport availability and change suggest also to also suggest
line 316: change If it allows to response to It may respond to
line 317: add the word but after difficult, change allow that all to allow for all and add the word care after the word quality.
line 318: delete the word the before the word know

We are sorry, but we don't understand this comment.
line 284-286: Revise sentence to read: The QUARITE trial showed that increasing the knowledge of clinicians by implementing training in emergency obstetric care led to a significant reduction in maternal mortality in the district hospitals.

We revised this sentence (line 295) as: “The QUARITE trial showed that health care professionals training in emergency obstetric care led to a significant reduction in maternal mortality in the district hospitals.”

Discretionary Revisions:

BACKGROUND:
line 75: your reference stating 80% of postpartum hemorrhages are related to uterine atony is based on high-resource settings. The work I have been involved in looking at obstetric hemorrhage in Africa found only about 30% of all hemorrhages were from uterine atony. While our studies included antepartum hemorrhages, there were also a significant proportion of hemorrhages from retained placenta and genital lacerations. I am not sure that changing this would make much of an impact or is important for this paper, but if you are trying to relate this work specifically to uterine atony you might want to consider the etiology and with such a large sample size you perhaps missed an opportunity by not breaking your data down by etiology, although perhaps it wasn't reliably available.

Thank you for this comment. We agree with you. We revised the sentence line 75 as follows: “The most cases are related to uterine atony, retained placenta and genital lacerations”.

MATERIALS AND METHODS

Setting
In line 110 you say that all participating hospitals offered CEmOC (comprehensive Emergency Obstetric Care) but yet transfusions were frequently unavailable - hospitals that cannot do cesarean section or give a blood transfusion are considered to have only Basic Emergency Obstetric Care (BEmOC) and it sounds as if some of the facilities in your sample might actually have been functioning at that level (as is common for district hospitals in many SSA countries). IF that is so, you might want to break that down and explain it.

We agree with you. We revised the sentences line 111 as follows: “The hospitals included in our study offered comprehensive emergency obstetric care in theory. However, transfusion could be sometimes unavailable due to lack of blood products”.

line 124: you describe women being included if they had excessive blood loss based on visual estimation - was there a specific threshold used? Typical diagnostic criteria for PPH is 500ml estimated blood loss following a vaginal delivery and 1000mL following a cesarian delivery. IF all of your facilities use that specific criteria you should say so. Equally if the diagnosis is just base on clinical assessment which included blood loss and patient status, but did not include a specific threshold that may explain some of the differences you saw between countries. Did your data collectors record PPh only if the clinician noted it, or did they include all patients with more than 50ml f blood loss as PPH? Explaining more clearly the criteria used may be helpful here.
We agree with you. We revised sentences line 125 as follows: “PPH was clinically assessed by the caregivers according to the visual estimation of excessive blood loss and patient status. The data collector recorded PPH only if the clinicians noted it in the clinical file.”

Study variables
line 145: you don't clarify here how the outcomes were tracked from transfers although you report results among transfers so you must have tracked them. Also it would be interesting to know the proportion of transfers that were transferred within the network of participating hospitals.

All women transferred in another hospital after delivery were tracked by the data collectors using mobile phones. If this information was lacking, the national coordinator of the trial asked to midwives or doctors of the hospital where the women were referred. So, maternal outcome was assessed in each case. We added the following sentence line 147: “All women transferred in another hospital after delivery were tracked by the data collectors or the national coordinator. The outcome was assessed in each case.”. 1.1% of women were transferred after delivery.

Khady Diouf’s report:

Major Compulsory Revisions:

1) How did the authors decide which risk factors for PPH to assess?

We selected well known individual risk factor from relevant literature. Institutional or contextual factors were selected from information based on our field experience and inputs from health providers in participating hospitals.

- Active management of the third stage of labor (administration of oxytocin, placenta delivery, and uterine massage) is a WHO-recommended guideline to avoid postpartum hemorrhage. It would be important to know if providers at the studied facilities are aware of this recommendation and whether or not it is implemented.

We agree with you. However, we did not collect this information in the Quarite trial.

-Additionally, there is no mention of the initial steps for PPH management under their "components of PPH management" category of risk factors for PPH-related deaths. Uterine massage, use of a balloon catheter for uterine tamponade and use of uterotonics such as misoprostol should all be done before transfusion of blood products and hysterectomy can be considered. Assessing these factors would help us answer the question of whether knowledge and performance of initial quick steps such as these would reduce deaths from PPH. For example, is misoprostol stocked and used in all facilities?

We agree that initial steps for PPH treatment is an important component of PPH management. However, this information was not collected in the Quarite Trial. We
are currently carrying out a survey in seven health care facilities in Benin and Mali to assess the initial steps for PPH management.

2) Can the authors offer an explanation as to the difference in PPH deaths found between the 2 countries, Mali and Senegal? Apart from offering "underdiagnosis of PPH" as an explanation, there are no other reasons offered. Do they think it is a personnel training difference? Is it a materials availability difference? Are the hospitals different in other characteristics?

Accordingly, we think that there are two other explanations. Firstly, the PPH definition might differ between the two countries. In Senegal, the diagnosis is mainly based on visual estimation of blood loss (i.e. estimation over 500 mL), while, in Mali, the diagnosis is mainly based on visual estimation AND patient status. The definition in Mali may lead to detect more severe PPH cases than in Senegal. This could explain why the case fatality rate is higher in Mali than in Senegal. Secondly, the number of regional hospitals participating in the Trial is higher in Senegal (11) than in Mali (4), while the number of district hospitals is higher in Mali (12) than in Senegal (7). Health care professionals are globally more qualified in regional hospitals than in district hospitals, and they are able to diagnose PPH cases more likely in the higher level of care.

We revised the final manuscript line 250 as follows: “The PPH definition might differ between the two countries. In Senegal, the diagnosis is mainly based on visual estimation of blood loss (i.e. estimation over 500 mL), while, in Mali, the diagnosis is mainly based on visual estimation and patient status. The definition in Mali may lead to detect more severe PPH cases than in Senegal. This could explain why the case fatality rate is higher in Mali than in Senegal. Otherwise, the number of regional hospitals participating in the Trial is higher in Senegal (11) than in Mali (4), while the number of district hospitals is higher in Mali (12) than in Senegal (7). Health care professionals are globally more qualified in regional hospitals than in district hospitals, and they are able to diagnose PPH cases more likely in the higher level of care.”

3) I agree that the observed association between PPH deaths and receipt of blood transfusion is most likely due to indication bias. What would be better to know is what the average estimated blood loss was for the patients who received the transfusion compared to those who did. For example, receiving 1 unit of blood for a blood loss of 3L of blood will not correct coagulopathy and such patients will be more likely to die.

We agree with you, but we have no data to assess the number of units of blood.

4) In the discussion section, the authors recommend to detect and treat chronic anemia, a risk factor for PPH-related death. In countries like Mali and Senegal, there is a high prevalence of sickle cell trait and disease and therefore baseline anemia is extremely common. Putting all patients on iron is certainly an option but will not correct the underlying pathology for certain anemias. Given a severely restricted blood bank capacity, transfusions have to be very selective, therefore the effort should be put on improving the capacity of the blood banks and making blood quickly accessible when needed.

We agree with you. We revised the final manuscript line 324 and the abstract as follows: “Severe antepartum anemia should be diagnosed more accurately and
treated before delivery, while effort should be put on improving the capacity of the blood banks and making blood quickly accessible when needed.”

5) In table 1, can authors clarify the difference between intrapartum and antepartum caesarean? I would recommend using different, universally accepted terminology (is it scheduled c-section vs unscheduled c-section? Or c-section before or after the onset of labor). Not clear.

⇒ We changed the terminology as “before the onset of labor” and “after the onset of labor”

Minor Essential Revisions:

⇒ We included all following minor essential revisions:

1) Under abstract: 2nd line of conclusion, remove “the” before anemia

2) Under background, 5th paragraph 1st line: instead of ”the more precise knowledge of the factors, change to ”better knowledge of the factors”; 3rd line, instead of the ”timeliest manner possible”, change to ”a timely manner”

4) in the 2nd paragraph of materials and methods, mentioning that ”blood supply is critically inadequate in SSA” should be moved to the introduction section.

3) Under materials and methods, in the 4th paragraph, the authors mention that the participant hospitals cover 10% of all deliveries in both countries, they should also mention where the remaining 90% of deliveries are thought to occur

⇒ According to available statistics in Mali and Senegal, we can say that approximately 50% of deliveries occurred at home and 40% in community health care centers in both countries.

Sincerely Yours,

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