Author's response to reviews

Title: Maternal near miss and mortality in a rural referral hospital in northern Tanzania: a cross-sectional study

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Maternal near miss and mortality in a rural referral hospital in northern Tanzania: a cross-sectional study
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Dear editor, dear reviewers,

Thank you for the editing and reviewing of this article. Many valuable points are raised that will certainly add to the quality of the paper. We are therefore happy to resubmit an improved version of our manuscript. Please find our response to the point-by-point comments below. As requested by the editor, we have also submitted our data abstraction form and the accompanying standard operating procedures.

Best regards, on behalf of all authors,

Ellen Nelissen

Reviewer 1:

1. Methods: in the section outcome measure, the authors describe MD, MNM and live births, but they do not consider the outcome measures of severe maternal complications or potentially life-threatening conditions as proposed by WHO.

Comment: That is correct, because the WHO near miss criteria were not all applicable in the low-resource setting of this hospital, we have modified the criteria as described in a recently published paper: Nelissen et al. Applicability of the WHO near miss criteria in a low resource setting. PLoS One 2013, 8(4):e61248. Several of the severe maternal complications or potentially life-threatening conditions have therefore been included in the locally modified definition of maternal near miss.

2. Inclusion criteria – admission to ICU, eclampsia, sepsis or severe systemic infection, and uterine rupture were considered as near miss factors in the present analysis. However this diverges from the WHO proposal that considers them only as potentially life-threatening conditions. Therefore this produces results that are not really comparable with others using the full definition and criteria recommended by WHO.

Comment: The conditions (admission to ICU, eclampsia, sepsis, and uterine rupture) that we have added to the inclusion criteria have case fatality rates ranging from 4.8% to 26.7%. We consider those conditions near miss factors and not merely potentially life threatening conditions. The applicability of the WHO near miss criteria depends on the level of health care. In hospitals in low-income countries, conditions such as PPH will result in a higher CFR than in hospitals in middle and high-income countries because of different treatment possibilities. This is also described in two recently published papers in PLOS one: van den Akker et al. The WHO Maternal Near Miss Approach: Consequences at Malawian District Level. PLoS One 2013, 8(1):e54805 and Nelissen et al. Applicability of the WHO near miss criteria in a low resource setting. PLoS One 2013, 8(4):e61248). We have stressed this issue in the discussion: "...for the collection of maternal near miss cases we have used modified WHO near miss criteria, as the original WHO near miss criteria were not applicable in the local context. This has to be taken into account when interpreting the results from this study, as more near miss cases have been collected with the modified criteria, than would have been with the original criteria."

3. Data collection: cases were collected as near miss and/or maternal death although authors refer that one underlying cause that started the cascade that led to maternal morbidity or mortality was identified after inclusion in the study. This condition was only possible due to the prospective design of the study. However, it is recommended the identification of severe complications of pregnancy as the first step in investigation of near miss, especially in audits. I suggest authors to highlight these conditions as a limitation of the study in the discussion section.

Comment: We have identified near miss cases according to the local modification of the WHO near miss criteria and not according to underlying cause. The underlying cause was identified after inclusion, but we don’t see how this can be a limitation of the study.
4. Statistical analysis: I suggest the inclusion of potentially life-threatening conditions as an outcome, as well as grouping cases of near miss and maternal death in order to increase the number of cases in the second group. So, it is possible to understand that every woman who proceeds to death was a near miss case before. Therefore, I do propose bivariate analysis with estimation of prevalence ratios for the assessment of possible associated demographic and clinical characteristics with the worst outcome.

Comment: For comment we would like to refer to point 1 and 2.

5. Table 1: admission to intensive care unit, eclampsia, sepsis or severe systemic infection and uterine rupture were considered near miss, as referred before, but these diagnosis increase the number of cases of near miss and change outcomes.

Comment: For comment we would like to refer to point 1 and 2.

6. In the footnote the letter K (eclampsia) is defined as preeclampsia and should be corrected.

Comment: the definition was correct and is not changed. "Eclampsia is defined as the presence of hypertension associated with proteinuria and fits. Hypertension is defined as a blood pressure ≥ 140 mmHg (systolic) or ≥ 90 mmHg (diastolic). Proteinuria is defined as excretion of ≥ 300mg protein/24hr or 300mg protein/litre urine or ≥ 1+ on a dipstick."

7. Table 2: I suggest including potentially life-threatening conditions, grouping near miss and maternal death, and calculate prevalence ratios for these variables (as previously cited).

Comment: For comment we would like to refer to point 1 and 2.

8. Table 4: identification of primary causes - the hypertensive disorders totaled 21 cases with two maternal deaths; did this total include all cases of eclampsia (15 cases)? What is the classification for other cases? Obstructed labor was the underlying cause in 30 cases with 3 maternal deaths; uterine ruptures are not included in these cases, are they? Why table 5 describes 21 cases of uterine rupture? The primary puerperal sepsis occurred in 9 cases and there were no cases of maternal death. Infections not attributable to obstetric causes totaled 11 cases. However, in Table 5, treatment for sepsis occurred in 30 cases and CFR of 26.7%. What were other causes of sepsis in these last 10 cases? Also in Table 4, explain cases of maternal death from unknown causes.

Comment: Table 4 describes underlying causes of maternal morbidity and mortality. For example: one primipara was admitted with obstructed labour and had a caesarean section. After caesarean section she developed sepsis. The underlying cause that started the cascade that led to maternal morbidity or mortality was obstructed labour. This table shows one diagnosis per woman (mutually exclusive, totally inclusive). This explains why there are discrepancies between table 4 and 5. Table 5 describes all women who experienced PPH. There are women who have had PPH and eclampsia and therefore will be shown in both parts. We have explained this difference better in the methods section, by mentioning the example as described above.

We have noticed that in table 4 the underlying causes, especially obstructed labour and uterine rupture, have caused confusion and therefore we have made a different division: obstructed labour with uterine rupture, obstructed labour without uterine rupture, and uterine scar rupture without obstructed labour.

Thank you for your comments and your efforts to improve the paper.

Reviewer 2:

9. The paper would benefit from re-working through the main messages and conclusion. The conclusion that “scaling up of evidence-based interventions by developing and implementing local guidelines is needed” is not really supported by the research. ‘Developing and implementing guidelines’ is not part of the research work. Same, audits are not part of this study. Both recommendations are generally ok, but the study only
proposes that key evidence-based interventions are not implemented in women with complication or women who died.

Comment: Thank you for this advice, we have adopted our conclusion accordingly in the abstract and main conclusion: Key evidence-based interventions are not implemented in the treatment for women with severe maternal morbidity and mortality. Progress can be made through up scaling the use of evidence-based interventions, such as the use of oxytocin for prevention and treatment of postpartum haemorrhage.”

10. Abstract: MMR data should refer to the latest WHO publication from 2012, which has indicated a much lower maternal mortality (also relevant for introduction, and discussion)

Comment: We have identified the article that you mean: “Trends in maternal mortality: 1990-2010" published by WHO in 2012, and have updated the maternal mortality ratios accordingly in the abstract, introduction, and discussion.

11. Was a ‘questionnaire’ or a ‘data abstraction form’ used? A questionnaire is rather asking people, but I’m not sure whether this was done?

Comment: We have used a data abstraction form and have changed this accordingly.

12. Make clear also in abstract that MMR is actually ‘hospital-based’ MMR. Maybe to reduce abbreviations in the abstract as there are a bit too many. The decimal places have no public health importance and could be omitted, particular in the abstract.

Comment: we have changed this in the abstract and throughout the manuscript.

13. Introduction: Millennium ‘project’ is a bit misleading as it is a declaration, which has triggered efforts and projects.

Comment: we have changed this in the introduction: “declaration of the Millennium Development Goals”

14. First paragraph: Jump in flow: The relative low absolute MD is mentioned, but for readers who might not be familiar why near-miss cases are used for audit and quality improvement work, might have difficulties to follow; thus the rational for near-miss could be better developed.

Comment: we have explained the rationale for the use of near miss cases: "Although the numbers of maternal deaths (MD) around the globe are high, absolute numbers in hospitals are low. Therefore, including cases of women who almost die, but survive pregnancy-related complications, is progressively being used to study the quality of obstetric care [5-8]. These near miss cases represent most of the characteristics of maternal deaths [9]. Combined, they create larger numbers and may lead to more rapid and precise reporting.”

15. The study rather focuses on a few aspects of quality of care, or better ‘implementation levels of key interventions’. One could put this a bit more in context (see for example the introduction to QoC in: Duysburgh, E., et al., Quality of antenatal and childbirth care in selected rural health facilities in Burkina Faso, Ghana and Tanzania: similar finding. Tropical Medicine & International Health, 2013

Comment: rather than using the term quality of care, we have specified the focus of the study: "This study aims to assess the occurrence of severe maternal morbidity and mortality in a referral hospital in rural Tanzania as proposed by the WHO near-miss approach and to assess implementation levels of key evidence-based interventions in women experiencing severe maternal morbidity and mortality."

16. It would be prudent to reformulate the aim (such as to study the occurrence of mortality and morbidity and the implementation levels of.... in women experiencing severe morbidity or who died....)

Comment: see comment 15.
17. Method: I recommend shifting the last two sentence of the first paragraph to the beginning of the paragraph as this puts the cross-sectional study done into the needed context.

Comment: we have changed this in the methods section.

18. Outcome measures: would specify that the LB are also the LB ‘in the hospital’

Comment: we have changed this in the methods section.

19. The second paragraph (outcome measures) is a bit difficult to read, the measures are all in the table 5, but then no helping footnote is available when looking at this table. Maybe one can make this more ‘reader’ friendly.

Comment: we have moved the definitions that are described in the second paragraph of the methods section to the footnote of table 5. In this way, the second paragraph flows better as well.

20. The secondary outcome measures are little defined (PPH = 500ml blood loss ?, only eclampsia or also pre-eclampsia? How was sepsis defined? and did the definition of ‘parental antibiotics’ include any antibiotic, and how long?).

Comment: the secondary outcome measures are process indicators and not outcome measures. Therefore we have removed these secondary outcome measures from the second paragraph of the methods section. The conditions that have not been defined before are defined in the footnote of table 5.

21. The rational for the change in definition is clear, but in the discussion the change of at least five units of blood transfusion to only ‘one’ should be taken up, and how this might have changed the indicators and results.

Comment: This issue is described in a recently published paper (Nelissen et al. Applicability of the WHO near miss criteria in a low resource setting. PLoS One 2013, 8(4):e61248). We have made a reference to this article in the methods section.

22. The description ‘general information and obstetric details’ were collected is a bit too vague and should be more concrete. How was the questionnaire / data abstraction form designed, what was the content, who abstracted data? How complete were they finally??

Comment: We have submitted the data abstraction form to the editor, along with the standing operating procedures. This form is based on the data extraction form that is used in the WHO near miss approach. The data was abstracted by either the principal investigator or one of the trained research assistant (nurse-midwives).


Comment: We used the previous version regarding underlying cause of death. "WHO: International statistical classification of diseases and related health problems, 10th revision, 2010". The 2012 version was published after our analysis.

24. Table 4: There is mentioning of pregnancy-related cases: are these co-incidental cases? (pregnancy-related in its definition also includes indirect and direct maternal deaths)

Comment: Yes, these are co-incidental cases. This has been changed in the text and table.

25. Table 5: This table might need some re-work as the messages are not easily to pick

   a. Eg: “all women who delivered in a hospital” is misleading, these are rather the complicated deliveries who did take place in the hospital,
b. “Treatment of PPH” is the first row. Is this about ‘any’ type of treatment?

Comment: We have adapted table 5 and changed the title of the table: “Process indicators among women with severe maternal morbidity and mortality”. Treatment of PPH is about the treatment options for PPH that have been used in this hospital. The reason why the use of routine uterotonics is mentioned in “treatment of PPH” is to show how many women who have experienced PPH, received oxytocin as part of active management of third stage of labour.

Discussion

26. First paragraph: Clearly there is too little knowledge about maternal morbidity and mortality in Tanzania, but there are actually quite a few studies published. Also other studies (e.g. from Kigoma Mbaruku et al if I recall right) pointed to many uterus ruptures in the hospital, other studies using audits have pointed to similar QoC issues, ...

Comment: We have searched Pubmed using the terms "maternal morbidity" OR "maternal mortality" OR "near miss" combined with "Tanzania" and 84 articles showed up. Two articles that describe maternal morbidity or mortality have been added to the references. Only articles of the past 15 years were included.

27. Second paragraph: Would be better to use the most recent data on MMR and to compare with other ‘hospital based MMR’. I was actually surprised that the in-hospital based MMR is still that high although the North is not among the least developed area in TZA.

Comment: We have adapted the MMR to the most recent data (WHO 2012). This hospital lies in a rural area, 300 km southwest of Arusha, and south of Lake Eyasi. This is not a very developed region in Tanzania.

28. Third paragraph: One could interpret maybe a bit more in light of the situation in TZA (nominal free care, transport,...). I would think this also a place a discussion where the change to ‘one’ unit of blood transfusion could be discussed.

Comment: See comment 21.

29. Fourth paragraph: good to see the background, maybe also refer to the studies from Sorensen, B.L who also describe similar deficiencies. I’m not sure whether the last sentence should be added, that is simply another topic: ‘How’ to improve QoC.


30. “CS is the most important risk factors...” I’m not sure whether this statement is clearly supported by the study, or better to reword ‘seems to be one of’ as we don’t know about other risk factors such as premature rupture of membranes, obstructed labour, ...

Comment: This statement is supported by two studies that we have added as references, and we have rephrased the sentence: “Caesarean section seems to be one of the most important risk factors for postpartum maternal infection”.

31. Limitations: maybe to develop here a bit more also in regard to definitions, completeness, ...

Comment: We have added the following section to the limitations: “…for the collection of maternal near miss cases we have used modified WHO near miss criteria, as the original WHO near miss criteria were not applicable in the local context. This has to be taken into account when interpreting the results from this study, as there have been more near miss cases collected with the modified criteria, than would have been with the original criteria.”
32. The main conclusion is that evidence based interventions are too little implemented. This study only gives indication on implementation levels in complicated cases but not normal deliveries, thus better to be more specific.

Comment: We have adapted our main conclusion accordingly: “Results show that there is a gap between actual and optimal use of evidence-based interventions in women experiencing severe maternal morbidity and mortality. Improvement in the quality of obstetric care can be made through up scaling the use of evidence-based interventions.”

33. The last paragraph I think could be dropped as the discussion does not lead to this point.

Comment: This has been changed in the discussion.

34. A point coming up in the conclusion but not in the discussion is the applicability of the WHO near-miss definition. One could add this earlier and also as an objective of the study and one might expand on this in the discussion.

Comment: Thank you for your comments. The last point, as mentioned earlier, is described in a recently published paper (Nelissen et al. Applicability of the WHO near miss criteria in a low resource setting. PLoS One 2013, 8(4):e61248).

Reviewer 3:
1. In the outcome measures paragraph, prophylactic oxytocin and prophylactic antibiotics are technically not outcome measures and should not be lumped with secondary outcome measures.

 Comment: the secondary outcome measures are indeed process indicators and not outcome measures. Therefore we have removed the term secondary outcome measures from the second paragraph of the methods section and replaced it by implementation levels of evidence-based interventions.

2. The limitations paragraph should mention that interpretation of the near-miss data must consider that the definitions are not the same as the WHO recommended definitions. There is potential for overestimation of near-misses, because of lower inclusion thresholds especially because of eclampsia, any blood transfusion, and ‘sepsis’ being included. The authors’ definitions will be more sensitive but less specific for severe morbidity, compared with the WHO’s definitions.

Comment: We have added the following section to the limitations: “…for the collection of maternal near miss cases we have used modified WHO near miss criteria, as the original WHO near miss criteria were not applicable in the local context. This has to be taken into account when interpreting the results from this study, as there have been more near miss cases collected with the modified criteria, then would have been with the original criteria.”

3. In table 4, underlying causes lack adequate definition. The authors must have faced difficult decision in assigning underlying causes. What is an underlying cause? A postpartum haemorrhage should have an underlying cause, whether this is uterine atony, caesarean section trauma or uterine rupture. In case of uterine rupture, this is a category in the table, and so those deaths are not included in ‘postpartum haemorrhage’. I have similar concerns with uterine rupture and puerperal sepsis, which so often are the result of obstructed labour. I noticed that there were 21 uterine ruptures, but only 6 of them were ‘underlying’. Presumably the other 15 were attributable to ‘obstructed labour’ as the underlying cause. Some clarification surrounding these definitions would be helpful.

Comment: Table 4 describes underlying causes of maternal morbidity and mortality. For example: one primipara was admitted with obstructed labour and had a caesarean section. After caesarean section she developed sepsis. The underlying cause that started the cascade that led to maternal morbidity or mortality was obstructed labour. This table shows one diagnosis per woman (mutually exclusive, totally inclusive). This explains why there are discrepancies between table 4 and 5. Table 5 describes all women who experienced PPH. There are women who have had PPH and eclampsia and therefore will be shown in both
parts. We have explained this difference better in the methods section, by mentioning the example as described above.

We have noticed that in table 4 the underlying causes, especially obstructed labour and uterine rupture, have caused confusion and therefore we have made a different division: obstructed labour with uterine rupture, obstructed labour without uterine rupture, and uterine scar rupture without obstructed labour.

4. Major compulsory revisions: Near the end of the inclusion criteria paragraph, the authors add ‘uterine rupture’ and other conditions to their modified case definition of maternal near miss. Uterine rupture should be better defined – the description of ‘complete rupture of a uterus during labour’ under Table 1 is not adequate. Detail is needed on the extent of extrusion of the fetus or fetal parts, and the meaning of ‘complete’.

Comment: We have adapted the definition of uterine rupture as follows: "Uterine rupture is defined as the complete rupture of a uterus (including peritoneum) with (partial) extrusion of the fetus during labour."

Thank you for your review and recommendations to improve the paper.