Author’s response to reviews

Title: Still births, neonatal deaths and neonatal near miss cases attributable to severe obstetric complications: a prospective cohort study in two referral hospitals in Uganda

Authors:

Annettee Nakimuli (anntettee.nakimuli@gmail.com)
Scovia N Mbalinda (snmbalinda@gmail.com)
Rose C Nabirye (rcnabirye@gmail.com)
Othman Kakaire (kakaireothman@gmail.com)
Sarah nakubulwa (sarahug@gmail.com)
Michael O Osinde (omoggg@yahoo.com)
Nelson Kakande (kakandeivan@yahoo.com)
Dan K Kaye (dankkaye@yahoo.com)

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Author’s response to reviews: see over
POINT BY POINT RESPONSE TO REVIEW COMMENTS

Reviewer's report
Title: Still births, neonatal deaths and neonatal near miss cases attributable to severe obstetric complications: a prospective cohort study in two referral hospitals in Uganda
Version: 1 Date: 17 February 2015
Reviewer: Cynthia Pileggi-Castro

Reviewer's report:
- Major Compulsory Revisions
  (which the author must respond to before a decision on publication can be reached)
  42 Neonatal near miss cases were defined according to the World Health Organization (WHO) criteria (which employs clinical features, management given and presence of organ-system dysfunction).
  Reviewer: To my knowledge, this concept is not correct. There are three proposed definition in the literature, two of them developed based on secondary analysis of WHO data, however WHO did not pronounced officially about this subject.

Response
We agree with the reviewer that the criteria cited as definition of the neonatal near miss was from a secondary analysis of WHO data from the 2005 WHO Global Survey on Maternal and Perinatal Health of 2005, but is not from an official WHO publication, and therefore it was erroneous to refer to it as such. We acknowledge this error and have cited the document as such.

80 As a related concept, a neonatal near miss case refers to a neonate that presents with a severe life-threatening complication during the neonatal period but survives [11]. They include newborns with very low Apgar score, very low birth weight or prematurity, and newborns with neonatal convulsions, septicaemia, or severe jaundice. Such babies require admission to the neonatal intensive care unit [NICU].
  Reviewer: The authors can decide on what definition to use in their study, but this definition is a proposition that requires referencing and, not less important the description of each criteria used should be precise. If the reader sees very low Apgar score, very low birth weight, or prematurity as pragmatic criteria or the described management criteria (sepsis, surrogates of asphyxia…) he/she won’t be able to classify their own cases.

Response
We agree with the reviewer that we needed to be explicit about our explicit pragmatic criteria used. We have thus corrected this as follows: They include newborns with very low Apgar score (less than 7 at 5 minutes), very low birth
weight (less than 1,500g) or prematurity (of 30 weeks of gestational age or less). Others may include newborns with neonatal convulsions, septicaemia, or severe jaundice, who very often require admission to the neonatal intensive care unit [NICU].

86 Like for maternal near miss, three types of criteria are used to diagnose a neonatal near miss.
87 [12-14]: The clinical criteria include features such as lethargy, failure to suckle, prematurity, low birth weight, respiratory complications and hypothermia. The laboratory criteria assess evidence of organ-system dysfunction (metabolic, respiratory, neurological or cardiovascular).
89 The evidence includes severe hypoglycaemia, severe jaundice, encephalopathy, sepsis, electrolyte imbalance or thrombocytopenia). The management-based criteria include, among others, total parenteral feeding, tracheal intubation, continuous positive airway pressure, surgery, or blood transfusion).

Reviewer: Line 86: “types” should be replaced by “categories of criteria"

Response
This has been corrected

As above, requires referencing.12-14 is not precise which definition or criteria proposed is used.

Response: We agree with the reviewer that the reference should be limited to reference 12: Avenant T. Neonatal near miss: a measure of the quality of obstetric care. Best Pract Res Clin Obstet Gynaecol. 2009 Jun; 23(3):369-374., and not all the three references 12-14. This has been corrected.

95-104

Response We acknowledge the utility of the suggested pragmatic criteria. However, we regret that we could not have employed this criteria since the criteria was published in March 2014, well after the study had been planned, and the data collected and analysed. We however acknowledge this important publication and have cited it in our discussion section (Reference 20).
The challenge of determining effective neonatal near miss indicators lies in the fact that these conditions are rarely diagnosed. Secondly, many indicators are not routinely registered in medical records, especially in low and middle-income countries.

Reviewer: Actually, the near miss concept is a proposal for epidemiologic studies to use as simple as possible criteria for identifying severe neonatal morbidities, targeting quality assessment of neo and perinatal health either in high complexity health facilities or at lower levels.

Response
We agree with the reviewer that the primary problem may not necessarily the paucity of such data, but the need to identify simple valid and reliable criteria for identification of severe neonatal morbidity, which could be used in quality improvement in health facilities or the community. We have elaborated on this in the discussion section. It reads as follows: The challenge of using neonatal near miss indicators is partly due to absence of simple valid and reliable criteria for identification of severe neonatal morbidity, which could be used in quality improvement in health facilities [20]. Pillegi-Castro et al [20] developed a criteria of pragmatic markers (birthweight <1750 g, Apgar score at 5 minutes <7, and gestational age <33 weeks), which were validated using data from the World Health Organisation Global Survey on maternal and perinatal health, and the WHO Multicountry Survey on Maternal and Newborn Health (WHOMCS). The diagnostic accuracy of the pragmatic and management markers of severity for identification of early neonatal deaths [20] showed high sensitivity, 92.8% (95% CI 91.8-93.7%), specificity, 92.7% (95% CI 92.6-92.8%), positive likelihood ratio, 12.7 (95% CI 12.5-12.9);

A prospective cohort study performed on 341 newborns with severe perinatal morbidity (secondary to severe obstetric complications) admitted to the neonatal intensive care unit found an incidence of early neonatal death of 109 deaths per 1000 live births [15]. In this study, 111 respiratory distress (adjusted risk ratio [aRR] 31.29, 95% CI, 4.17-234.20, p=0.001) and inadequate fetal heart monitoring during labor (aRR 6.0, 95% CI 1.40-25.67, p=0.016) were significantly associated with early neonatal death.
Reviewer: Unclear which criteria was used for case definition and measures of health indicators.

Response
In this study, respiratory distress was defined as a low 5-minute apgar score less than 7.
114 birth survey in Brazil [16], 115 show that obstetric complications have a significant impact on the risk of perinatal and neonatal 116 deaths. Reviewer: This study proposed another case definition criterion, slightly different, considering congenital malformation. Each study used different criteria for case definition which makes difficult to compare.

Response:
We agree with the reviewer that the criteria used are different, but most of the indicators used as criteria are related to severe obstetric complications, and this is the point we wanted to emphasize.

116-118
Reviewer: Unclear if this objective is from the commented paper or the current manuscript.

Response:
We have clarified that these were was our study objectives as follows: The objectives of our study were to assess the attributable risk of still births and neonatal deaths from severe obstetric morbidity, as well as evaluate risk factors for perinatal deaths and neonatal near miss cases.

METHODS SECTION
Reviewer: The inclusion of an analysis flowchart is required to make easier for the reader to understand what has been done by the authors.

Response
This has been added

129 Data collection
Reviewer: Please include time period of data collection.

Response:
This has been added

134 classified using the respective WHO criteria for maternal and neonatal near misses [7, 15]. Reviewer: Reference 7 is not the WHO criteria for maternal near miss definition, mistyped reference 6 (?) and, does not exist a WHO criteria for neonatal near miss case definition. Very important: the authors must state clearly which criteria they used for case definition, wasn’t the Avenant’s proposed criteria? It should be referenced (lines 136-146).

Response
The criteria used has been clarified in the introduction and methods sections. This was a modification of the criteria used by Avenant et al and is reads as follows: The neonatal near miss cases were after modification of the criteria by Avenant et al [12]as follows: an Apgar score of less than 7 at 5 minutes after
birth, gestational age based on the last menstrual period less than 30 weeks, and birth weight less than 1500g

Reviewer: Khan’s formula requires reference.

Response: This section on sample size has been revised as follows: Assuming a power of 80% at the 95% significance level, a maximum accepted error of 2%, and an assumed incidence ratio of neonatal near miss of 424 per 15,169 deliveries [15], our sample size was estimated to be 279 newborns with neonatal complications.

155 We further analyzed the risk factors

Reviewer: Unclear which risk factors were explored.

Response: At bivariate analysis, we initially assessed risk factors for severe neonatal outcomes (which include newborn deaths, both still birth and neonatal deaths, and or neonatal near miss cases). Later we analysed factors associated with risk of newborn deaths only (still births or neonatal deaths, excluding the neonatal near miss cases).

This clarification now reads as follows: At bivariate analysis, we analyzed risk factors for severe neonatal outcomes (neonatal near miss or neonatal death). Categorical variables were compared with $\chi^2$ square or Fisher’s exact test and continuous variables with a two-tailed student t test. In addition, we analyzed factors associated with risk of newborn deaths (still births and neonatal deaths) using log binomial regression analysis, where characteristics of newborn deaths (still births and neonatal deaths) and those of survivors (neonatal near miss and babies with no or minimal complications) were compared and adjusted relative risks computed. Newborns that presented with at least one of the predictors selected for multivariable analysis and survived the neonatal period were considered neonatal near miss cases.

158 minimal complications
Reviewer: Unclear what the authors considered as minimal neonatal complications.

Response: Newborns with no or minimal complications referred to babies who survived the neonatal period but did not have any of the features used as clinical criteria, management-based criteria or organ-system dysfunction criteria for neonatal near miss.

RESULTS SECTION
411 * The remainder of still births and neonatal deaths were from other causes; Reviewer: This numbers must be included in the table, seems at first read that there are missing numbers there.

Response:
This has been corrected. The remainder of still births and neonatal deaths were from other causes unrelated to obstetric complications of childbirth, since the obstetric complications were the focus of interest as risk factors for newborn deaths or severe neonatal morbidity.

202 gravidity,
Reviewer: Unclear how maternal gravidity was measured

Response
Gravidity refers to number of all pregnancies in the woman, including abortions.

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests
Reviewer’s report
Title: Still births, neonatal deaths and neonatal near miss cases attributable to severe obstetric complications: a prospective cohort study in two referral hospitals in Uganda
Version: 1 Date: 14 February 2015
Reviewer: Olufemi A Oloyede

Reviewer’s report:
- Major Compulsory Revisions
  The statistics on concerning obstructed labour and severe obstructed labour must be addressed
  The statistics on following items mentioned earlier- obstetric haemorrhage, hypertensive disorders in pregnancy, obstructed labour, chorioamnionitis and pregnancy-specific complications such as malaria, anemia and premature rupture of membranes, should be provided or accounted/explained appropriately)

Response
Details of the cases of complications of childbirth are given in Table 1. For other obstetric but not child-birth related complications, the data was not available. We acknowledge this as a limitation and have indicated this in our results and discussion sections.

- Minor Essential Revisions
  Author should reference the statement (discussion)- While a study in six developing countries showed that training on Essential Newborn Care (including training on basic resuscitation) had no effect on early neonatal mortality, it revealed significant reduction in the rate of fresh stillbirths primarily fresh.

Response
This has been done

Author should recalculate and correct the figures as shown below-
Line 48 (Results)- Of the remainder, there were 2142 (69.1%) deliveries. This should actually be 73.1%, considering that the denominator should be 2908 and not 3100. Please check again and confirm.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:
‘I declare that I have no competing interests’
Reviewer’s report
Title: Still births, neonatal deaths and neonatal near miss cases attributable to severe obstetric complications: a prospective cohort study in two referral hospitals in Uganda
Version: 1 Date: 6 February 2015
Reviewer: Anup Katheria
Reviewer’s report:
Major Compulsory Revision
The last two paragraphs in the discussion about therapies for neonatal asphyxia and respiratory distress syndrome have nothing to do with near misses and should be removed.
Response: This has been done

Minor Revisions
Correct p values are 0.01 etc. please check where there are additional decimals.

Response: This has been done

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:
No