Author's response to reviews

Title: Bubble CPAP to support preterm infants in rural Rwanda: a retrospective cohort study

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Version: 4 Date: 30 April 2015

Author's response to reviews: see over
** We thank the editor and the reviewers for their thoughtful comments. We appreciate the opportunity to revise our paper and believe that this new version is much improved. We have indicated all changes with red font in the manuscript and provide specific responses to reviewers below (begin with **).

Editor's comment:

1. Copyediting:
   We recommend that you copyedit the paper to improve the style of written English. If this is not possible, you may need to use a professional language editing service. For authors who wish to have the language in their manuscript edited by a native-English speaker with scientific expertise, BioMed Central recommends Edanz (www.edanzediting.com/bmc1). BioMed Central has negotiated a 10% discount to the fee charged to BioMed Central authors by Edanz. Use of an editing service is neither a requirement nor a guarantee of acceptance for publication. For more information, see our FAQ on language editing services at http://www.biomedcentral.com/authors/authorfaq/editing.

** Thank you for your feedback. Our team has paid close attention to copyediting the paper and hope that the new version has an improved style of written English.

Reviewer's report 1: (Angela Okolo)

The retrospective chart review utilised for this study was reasonable approach as it allowed for the assessment of the reality of the situation on ground in these rural health facilities that lacked availability of specialist paediatricians who could have monitored more closely in real time the completeness of the documentation of data.

Line 128 to 130:
It would be more precise if the method of measurement of oxygen saturation were indicated.

** Thank you for the comment. We have added the method used for oxygen measurement which is the pulse oximeter. Line 130 now has this additional sentence “Oxygen saturation was measured using pulse oximeter.”

On table 1, the home deliveries were 10.3% of the 136 preterm or Very low birth weight infants and 4.4% of the 726 near term none very low birth weight, yet the Birth weight Unknown in the category of VLBW babies was 0 ( 0%) and 65 (9.0 %) in the term and near term infants. Does it mean that the babies born at home were all brought to hospital in the first hour or two of birth for the VLBW and for a greater proportion of the larger babies there was a delay in presenting at the health facility and so birth weight could not be ascertained?
Thank you for the question raised. In the study we were able to find birth weight for all preterm or very low birth weight infants whereas for 9% of the term and near term infants, birth weight was not found. We think that more attention was given to preterm or VLBW whether born at the health facility or transferred from home to a health facility given their increased need for medical attention and therefore documentation was better for this group than for term or near term infants who were not VLBW. We demonstrate this challenge in the paper in line 138-140 when we exclude the term and near term babies from further analysis due to poor documentation of the severity of their respiratory distress. Line 138 to 140 reads, “Term and near term infants (GA≥33 weeks and/or birth weight≥1500 grams) were excluded as the severity of their respiratory distress was not captured in the patient charts and therefore eligibility for bCPAP could not be ascertained.”

**Table 2** Would transformation of the information obtained into a scoring system for the rating of the degree of severity of the respiratory distress be have been more objective way of categorizing the severity of the respiratory distress?

**Thank you for the constructive and important question.** We agree that scoring the severity of the respiratory distress into mild, moderate and severe would be a much more objective approach in presenting Table 2. However, for all the infants, we could determine from the patient charts if an infant had a sign of respiratory distress, but we could not determine whether those signs were mild, moderate or severe. Secondly, based on CPAP indications in Figure 1, this categorization is important for term and near term infants who were excluded from further analysis because of limited information in their patient charts to help us determine the severity of their respiratory distress. Our study population was only restricted to PT/VLBW infants who according to the protocol, should be put on CPAP if they show any sign of respiratory distress, regardless of the severity. This is indicated in the line 132 to 134 “Furthermore, preterm (gestational age (GA) < 33 weeks) or very low birth weight (< 1500 grams) infants with any degree of respiratory distress (mild, moderate or severe) should have been initiated on bCPAP.”

**Level of interest**: This article represents an issue of public health interest in Neonatal health particularly to developing countries’ policy makers and researchers. It serves as an example for introduction of policy change that supports task shifting. It clearly illustrates how mentorship and supportive supervision can greatly enhance the safe use of what would have been considered sophisticated technology for application at that level of care where there are no specialists. This is a commendable model for emulation and scale up if significant neonatal mortality reduction is to be addressed in low income countries.

**Thank you for this positive feedback and we are hopeful that this paper will encourage others to consider this technology in the future.
Reviewer's report (Fidelis Njokanma)
Minor essential revisions
1. Abstract Lines 53 to 54 of the manuscript reads as follows: "Of the 43 bCPAP-eligible infants for whom bCPAP was and was not initiated, 18 (41.8%) and 13 (56.5%) recovered, respectively." It should be recast to give more clarity. For instance: "Among the bCPAP eligible infants, the survival rates were 41.8% (18 of 43) for those in whom the procedure was initiated and 56.5% (13 of 23) for those in whom it was not initiated."

** Thank you for the comment. The proposed changes were made in the manuscript and line 53 to 54 now reads “Among the bCPAP eligible infants, the survival rates were 41.8% (18 of 43) for those initiated on the procedure and 56.5% (13 of 23) for those who were not initiated.”

2. Results Lines 177 to 180 of the manuscript reads: "Of the 23 bCPAP-eligible infants for whom bCPAP was not initiated, 56.5% (n=13) recovered, 39.1% (n=9) died and 6.9% (n=3) were referred for tertiary care. Outcome information was missing for 1 (2.3%) infant.
Comment
The phraseology used by the authors gives the impression of wrong arithmetic because 13 + 9 + 3 + 1 will not give 23. It would however appear that the three infants listed as having been transferred to a tertiary institution were among the survivors or fatal cases. If that is so, the facts should be expressly stated.

** Thank you for the constructive feedback. We realized there was a mistake around the three infants listed as having been transferred to a tertiary institution as they were actually among the infants for whom CPAP was initiated. We made the changes and line 178 to 179 now reads, “Of the 23 bCPAP-eligible infants for whom bCPAP was not initiated, 56.5% (n=13) recovered, 39.1% (n=9) died and outcome data was missing for 4.4% (n=1).”

3. Figure 1: The box for “Initiate CPAP” did not show the pressure to be used for CPAP. This should be corrected.

** Thank you for the comment. We have reviewed the entire figure and formatted it further. The specific question on pressure is now addressed. We have added “6” and it now reads “Start CPAP @ 6 cm H₂O”, Included respiratory rate in the Mild distress box, added the arrow from PT/VLBW to order Caffeine, and ensured the oxygen saturation indications are right.

Reviewer's report (Olukemi Tongo)
Minor essential revisions
1. Line 53: “Of the 43 bCPAP-eligible infants for whom bCPAP was and was not initiated” probably should read ‘Of the bCPAP-eligible infants for whom bCPAP was and was not initiated”
** Thank you for the comment. We agree that as stated, the sentence was confusing. We have made changes to improve clarity and now line 52 to 54 reads as, “Among the bCPAP eligible infants, the survival rates were 41.8% (18 of 43) for infants initiated on the procedure and 56.5% (13 of 23) for infants who were not initiated on the procedure.”

2. Line 76: “intensive care unit technology for respiratory support” instead of “intensive care unit technology for respiratory distress”

** Thank you for this comment again. We have changed “distress” to “support” and now line 76 reads, “Specifically, intensive care unit technology for respiratory distress, such as a mechanical ventilation, is often not available due to high costs, maintenance demands and the need for highly trained staff.”

Results

3. Line 179: How come the unusual outcome of more survivors in the bCPAP eligible but not initiated than eligible and initiated. Also there were referrals in the eligible and initiated group whereas the eligible and not initiated did not have any referrals? Yet no record of complications Could this in anyway be suggesting that bCPAP in that setting portends more danger than not giving it? Possible selection bias was suggested in the discussion but with the guidelines provided for the identification of respiratory distress, is it possible to carry out a subgroup analysis to determine the severity of respiratory distress in those eligible who had bCPAP or did not anyway, this is one of the drawbacks of retrospective reviews

** We understand your concern. The fatality rate among the CPAP eligible and initiated infants was higher than those eligible but not initiated. Because of limitations in patient chart documentation, we could identify signs of respiratory distress but could not determine the severity of these symptoms. We suspect that those who were eligible and for whom CPAP was initiated were likely to be more severely ill with potential comorbidities. We have indicated this in line 207 to 209 “Given the low sensitivity of CPAP initiation, we suspect that this group had a higher severity of respiratory distress and other comorbidities compared to infants who were not initiated on CPAP”.

** The point you raise about a subgroup analysis is critical. However, with the incomplete documentation on the severity of respiratory distress, such analysis might not be objective with the data we have. We agree with you that the question of high mortality among infants put on CPAP as observed in other studies too, we document this in line 211 to 214 “In addition, our study was conducted in rural hospitals without full-time pediatric specialists on staff; however, similarly high mortality rates among bCPAP initiated infants have been reported in studies conducted in teaching hospitals with more specialized staff [15-17, 21]”, needs further investigation. We have added this in line 241 to 243 “Future qualitative and prospective research is needed to determine challenges encountered by clinicians in using
bCPAP as well as delineate the reasons for high mortality among infants put on CPAP” to further bring out this point more strongly.

4. Though not specified in the methodology, but I presume the oxygen saturation in the study was measured by pulse oximetry, if it is so, I suggest the abbreviation SaO2 be replaced with SpO2

** Thank you for your comment. The pulse oximetry was used to measure the oxygen saturation. The suggested change from SaO2 to SpO2 has been made in line 163, 255 and Table 2. Also, line 130 now has this additional sentence “Oxygen saturation was measured using pulse oximeter.”