

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Feasibility of using an Early Warning score for preterm or low-birth weight infants in a low resource setting: results of a mixed-methods study at a national referral hospital in Kenya
AUTHORS	Mitchell, Eleanor; Qureshi, Zahida; Were, Fredrick; Daniels, Jane; Gwako, George; Osoti, Alfred; Opira, Jacqueline; Bradshaw, Lucy; Oliver, Mary; Pallotti, Phoebe; Ojha, Shalini

VERSION 1 – REVIEW

REVIEWER	Anne Lee Solevåg Department of Paediatric and Adolescent Medicine, Oslo University Hospital, Norway
REVIEW RETURNED	22-Apr-2020

GENERAL COMMENTS	<p>Dear Editor of BMJ Open and the authors of original paper entitled 'Development of an Early Warning Track and Trigger system for preterm or low-birth weight infants in a low resource setting: results of a mixed-methods study at a national referral hospital in Kenya' by Mitchell and coworkers.</p> <p>Thank you for the opportunity to review this mixed-methods study. The topic is highly relevant and the paper is well written. A very useful part of the study is the stakeholder meeting to identify enablers and barriers to implementing NEWTT in this LMIC context. The observational/charting part of the study could be much more useful if the authors addressed the fact that reference ranges for term infants do not necessarily pertain to preterm infants. Their data suggest that some of the infants were quite small and immature, and (at least) amber, and perhaps even red recordings may not be a true warning sign in these infants as physiological heart rate and respiratory rate is higher in these infants. I therefore think that the study may overestimate the need for escalation and resources. I wish that the authors would stratify their chart results to different groups of premature infants.</p> <p>The title of the paper is: "Development of an Early Warning Track and Trigger system for preterm or low-birth weight infants" – but I cannot find anything about system development in the paper. It would be useful if the (modified) NEWTT chart that they used was submitted at least as supplementary material.</p> <p>Another important topic that the authors address is the high number of infants that were hypothermic and the low rate of infants put in KMC after birth. To reduce morbidity and mortality in these infants, perhaps implementing early KMC should be addressed before implementing an EWS? I suspect that this would in itself be</p>
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	<p>a very powerful intervention that would reduce morbidity and mortality in preterm infants.</p> <p>Below are some comments to some of the manuscript sections:</p> <p>Abstract "Using hospital records, data were collected on all live born infants born at <37 weeks and/or <2500g (n=294, 255 mothers) in the first week of life" -Please state the period of observations (not only in the main manuscript text)</p> <p>Background "All available scoring systems were developed in high income countries where continuous vital sign monitoring is standard "</p> <p>Comment: The NEWTT was developed for use in maternity/post partum wards, not NICU. Even in high income country maternity wards, continuous vital signs monitoring is not standard.</p> <p>Methods Stata version 15</p> <p>Comments: Please provide manufacturer and country</p> <p>Stakeholder meeting – How was the feedback collected for analysis– Written? Audiotape? Video?</p> <p>Results "Ten infants were excluded as they had a birth weight >2500g" Comment: It is stated that the target group had GA <37 w and/or bw <2500. It would then be incorrect to exclude infants with bw >2500g if they had a GA < 37 weeks.</p> <p>Tables Please make sure that numerical results are not duplicated in table and main manuscript text</p> <p>Supplementary material Please explain the meaning of the abbreviation NGO</p> <p>In conclusion, this is an important and relevant study. I would have hoped for more information about adaptation(s) of the NEWTT tool to the context and to the premature population.</p>
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REVIEWER	Sue Chapman Great Ormond Street Hospital for Children, London
REVIEW RETURNED	02-May-2020

GENERAL COMMENTS	<p>Thank you for inviting me to review this manuscript. I very much enjoyed reading it. It is well written, clearly presented and demonstrates the opportunities and challenges of introducing a EWS into a low resource setting.</p> <p>I have a few comments: Was there any verification of the research midwives accuracy in collecting the data? Did they enter the data into the database or was this done by a third party? What was the process for</p>
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	<p>identifying the infant participants and how was it verified that all eligible infants were captured? More detail on the qualitative 'stakeholder meeting' methodology would be welcome, particularly around how data was collected and analysed. There is also relatively little reporting of the findings, which I think would be interesting to the reader. It is quite difficult to identify where you discuss the limitations of the study so a paragraph on this would be helpful.</p> <p>Overall a very interesting study which has the potential to impact on infant mortality. Many thanks for undertaking such valuable research.</p>
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REVIEWER	Muhammad Chutiya Macquarie University, Australia Shehu Sule College of Nursing and Midwifery, Damaturu, Nigeria
REVIEW RETURNED	02-May-2020

GENERAL COMMENTS	<p>I found the manuscript well written and insightful The introduction provided a strong overview of preterm/low birth weight infants globally, and then narrowed to resource poor settings like Kenya It has a clearly stated aim, which was to investigate whether an early warning score system in preterm/low birth weight infants could be implemented in a low resource setting.</p> <p>The methods provide sufficient information to allow for replication if the need be, particularly the observational study aspect. The result presentation was clear, with findings easily interpretable and well used to deduce conclusions for the study. Overall, the outcome of the study will contribute toward overcoming a major neonatal health concern in African continent as a whole, by emphasising the need for implementing newborn monitoring tools to promote care of preterm/underweight, taking into account local available resources.</p> <p>Good manuscript</p>
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VERSION 1 – AUTHOR RESPONSE

<p>Reviewer(s)' Comments to Author:</p> <p>Reviewer: 1 Reviewer Name: Anne Lee Solevåg Institution and Country: Department of Paediatric and Adolescent Medicine, Oslo University Hospital, Norway Please state any competing interests or state 'None declared': None declared</p> <p>Please leave your comments for the authors below Dear Editor of BMJ Open and the authors of original paper entitled 'Development of an Early Warning Track and Trigger system for preterm or low-birth weight infants in a low resource setting: results of a mixed-methods study at a national referral hospital in Kenya' by Mitchell and coworkers.</p> <p>Thank you for the opportunity to review this mixed-methods study. The topic is highly relevant and</p>

the paper is well written. A very useful part of the study is the stakeholder meeting to identify enablers and barriers to implementing NEWTT in this LMIC context. The observational/charting part of the study could be much more useful if the authors addressed the fact that reference ranges for term infants do not necessarily pertain to preterm infants. Their data suggest that some of the infants were quite small and immature, and (at least) amber, and perhaps even red recordings may not be a true warning sign in these infants as physiological heart rate and respiratory rate is higher in these infants. I therefore think that the study may overestimate the need for escalation and resources. I wish that the authors would stratify their chart results to different groups of premature infants.

Response: Thank you for your positive feedback. We accept the feedback relating to the differences between physiological reference ranges for preterm and term infants and have added additional text to the background section of the manuscript. As this was an exploratory study to understand current practice, we did not adjust the reference ranges given in the NEWTT and accept this could be considered a limitation of the study. As such, we have added further text to the discussion section and the “strengths and limitations” section of the manuscript to address this. The title of the paper is: “Development of an Early Warning Track and Trigger system for preterm or low-birth weight infants” – but I cannot find anything about system development in the paper. It would be useful if the (modified) NEWTT chart that they used was submitted at least as supplementary material.

Response: We have amended the title of the manuscript to reflect the fact that the NEWTT was used to plot vital signs, rather than developing an alternative early warning track and trigger system. We have also added the NEWTT as supplementary material.

Another important topic that the authors address is the high number of infants that were hypothermic and the low rate of infants put in KMC after birth. To reduce morbidity and mortality in these infants, perhaps implementing early KMC should be addressed before implementing an EWS? I suspect that this would in itself be a very powerful intervention that would reduce morbidity and mortality in preterm infants.

Response: Thank you for your feedback. We agree early implementation of KMC is important since there is strong evidence that it reduces neonatal mortality, when compared to standard care. The Ministry of Health in Kenya support roll-out of this initiative across the country. It will be important to address implementation of KMC alongside the development and implementation of any new initiatives such as an EWS. We have added a paragraph to the discussion section of the manuscript.

Below are some comments to some of the manuscript sections:

Abstract

“Using hospital records, data were collected on all live born infants born at <37 weeks and/or <2500g (n=294, 255 mothers) in the first week of life”

-Please state the period of observations (not only in the main manuscript text)

Response: The period of observations has been added to the methods section of the abstract.

Background

“All available scoring systems were developed in high income countries where continuous vital sign monitoring is standard ”

Comment: The NEWTT was developed for use in maternity/post partum wards, not NICU. Even in high income country maternity wards, continuous vital signs monitoring is not standard.

Response: We have revised the text in the background section of the manuscript to reflect this.

Methods

Stata version 15

Comments: Please provide manufacturer and country

Response: The manufacturer and country have been added.

Stakeholder meeting – How was the feedback collected for analysis– Written? Audiotape? Video?

Response: Flipchart paper was used by each group to record their opinions. Additional notes were taken when groups gave verbal feedback. We have added a sentence to the methods section to explain this.

Results

“Ten infants were excluded as they had a birth weight >2500g”

Comment: It is stated that the target group had GA <37 w and/or bw <2500. It would then be incorrect to exclude infants with bw >2500g if they had a GA < 37 weeks.

Response: We have revised this sentence to make it clearer that these infants, from multiple births, did not meet the eligibility criteria (birth weight and/or gestational age).

Tables

Please make sure that numerical results are not duplicated in table and main manuscript text

Response: We have deleted the written numerical results relating to infants' characteristics from the manuscript to avoid duplication with Table 1.

Supplementary material

Please explain the meaning of the abbreviation NGO

Response: NGO means Non-Government Organisation. We have added this definition to the supplementary material.

In conclusion, this is an important and relevant study. I would have hoped for more information about adaptation(s) of the NEWTT tool to the context and to the premature population.

Response: Thank you for your positive feedback. We have revised the manuscript to make it clearer that the NEWTT was not adapted for the purpose of this observational study and that reference ranges for preterm infants will be important to consider in future studies considering an EWS in this setting.

Reviewer: 2

Reviewer Name: Sue Chapman

Institution and Country: Great Ormond Street Hospital for Children, London

Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

Thank you for inviting me to review this manuscript. I very much enjoyed reading it. It is well written, clearly presented and demonstrates the opportunities and challenges of introducing a EWS into a low resource setting.

Response: Many thanks for your positive feedback.

I have a few comments:

Was there any verification of the research midwives accuracy in collecting the data? Did they enter the data into the database or was this done by a third party? What was the process for identifying the infant participants and how was it verified that all eligible infants were captured?

Response: The research midwives recorded data using a paper data collection booklet. The data was then entered into an electronic database by the study coordinator. Infants were identified using records on Labour Suite and infants were recorded on an enrolment log, maintained by the research midwives and study coordinator. Due to resource restrictions we were unable to check accuracy of data collection by the research midwives. However, data quality checks were undertaken by the data management team in the UK. We have added a sentence to the methods section of the manuscript.

More detail on the qualitative 'stakeholder meeting' methodology would be welcome, particularly around how data was collected and analysed. There is also relatively little reporting of the findings, which I think would be interesting to the reader.

Response: Further to Reviewer 1's feedback, we have added a sentence to explain how data was collected during the stakeholder meeting. We feel we have included the main findings from the stakeholder meeting and have therefore not added any additional text with regards to this. In addition, we conducted a separate qualitative study (using focus groups and interviews) on this subject which includes the views of mothers, families, healthcare professionals and other stakeholders, which will be reported separately.

It is quite difficult to identify where you discuss the limitations of the study so a paragraph on this would be helpful.

Response: We have added a sentence to make it clearer where the limitations are discussed within the manuscript. In addition, further to the editor's feedback, we have made the "strengths and limitations" section of the manuscript clearer.

Overall a very interesting study which has the potential to impact on infant mortality. Many thanks for undertaking such valuable research.

Response: Thank you for your kind comments.

Reviewer: 3

Reviewer Name: Muhammad Chutiyami

Institution and Country: Macquarie University, Australia

Shehu Sule College of Nursing and Midwifery, Damaturu, Nigeria

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below

I found the manuscript well written and insightful

The introduction provided a strong overview of preterm/low birth weight infants globally, and then narrowed to resource poor settings like kenya

It has a clearly stated aim, which was to investigate whether an early warning score system in preterm/low birth weight infants could be implemented in a low resource setting.

Response: Many thanks for your positive feedback.

The methods provide sufficient information to allow for replication if the need be, particularly the observational study aspect.

The result presentation was clear, with findings easily interpretable and well used to deduce conclusions for the study.

Overall, the outcome of the study will contribute toward overcoming a major neonatal health concern in African continent as a whole, by emphasising the need for implementing newborn monitoring tools to promote care of preterm/underweight, taking into account local available resources.

Good manuscript

Response: Thank you.

VERSION 2 – REVIEW

REVIEWER	Anne Lee Solevåg Oslo University Hospital Norway
REVIEW RETURNED	28-Jul-2020

GENERAL COMMENTS	<p>Dear Editor of BMJ Open and the authors of the revised paper entitled 'Feasibility of using an Early Warning score for preterm or low-birth weight infants in a low resource setting: results of a mixed-methods study at a national referral hospital in Kenya' by Mitchell and coworkers.</p> <p>I find that the authors have addressed the reviewers' comments in a satisfactory manner, and made revisions accordingly.</p> <p>I still have a few minor comments, though:</p> <p>Strengths and limitations "The tool includes physiological parameters for term and late preterm infants, whereas our study included any preterm or low-birth weight infant"</p> <p>Consider revising to:</p> <p>"The tool includes physiological reference ranges for term and late preterm infants, whereas we studied preterm or low-birth weight infant"</p> <p>In the background section 2nd paragraph, it is stated that:</p> <p>"In Kenya, where the most recent NMR was 19.6 per 1000 live births(5), infants born prematurely are currently managed in accordance with national and international guidance for essential newborn care(6-8). This includes a range of evidence-based recommendations for care in the first week of life, e.g. provision of Kangaroo Mother Care (KMC) for all clinically stable infants weighing <2000g, which is recommended for hypothermia prevention (6, 8, 9)."</p> <p>Comment: This sentence seems incorrect, as the large referral hospital Kenyatta National Hospital does in fact not provide the evidence-based recommendation KMC.</p> <p>Results</p>
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	<p>"A respiratory rate of <30 beats/min (red zone) was recorded at least once in 9/155 (6%) and 73/155 (47%) had at least one recording of 30-39 beats/min"</p> <p>Comment: The unit for respiratory rate is not beats/min, but breaths/min or simply X/min</p> <p>I would suggest, in addition to repeating the fact that NEWTT reference ranges are not tailored to all ranges of preterm infants, to include a statement that references for respiratory rate and heart rate are likely to be higher than those of term infants. Thus, the need for escalation might be overestimated when using the "unadjusted" NEWTT in this patient population.</p> <p>Some of the numerical results still appear in both table and manuscript text: "Very few infants had vital signs recorded in the first hour of life; only 10/294 (3%) infants had a recorded temperature, 58/294 (20%) had a recorded heart rate and 70/294 (24%) had a recorded respiratory rate. In addition, Kangaroo Mother Care was not recorded as having been initiated in any of the 180 clinically stable infants soon after birth. "</p>
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REVIEWER	Sue Chapman Great Ormond Street Hospital for Children, London, UK
REVIEW RETURNED	08-Aug-2020

GENERAL COMMENTS	<p>Thank you for asking me to review this revised manuscript. Many thanks to the authors for addressing the recommendations of myself and other reviewers. What was already a good manuscript has been strengthened as a result.</p> <p>I only have one comment. In the second paragraph there is an inference that infants born prematurely in Kenya are currently managed in accordance with national and international guidance (such as KMC) but the evidence from your study, particularly around KMC, does not align with this. This sentence may need amending to reflect that practice 'on the ground' may not align with government recommendations.</p> <p>Otherwise I think the is a very well written manuscript on an interesting topic which informs the management of premature infants in LMIC. Many thanks for your hard work.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer 1

Dear Editor of BMJ Open and the authors of the revised paper entitled 'Feasibility of using an Early Warning score for preterm or low-birth weight infants in a low resource setting: results of a mixed-methods study at a national referral hospital in Kenya' by Mitchell and coworkers. I find that the authors have addressed the reviewers' comments in a satisfactory manner, and made revisions accordingly. I still have a few minor comments, though:

Strengths and limitations: "The tool includes physiological parameters for term and late preterm infants, whereas our study included any preterm or low-birth weight infant". Consider revising to: "The tool includes physiological reference ranges for term and late preterm infants, whereas we studied preterm or low-birth weight infant"

Response: Thank you for your recommended revision; we have made this change.

In the background section 2nd paragraph, it is stated that: "In Kenya, where the most recent NMR was 19.6 per 1000 live births(5), infants born prematurely are currently managed in accordance with national and international guidance for essential newborn care(6-8). This includes a range of evidence-based recommendations for care in the first week of life, e.g. provision of Kangaroo Mother Care (KMC) for all clinically stable infants weighing <2000g, which is recommended for hypothermia prevention (6, 8, 9)." Comment: This sentence seems incorrect, as the large referral hospital Kenyatta National Hospital does in fact not provide the evidence-based recommendation KMC.

Response: Thank you for this observation, which was also noted by Reviewer 2. We have adapted the text in paragraph 2 (background) to make it clear that whilst infants *should* be managed in accordance with guidance and evidence-based recommendations, this is not always the case.

Results: "A respiratory rate of <30 beats/min (red zone) was recorded at least once in 9/155 (6%) and 73/155 (47%) had at least one recording of 30-39 beats/min". Comment: The unit for respiratory rate is not beats/min, but breaths/min or simply X/min

Response: Apologies for this oversight. We have made this change.

I would suggest, in addition to repeating the fact that NEWTT reference ranges are not tailored to all ranges of preterm infants, to include a statement that references for respiratory rate and heart rate are likely to be higher than those of term infants. Thus, the need for escalation might be overestimated when using the "unadjusted" NEWTT in this patient population.

Response: Thank you for this observation; we have added an additional sentence to the discussion section.

Some of the numerical results still appear in both table and manuscript text: "Very few infants had vital signs recorded in the first hour of life; only 10/294 (3%) infants had a recorded temperature, 58/294 (20%) had a recorded heart rate and 70/294 (24%) had a recorded respiratory rate. In addition, Kangaroo Mother Care was not recorded as having been initiated in any of the 180 clinically stable infants soon after birth. "

Response: We have edited this paragraph based on your feedback.

Reviewer: 2

Thank you for asking me to review this revised manuscript. Many thanks to the authors for addressing the recommendations of myself and other reviewers. What was already a good manuscript has been strengthened as a result.

I only have one comment. In the second paragraph there is an inference that infants born prematurely in Kenya are currently managed in accordance with national and international guidance (such as KMC) but the evidence from your study, particularly around KMC, does not align with this. This sentence may need amending to reflect that practice 'on the ground' may not align with government recommendations.

Otherwise I think the is a very well written manuscript on an interesting topic which informs the management of premature infants in LMIC. Many thanks for your hard work.

Response: Thank you for your positive feedback. We have noted your observation, which was also noted by Reviewer 1. We have edited the text in paragraph 2 (background) to ensure it is clear that whilst guidance *should* be followed, in practice this is not always the case.

VERSION 3 – REVIEW

REVIEWER	Anne Lee Solevåg Oslo University Hospital Norway
REVIEW RETURNED	13-Sep-2020
GENERAL COMMENTS	No further comments.