Identification of thresholds for accuracy comparisons of heart rate and respiratory rate in neonates [version 1; peer review: 1 not approved]

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Abstract

Background: Heart rate (HR) and respiratory rate (RR) can be challenging to measure accurately and reliably in neonates. The introduction of innovative, non-invasive measurement technologies suitable for resource-constrained settings is limited by the lack of appropriate clinical thresholds for accuracy comparison studies.

Methods: We collected measurements of photoplethysmography-recorded HR and capnography-recorded exhaled carbon dioxide across multiple 60-second epochs (observations) in enrolled neonates admitted to the neonatal care unit at Aga Khan University Hospital in Nairobi, Kenya. Trained study nurses manually recorded HR, and the study team manually counted individual breaths from capnograms. For comparison, HR and RR also were measured using an automated signal detection algorithm. Clinical measurements were analyzed for repeatability.

Results: A total of 297 epochs across 35 neonates were recorded. Manual HR showed a bias of -2.4 (-1.8%) and a spread between the 95% limits of agreement (LOA) of 40.3 (29.6%) compared to the algorithm-derived median HR. Manual RR showed a bias of -3.2 (-6.6%) and a spread between the 95% LOA of 17.9 (37.3%) compared to the algorithm-derived median RR, and a bias of -0.5 (1.1%) and a spread between the 95% LOA of 4.4 (9.1%) compared to the algorithm-derived RR count. Manual HR and RR showed repeatability of 0.6 (interquartile range (IQR) 0.5-0.7), and 0.7 (IQR 0.5-0.8), respectively.

Conclusions: Appropriate clinical thresholds should be selected...
priori when performing accuracy comparisons for HR and RR. Automated measurement technologies typically use median values rather than counts, which significantly impacts accuracy. A wider spread between the LOA, as much as 30%, should be considered to account for the observed physiological nuances and within- and between-neonate variability and different averaging methods. Wider adoption of thresholds by data standards organizations and technology developers and manufacturers will increase the robustness of clinical comparison studies.

**Keywords**
neonatal vital sign measurement, monitoring, heart rate, respiratory rate, accuracy, validation

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Introduction
There is a high risk of mortality during the neonatal period, particularly in resource-constrained settings. Continuous monitoring of neonatal vital signs enables early detection of physiological deterioration and potential opportunities for lifesaving interventions. The development of innovative, non-invasive, multiparameter continuous physiological monitoring (MCPM) technologies specifically for neonates offers the promise of improving clinical outcomes in this vulnerable population.

A neonate’s marked physiological variability, small size, and often fragile condition can offer challenges when measuring and monitoring vital signs. A lack of neonatal clinical validation standards further undermines the development of MCPM technologies clinically validated specifically for neonates. Determining the accuracy of new MCPM technologies is an essential step in bringing these technologies to market.

The Evaluation of Technologies for Neonates in Africa (ETNA) platform aims to independently establish the accuracy and feasibility of novel MCPM technologies suitable for use in neonates in resource-constrained settings. To determine accuracy and agreement, new technologies are compared against existing reference methods or technologies. However, before the comparison process can proceed, a clinical reference verification step is necessary to determine appropriate accuracy thresholds. These a priori thresholds determine the target level of agreement required and thus, the success or failure of an investigational technology. This study describes the clinical reference technology verification processes conducted to determine appropriate heart rate (HR) and respiratory rate (RR) thresholds in subsequent accuracy comparisons.

Methods
Study design
This was a cross-sectional study which aimed to identify the natural variation in neonatal HR and RR in order to identify appropriate accuracy thresholds for use in an accuracy comparison of MCPM technologies.

Setting and participants
Study participants were neonates admitted for observation and care in the maternity ward, neonatal intensive care, and the neonatal high dependency units at Aga Khan University Hospital in Nairobi, Kenya (AKUHN). Between June and August 2019, caregivers were approached, recruited, and sequentially screened for enrolment by trained study staff during routine newborn intake procedures. To minimize potential selection bias, all caregivers were approached in a sequential manner, as much as possible and introduced to the study using a standardized recruitment script. Final eligibility determination was dependent on medical history results, physical examination, an appropriate understanding of the study by the caregiver, and completion of the written informed consent process (Table 1).

Table 1. Study eligibility criteria and definitions.

<table>
<thead>
<tr>
<th>Eligibility criteria</th>
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<tr>
<td><strong>Inclusion criteria</strong></td>
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<tr>
<td>- Male or female neonate, corrected age of &lt;28 days</td>
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<tr>
<td>- Willingness and ability of neonate’s caregiver to provide informed consent and to be available for follow-up for the planned duration of the study</td>
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<tr>
<td><strong>Exclusion criteria</strong></td>
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<tr>
<td>- Receiving mechanical ventilation or continuous positive airway pressure</td>
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<td>- Skin abnormalities in the nasopharynx and/or oropharynx</td>
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<td>- Contraindication to the application of skin sensors</td>
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<td>- Known arrhythmia</td>
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<tr>
<td>- Any medical or psychosocial condition or circumstance that, in the opinion of the investigators, would interfere with the conduct of the study or for which study participation might jeopardize the neonate’s health</td>
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<table>
<thead>
<tr>
<th>Study definitions</th>
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<tr>
<td><strong>Epoch</strong></td>
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<tr>
<td>A 60-second period of time</td>
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<tr>
<td><strong>Heartbeat</strong></td>
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<tr>
<td>One pulsation of the heart, including one complete contraction and dilatation</td>
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<tr>
<td><strong>Heart rate (HR)</strong></td>
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<tr>
<td>Number of heart beats within an epoch</td>
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<tr>
<td><strong>Breath</strong></td>
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<tr>
<td>One cycle of inhalation and exhalation</td>
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<tr>
<td><strong>Breath duration</strong></td>
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<tr>
<td>Length of time from the start to the end of a single breath</td>
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<tr>
<td><strong>Respiratory rate (RR)</strong></td>
</tr>
<tr>
<td>Number of breaths initiated within an epoch</td>
</tr>
<tr>
<td><strong>Pulse oximetry signal quality index (PO-SQI)</strong></td>
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<tr>
<td>Automated indicator of signal quality from the plethysmographic recording.</td>
</tr>
<tr>
<td><strong>CO₂-SQI</strong></td>
</tr>
<tr>
<td>Algorithm-defined indicator of signal quality from the capnography channel</td>
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</table>
Study procedures
The Masimo Rad-97 Pulse CO-Oximeter® with NomoLine Capnography (Masimo Corporation, Irvine, CA, USA) was selected as the reference technology based on validated oxygen saturation (SpO₂) accuracy measurement in neonates. During study participation, trained and experienced study nurses attached the Rad-97 to neonates and conducted manual HR measurements (counting over 60-second epochs) every 10 minutes for the first hour and once per hour of participation thereafter, following World Health Organization (WHO) guidance for HR measurement in neonates. Photoplethysmographic HR was also measured via the Masimo Rad-97 pulse oximetry skin sensor attached to the neonate’s foot. RR was measured by capnography using an infant/pediatric nasal cannula to collect the neonate’s exhaled carbon dioxide (CO₂) levels. Duration of data collection length was set at a minimum of one hour, with no upper limit. Neonates exited from the study upon discharge from the ward or by caregiver request.

Data collection and analysis
Using a custom Android (Google, Mountain View, CA, USA) application, raw data was collected from the Masimo Rad-97 in real-time through a universal serial bus (USB) asynchronous connection and parsed in C (Dennis Ritchie & Bell Labs, USA). Instantaneous HR was obtained from the timing of the pulse oximetry signal quality index (PO-SQI). The plethysmogram waveform was sampled at 62.5 Hz with the PO-SQI identified by the Masimo Rad-97 at the peak of each heartbeat. The CO₂ waveform was sampled at approximately 20 Hz from the capnography channel. The parsed output included an accurate time stamp for each entry in the waveform data output to facilitate synchronization and analysis. Data were recorded and stored on a secure AKUHN-hosted REDCap server.

We analyzed the CO₂ waveform data using a breath detection algorithm developed in MATLAB (Math Works, USA) and based on adaptive pulse segmentation. In addition to providing a RR, the algorithm analyzed the waveform’s shape and identified the breath duration (waveform trough to trough) for each breath. From the breath duration, we calculated a RR based on the median breath duration within the epoch. We developed a custom capnography quality score (CO₂-SQI) based on capnography features to assist with data selection.

Measurement repeatability was estimated using linear mixed-effects models based on the between- and within-neonate variability for each data source using R version 4.0.3. Agreement between data collection methods was assessed using the method described by Bland-Altman for replicated observations and reported as a mean bias with 95% confidence intervals (CIs), 95% upper and lower limits of agreement (LOA), and as a root mean square deviation (RMSD). The aim was to identify practical threshold limits using data from the clinical reference technology verification process.

Sample size
We estimated that 20 neonates with ten replications each would give a 95% CI LOA between two methods of +/-0.76 times the standard deviation (SD) of their differences. Sample size estimates for method comparison studies typically depend on the CI required around the LOA, and sample sizes of 100 to 200 provide tight CIs. We aimed for a sample size of at least 30 neonates to ensure a diverse population and sufficient replications for tight CIs.

Ethical approval
The study was conducted per the International Conference on Harmonisation Good Clinical Practice and the Declaration

Table 2. Rules for identifying breaths based on graphical waveform plots.

<table>
<thead>
<tr>
<th>Rule</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>1.</td>
<td>Count peaks of the waveform that are within the white background. Ignore peaks that are within the grey background on either side of the image.</td>
</tr>
<tr>
<td>2.</td>
<td>A peak should be counted as a breath when the peak of the waveform is above 15 mmHg, the lower horizontal blue line.</td>
</tr>
<tr>
<td>3.</td>
<td>If the peak does not reach the lower horizontal blue line at 15 mmHg, to be counted as a breath, the peak should reach at least 50% of the mean peak.</td>
</tr>
<tr>
<td>4.</td>
<td>The waveform should dip down to the normal baseline (either below 15 mmHg, the lower horizontal blue line, or based on other breaths). If the waveform does not reach below this point, then this is considered part of the same (double) peak and only counted as a breath once.</td>
</tr>
</tbody>
</table>
of Helsinki 2008. The protocol and other relevant study documents were approved by Western Institutional Review Board (20191102; Puyallup, Washington, USA), Aga Khan University Nairobi Research Ethics Committee (2019/REC-02 v2; Nairobi, Kenya), Kenyan Pharmacy and Poisons Board (19/05/02/2019(078)) and Kenyan National Commission for Science, Technology and Innovation (NACOSTI/P/19/68024/30253). Written informed consent was obtained in English or Swahili by trained study staff from each neonate’s caregiver according to a checklist that included ascertainment of caregiver comprehension.

Results
Between June and August 2019, 35 neonates were enrolled, and 297 clinical observations were completed with a mean of 8.4 (SD 1.7) observations per neonate (Table 3; Figure 1) and a median data collection time of 4 hours, 5 minutes (interquartile range (IQR) 3:52-4:45). The manual HR measurements were found to have a non-normal distribution with skewness of 0.76 and kurtosis of 3.60 (p<0.001). The median manual HR measurement for all observations was 134 (IQR 126-143) beats per minute (bpm).

The manual HR demonstrated a negative bias of -2.4 (-1.8%) compared to the median PO-SQI HR, and a marked spread between the 95% LOA of 40.3 (29.6%). The RMSD was 10.5 (7.7%). Removing data from a single outlier neonate resulted in a smaller bias of -1.4 (-1.0%), a tighter spread between the 95% LOA of 24.7 (18.2%), and a lower RMSD of 6.4 (4.7%) (Table 4; Figure 2).

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age at participation (days)</th>
<th>Gestation at birth (weeks)</th>
<th>Weight at birth (grams)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>Male</td>
<td>Other</td>
<td>Median</td>
</tr>
<tr>
<td>22</td>
<td>13</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 3. Neonate demographic data.

Figure 1. Recruitment flow chart.
Moderate repeatability was demonstrated with approximately 62% (95% CI 47%-73%) of the manual HR variability being due to differences between neonates (Table 5, Figure 3A). Since the 95% CI for manual HR crossed 50%, the between- and within-neonate variability appeared to be comparable, with neither causing significantly more variability than the other.

Manual RR from capnograms were found to have a non-normal distribution with skewness of 0.61 and kurtosis of 2.96 (p=0.027). The median manual RR measurement for all observations was 47 (IQR 39-56) breaths per minute. The manual RR compared to the algorithm-derived median RR showed a negative bias of -3.2 (-6.6%) and a marked spread between the 95% LOA of 17.9 (37.3%). The RMSD was 5.5 (11.4%). Comparing the manual RR to the algorithm-derived RR count showed a smaller bias of -0.5 (-1.1%) and a tighter spread between the 95% LOA of 4.37 (9.1%). The RMSD was 1.2 (2.5%).

The repeatability was moderate with approximately 66% (95 CI 47%-79%) of the manual RR variability due to differences between neonates (Table 5, Figure 3C). Since the 95% CI crossed 50%, the amount of between- and within-neonate variability appeared similar, with neither one resulting in significantly more variability than the other.

Discussion
This reference technology clinical verification study showed minimal measurement bias with a wide spread of 95% upper and lower LOAs and similar repeatability compared with manual clinical measurements. The agreement results allowed us to identify practical HR and RR thresholds for our subsequent technology comparison evaluation. Specifically, we identified a 30% spread between the 95% upper and lower LOA. These a priori-defined thresholds were based on variability observed ten and sixty minutes apart in the same neonate and considered the natural within-neonate physiologic variability. Variability was found to be more marked in some neonates. In part, the 30% spread between 95% upper and lower LOA was selected based on the idea that thresholds should not be more stringent than the observed physiological variability, and in part, based on results from the different averaging methods (manual RR vs algorithm-derived median RR). Given the large difference in results between the two averaging methods, considerable thought should be given prior to choosing an averaging method. A random selection of real clinical data can provide appropriate guidance for selecting suitable neonatal accuracy thresholds.

Of note, one neonate (PTID9) significantly impacted the LOA for HR. Five of nine of this neonate’s manual HR measurements significantly diverged from the same epoch’s PO-SQI HR values and were significantly lower than their mean PO-SQI HR, despite having acceptable signal quality scores. This irregularity suggests a HR reading or data entry error by the study nurse. Removing this neonate’s data and re-analyzing it resulted in a smaller bias and tighter LOAs (Figure 2B).

Results from this clinical verification highlight the difficulty with existing performance thresholds. Current United States Food and Drug Administration performance thresholds for HR measurement, based on electrocardiogram measurements, may not be applicable for use in neonates or when using photoplethysmography for estimating HR\(^9\). The current UNICEF target product profile for RR measurement technology

| Table 4. Bland-Altman analysis of heart rate (HR) and respiratory rate (RR) methods. |
|-------------------------------------------------|---------------------------------|---------------------------------|---------------------------------|
| | Bias (normalized) | 95% upper/lower limits of agreement | Spread of 95% limits of agreement (normalized) | Root-mean-square deviation (normalized) |
| Heart rate | | | | |
| Manual HR vs median pulse oximetry signal quality index HR | -2.39 (-1.8%) | -22.53/17.74 | 40.27 (29.6%) | 10.5 (7.7%) |
| Manual HR vs median pulse oximetry signal quality index HR (outlier neonate removed) | -1.4 (-1.0%) | -13.71/10.97 | 24.67 (18.2%) | 6.4 (4.7%) |
| Respiratory rate | | | | |
| Manual RR vs algorithm-derived median RR | -3.16 (-6.6%) | -12.1/5.8 | 17.9 (37.3%) | 5.5 (11.4%) |
| Manual RR vs algorithm-derived RR count | -0.52 (-1.1%) | -2.7/1.66 | 4.37 (9.1%) | 1.2 (2.5%) |
Heart rate (A, B)

A

B

* With participant 9 (PTID9) removed due to significant outliers
Figure 2. Bland-Altman plots comparing manual heart rate (HR) vs median pulse oximetry signal quality index (PO-SQI) HR for all epochs (A), modified* manual HR vs median PO-SQI HR (B), manual respiratory rate (RR) vs algorithm-derived median RR (C), and manual RR vs algorithm-derived RR count (D).
Table 5. Repeatability results for heart rate (HR) and respiratory rate (RR) measurements for all included epochs.

<table>
<thead>
<tr>
<th></th>
<th>Repeatability (95% Confidence Intervals)</th>
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<tbody>
<tr>
<td>Heart rate (n=297 epochs)</td>
<td></td>
</tr>
<tr>
<td>Manual HR</td>
<td>0.62 (0.47-0.73)</td>
</tr>
<tr>
<td>Median pulse oximetry signal quality index HR</td>
<td>0.75 (0.62-0.83)</td>
</tr>
<tr>
<td>Respiratory rate (n=130 epochs)</td>
<td></td>
</tr>
<tr>
<td>Manual RR</td>
<td>0.66 (0.47-0.79)</td>
</tr>
<tr>
<td>Algorithm-derived median RR</td>
<td>0.50 (0.28-0.67)</td>
</tr>
<tr>
<td>Algorithm-derived RR count</td>
<td>0.66 (0.46-0.79)</td>
</tr>
</tbody>
</table>

Repeatability = (between-neonate variance/(between-neonate variance + within-neonate variance))

Performance thresholds identified using this method are influenced by the characteristics of the neonates studied, the data selection methods, and the number of comparisons. For this reason, the thresholds we identified may not be applicable in different neonate cohorts, such as those receiving mechanical ventilation or immediately following birth, among others. Variability will be influenced by disturbances in the environment such as routine procedures, feeding, noise, and time of day. To minimize variability in our data set, we used only RR epochs that appeared to be regular based on visual inspection. Although these segments were selected based on predefined criteria, a majority (167/297) were discarded as the extreme variability seen in some recordings would have made reproducible manual counting of breaths impossible.

**Conclusion**

Appropriate clinical thresholds should be selected *a priori* when performing accuracy comparisons for HR and RR. The magnitude and importance of sample size, as well as within-neonate variability requires further investigation. A larger sample size could allow the development of an error model that more clearly describes the error due to various factors such as the measurement technology, averaging method, the observer, and the natural variability of neonatal HR and RR.

We strongly support the creation of international standards for technology comparison studies in neonates. These standards should include thresholds for HR and RR based on the specific neonatal population studied and provide details of the experimental conditions, data selection methods, and analysis methods used. Together, such standards would lay the groundwork for a robust MCPM technology comparison field.
**Data availability**

Underlying data

Dryad: Identification of thresholds for accuracy comparisons of heart rate and respiratory rate in neonates. [https://doi.org/10.5061/dryad.1c59zw3vb](https://doi.org/10.5061/dryad.1c59zw3vb).

This project contains the following underlying data:

- Coleman-2021-ETNA-DemographicData.csv
- Raw data folder (contains all raw capnography and pleth data)
- Coleman-2021-ETNA-ProcessedPulseValues.csv

Data are available under the terms of the Creative Commons Zero “No rights reserved” data waiver (CC0 1.0 Public domain dedication).

**Acknowledgments**

We thank Dorothy Chomba, Millicent Parsimei, Annah Kasyoka, and the dedicated staff at Aga Khan University-Nairobi Hospital for providing patient care, and the neonatal participants, their caregivers, and the local community in Nairobi, Kenya, for their participation.

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**Figure 3. Variability plots (vertical for between-neonate variability, horizontal for within-neonate variability).** Manual heart rate (HR) between-neonate variability accounts for 62% of total variability (A); median pulse oximetry signal quality index (PO-SQ) HR between-neonate variability accounts for 75% of total variability (B); manual respiratory rate (RR) between-neonate variability accounts for 66% of total variability (C); algorithm-derived median RR between-neonate variability accounts for 50% of total variability (D); and algorithm-derived RR count between-neonate variability accounts for 66% of total variability (E).
References


15. R Core Team: R: A language and environment for statistical computing. Reference Source


19. American National Standards Institute, Inc: Cardiac monitors, heart rate meters, and alarms. (Association for the Advancement of Medical Instrumentation) 2002.


Open Peer Review

Current Peer Review Status: 

Version 1

Reviewer Report 03 August 2021

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The exact hypothesis of this study is hard to discern. In their abstract and introduction, the authors imply that innovative, non-invasive measurement technologies that use advanced measures of vital signs such as heart rate variation and transient deceleration (citation 2) can be used to improve outcome in infants in resource-constrained settings such as low and middle income countries, but the paper then describes a comparison of nurse observation with continuous measures available from electronic monitors, with the stated aim of defining the accuracy of methods to continuously measure physiological events. Such comparisons have been done, and they cite a substantial review (citation 4).

The introduction then ends with this statement of the study aim: “the clinical reference technology verification processes conducted to determine appropriate heart rate (HR) and respiratory rate (RR) thresholds in subsequent accuracy comparisons.” However the methods then state the aim is “to identify the natural variation in neonatal HR and RR in order to identify appropriate accuracy thresholds for use in an accuracy comparison of MCPM technologies.”

So, we have at least three alternative study aims: the third I’d consider to be the most useful aim, comparing MCPM methods: unlikely to be answered when comparing clinicians with monitors, but could be answered with the data gathered.

At this point, I felt that some sensible and more exact definitions are required, for words such as accuracy, repeatability, agreement, threshold, precision perhaps – as stated in citation 6, by two of the authors of the present paper.

What is “Repeatability”? If we accept that the result of a 60 second counting period will differ, from one observation to the next, because the components of the measure (the duration of each breath, or the interval between photoplethysmograph pulse waves) are randomly different, then the only mechanism available to improve the estimate of the overall frequency is to increase the size of the sample: this is the law of large numbers, a statistical rule that has been known for several centuries in one form or another.
Bland and Altman, when first introducing their extremely popular method, used an example of spirometry: a single measure made first with one device and then with an alternative device. It’s quite possible that two repeat FVC manoeuvres with the same device would differ: within subject variation. This is a more substantial problem in this study, as the authors state: “Furthermore, a ±2 breaths per minute or 5% spread in LOA is smaller than random and natural within-neonate physiologic variability (11.5% in this study [unpublished data]) and would result in unrealistically stringent thresholds”. The degree of within subject variation is evident also from Figure 3. The phenomenon was noted by Simoes et al. (1991).

So we have a small number of intrinsically variable events. So, for a fair comparison of two methods, a necessary requirement is to ensure that the events being measured are the same, exactly the same sample has been taken. If the pulse-wave derived rate from the machine is of a different series of waves (i.e the time period is not EXACTLY the same) than those counted by the nurse, they are already going to be affected by within subject variation as well as the variation between the methods. The methods state: “Manual measures were every 10 minutes for the first hour and once per hour of participation thereafter: were the manual and monitor measures exactly timed to coincide? And, was there any time trend in the patients studied for longer times?

Of course, Bland and Altman had to subsequently refine their method, to separately account for repeated measures in multiple subjects, and at the same time they introduced the concept of confidence intervals for the limits of agreement. Looking at figure 3, there’s a lot of variation: it would be helpful to plot the CI for the LOA on the Bland and Altman plots. However, I would suggest that the most useful thing to do would be to carefully analyse repeated random samples from the electronic records, looking at precise time intervals, so that the intrinsic variation could be quantified, and study how different sample sizes might affect reliability of the rate values. We have done this for respiratory rate in acutely ill adults (Drummond et al., 2020).

Using 30 second periods of observation gave an interquartile range of respiratory rates of 3.4 breath/minute, whereas samples taken for 120 seconds had an IQR of 2.5. Using the techniques the authors describe here, why not sample for 5 minutes?

Availability of these records would be very useful to other workers! More analysis of the monitor records is also important since it appears that rate is not, in itself, perhaps the most important signal. For example, others have found that short-term heart and respiratory rate variability make a significant contribution to illness scoring systems (Saria et al., 2010).

Small points:

- Abstract: “Automated measurement technologies typically use median values”. I'm afraid that my experience is that manufacturers of monitors rarely tell what they use: some sort of exponential averaging or filtering seems more likely. It would be good to have this statement substantiated (if possible).

- Abbreviations make reading difficult. “multiparameter continuous physiological monitoring (MCPM) technologies” is subsequently used as MCPM technologies (17 characters) throughout the paper. Why not just use “continuous monitors” (19 characters)?

- Pulse plethysmography may not be an accurate measure of heart rate variability. ECG
monitoring might be better. I realise that ECG has its drawbacks!

References

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
No

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?
No

Are the conclusions drawn adequately supported by the results?
No

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Expertise in respiratory monitoring and data analysis

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.