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A systematic review of novel technology for monitoring infant and newborn heart rate. (title)

Novel technology for infant and newborn heart rate. (short title)

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ABSTRACT

Heart rate is a vital sign for assessing the need for resuscitation. We performed a systematic review of studies assessing novel methods of measuring heart rate in newborns and infants in the neonatal unit. Two investigators completed independent literature searches. Identified papers were independently evaluated and relevant data were extracted and analysed. **Conclusion:** This systematic review identified seven new technologies, including camera-based photoplethysmography, reflectance pulse oximetry, laser Doppler methods, capacitive sensors, piezoelectric sensors, electromyography, and a digital stethoscope. Clinicians should be aware of several of these, which may become available for clinical use in the near future.

Keywords: Neonatology, newborn and infant, heart rate monitoring, delivery room management, NICU environment

Key Notes:

- Current established methods of heart rate assessment for newborns and infants are disadvantaged by inaccuracy, intrusiveness and time-consuming application, whereas novel methods require appraisal
- Our systematic review evaluates novel techniques for heart rate assessment including camera-based photoplethysmography, reflectance pulse oximetry, laser Doppler, capacitive sensors, piezoelectric sensors, electromyography, and a digital stethoscope
- Although not yet suitable for widespread clinical use, several technologies are promising and clinicians should be aware of them

INTRODUCTION

Background

Monitoring neonatal and infant heart rate (HR) accurately is important to clinicians around the world. HR is a vital sign with an important role in assessing the need for, and response to resuscitation (1, 2) and may serve as a marker to identify critically unwell infants requiring escalation of medical attention (3). For newborns, the International Liaison Committee on Resuscitation (ILCOR) guidelines

emphasise the importance of rapid, accurate heart rate determination in guiding emergency care immediately after birth. These stipulate heart rate assessment within the first minute of life, with ventilatory assistance to be provided if the heart rate is below 100 beats per minute (bpm) and chest compressions if less than 60 bpm (4).

Rationale

Although rapid, chest auscultation and pulse palpation have been shown to be inaccurate to an extent that impairs adherence to resuscitation guidelines (5, 6). Electrocardiography (ECG) and pulse oximetry (PO) are both more precise, but multiple studies have shown that the time elapsed from birth to successful establishment of heart rate display using these devices often exceeds one to two minutes (7, 8). Both of these modalities can become inaccurate with movement artefact (9, 10). In the neonatal unit, application of monitoring leads with adhesives to sensitive skin, especially in preterm infants, may cause trauma through burns and pressure ulcers (11-13). Skin damage can in turn increase an individual's susceptibility to infection (14); a potentially life-threatening risk in this vulnerable group of patients.

These challenges, combined with increasingly sophisticated scientific advancements, have driven the development of novel technologies to assess newborn and infant heart rate in ways that seek to overcome the limitations of currently available devices. However, assessing the performance and accuracy of novel devices is vital given that critical clinical decisions are made on the basis of heart rate. The aim of this systematic review was to critically appraise the evidence on the application and accuracy of novel technologies for monitoring the heart rate of newborns and hospitalised young infants compared to current reference standards.

OBJECTIVES

The primary objectives of this systematic review were

- To identify and describe novel technologies for monitoring the heart rate of infants in the delivery room (DR) and neonatal unit, and
- To provide a summary of the performance of these technologies, including an analysis of their applicability to the study population

Where studies presented the diagnostic accuracy of devices in similar ways, we compared their

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diagnostic performance.

METHODS

Criteria for Study Consideration

Types of Studies

We included studies of original research describing novel technology for assessing heart rate with the following limits applied

1. Published in the last ten years
2. Evaluated the technology in a relevant clinical population, defined as neonates and/or young infants <6 months of age in a neonatal unit
3. Performed a comparison against an established reference standard for heart rate assessment, defined as transmission pulse oximetry or electrocardiography

Although review articles were not included in the systematic review, we included information from several reviews identified during our search. These originated from sources bridging diverse disciplines, such as engineering, biotechnology, and medicine, and were used to inform our discussion (15-17).

Participants

Participants were neonates and young infants less than six months of age in the hospital neonatal unit.

Index Test(s)

Index tests were novel technologies for heart rate assessment.

Target Condition

The target condition of this review was defined as newborn and/or infant heart rate.

Reference Standard(s)

Reference standards were designated as heart rate obtained by either ECG or transmission PO.

ECG was chosen as a reference standard because it is the established gold standard for assessment of neonatal HR (18). In particular, ECG may be the fastest way of accurately determining heart rate in

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resuscitation (8, 19) and for hospitalised young infants there are a variety of situations in which ECG monitoring is indicated, including episodes of apnoea and bradycardia, perioperative assessment and critical illness (20).

Transmission PO was also considered a reference standard because it is commonly used in the delivery room (DR) to measure oxygen saturations, as well as HR, accurately (21, 22). In this setting, it is used to guide resuscitation (4) and in the neonatal intensive care unit (NICU), it is an essential element of patient monitoring for both oxygen saturations and for assessment of heart rate (20, 23).

Search Methods for Identification of Studies

Electronic Searches

We searched the following electronic databases to identify reports of relevant studies:

- MEDLINE, through OVID (15/04/2016)
- EMBASE, through OVID (18/04/2016)
- Science Citations Index (Expanded), through Web of Science (21/04/2016)
- Conference Proceedings Citation Index – Science, through Web of Science (21/04/2016)

The keyword search terms (with MeSH terms additionally used whenever available) we used were:

Neonat* OR infant OR newborn [neonatology] [infant] [newborn]; Heart rate OR heartbeat [heart rate]; Monitoring [monitoring,physiologic]. Full details of each search are listed in Appendix 1.

Other Considerations and Searches

Given our focus on newly developing technologies, we limited our search to articles published in the last ten years. We also reviewed the reference lists of publications eligible for inclusion, and lists of articles citing eligible publications (as found on Google Scholar), to identify additional relevant works.

Data Collection and Analysis

Selection of Studies

The initial searches were undertaken independently by two reviewers (AK, DB), and studies assessing heart rate monitoring were identified based on the title of the articles. Review articles and articles assessing only well-established methodologies for heart rate assessment, such as ECG and transmission PO, were excluded from analysis. The two reviewers then independently assessed the abstract of each reference against the remaining inclusion criteria. Additional relevant works identified by reviewing the reference lists of publications eligible for inclusion, and list of articles citing those eligible studies,

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underwent the same process. Any disagreements that arose between authors were resolved through discussion.

Data Extraction and Management

We extracted the following data from each included study:

- Study design
- Study population
- Reference standard and information relating to performance of the reference standard
- Index test and data relating to the performance of the index test
- Technical details of the index test method(s) used; we classified the diagnostic modalities of studies' index testing methods by grouping similar technologies

Two review authors (AK, DB) extracted the data. Disagreements were resolved by discussion, including discussion with a third author (PD) where necessary.

Assessment of Methodological Quality

As quality assessment of diagnostic accuracy studies is strongly recommended by STARD (Standards for Reporting of Diagnostic Accuracy) (24), all included studies were independently assessed by two reviewers (AK, DB) using the Quality Assessment Tool for Diagnostic Accuracy Studies - Revised Version (QUADAS-2) (25). The QUADAS-2 assessment tool lists four key domains: patient selection; index test; reference standard; flow and timing.

Each study was evaluated for risk of bias under each of these four domains and each study was also evaluated for applicability under each of the first three of these domains. This evaluation was undertaken following recommendations of the QUADAS-2 framework by use of appropriate signaling questions, which are listed in Appendix 2, to form judgements. The outcomes were discussed and consensus between the reviewers was reached. Where consensus could not be reached, a third reviewer (PD) was consulted. The only exception to this process was in the evaluation of studies in which the reviewer was a contributing author. In this case, in order to avoid bias, only the opinion of other reviewer(s) was used in presenting the methodological quality analysis.

Statistical Analysis and Data Synthesis

The data from each study were collated and presented in tabular and graphical format. For each study,

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we have presented data relating to the number of patients and/or recordings included and, if possible, the number of minutes of recording(s) analysed.

Where studies presented the mean difference and standard deviation (SD) and/or 95% confidence intervals in bpm between the novel technology index test and the reference standard, we displayed these data across differing index tests in order to facilitate comparison of the novel technologies. Where studies did not present this data, we contacted listed corresponding authors by electronic mail to request this data and in instances where this was made available, we have included it. We also present information relating to data exclusions disclosed by each eligible publication.

RESULTS

Results of the Search

The initial search strategy identified 1672 references (Figure 1). After screening titles and abstracts, we identified 25 articles for full-text review. Of these, we excluded fourteen studies for the following reasons: two studies did not include new original research data relating to the study question (26, 27), five studies had no comparison of novel technology with an appropriate reference standard (28-32), and seven studies reported no actual testing on our target population (33-39).

After inclusion of four additional studies identified through references and citation of eligible studies (40-43), fifteen articles were identified for analysis in this review (40-54).

The technologies assessed by these studies were camera-based photoplethysmography (42-44, 49, 51), reflectance pulse oximetry (45, 47), laser Doppler methods (54), capacitive sensors (40, 46), piezoelectric sensors (41, 52, 53), transcutaneous electromyography (50), and a digital stethoscope (48). Appendix 3 contains brief, plain-language descriptions of these technologies.

The main characteristics of the studies are summarised in Appendix 4. Collectively in these studies, data on novel methods of heart rate detection compared to an appropriate reference standard device were collected and examined for a total of 327 neonates and infants less than two years of age. Fifty-six participants underwent camera-based heart rate detection, 102 were tested with reflectance pulse oximetry and twenty were assessed by laser Doppler vibrometry. Nineteen and 35 children less than two years of age had heart rate detection performed by capacitive and piezoelectric sensors

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respectively. Kraaijenga and colleagues assessed 31 neonates using transcutaneous electromyography (50), and a total of 57 neonates and infants were auscultated for automated heart rate detection using a digital stethoscope by Kevat and colleagues (48).

Methodological quality of included studies

The results of the QUADAS-2 tool assessment (Figure 2) show that one of the main limitations identified was patient selection as a potential source of bias. Only one of the articles specified randomised patient selection (51), and most of the articles did not describe how patients were selected (40-47, 49, 50, 52-54). In addition, it was deemed that a number of studies used restrictive inclusion criteria in selecting patients without providing a suitable justification.

All of the studies applied the index and reference tests simultaneously. However, many studies analysed the index test results after obtaining results of the reference test, especially studies of photoplethysmography (43-45, 47, 49, 51, 54). We deemed this process to increase the risk of bias due to the generation of novel technology results after obtaining results of the reference test.

Post-hoc data exclusion and selective data analysis also affected the methodological quality of several studies. Some studies did not report data for all patients (40, 44) whereas others excluded data arising affected by a poor trace (42, 43, 45, 47) or when movement, apnoea or arrhythmia occurred (49, 52). Only one study declared having devised an *a priori* method for selecting data suitable for their analysis (48).

Almost all studies effectively reported and appropriately used a gold-standard reference standard. However, some studies were unclear in specifying which reference standard was used and/or whether the same reference standard tool was applied to all studied infants (44, 45).

Another notable source of bias includes the practice of obtaining data from one patient on more than one occasion, affecting two studies (40, 49).

With regard to the QUADAS-2 category of applicability, some novel technologies were trialled on a very specific subgroup of infants, raising concerns. Five studies trialled their devices only on preterm neonates (41, 43, 46, 50, 53). Whilst most studies had small numbers of recruited participants, several

publications were able to demonstrate appropriate demographic variability in their selected population (42, 47, 49).

Findings

Results of the analysis

Data extracted for statistical analysis from the included studies are presented in Table 1. Many of the studies did not provide sufficient data to derive mean difference and/or standard deviation in bpm for comparison, but where they do they are compared in Figure 3. Considerable heterogeneity exists between the statistical reporting methods employed, both across the assorted technologies investigated and between different studies utilising the same basic technological approach.

Heterogeneity and Related Analysis

Camera-based photoplethysmography

Non-contact photoplethysmography was the novel method that was described by the greatest number of studies. This technology derives a heart rate by detecting and amplifying small changes in the colour of skin occurring with each heartbeat. All of the five trials were small, initial studies based in intensive care departments, with less than twenty reported participants each. They derived device HR from post hoc analysis of recordings, not in real-time. Movement artefact was a key factor in all of these studies reducing accuracy; other factors affecting accuracy included illumination (42-44) and infant positioning (49). Interestingly, the presence of staphylococcal scalded skin syndrome and phototherapy seemed to be associated with increased signal clarity and improvements in non-contact technology precision (44), although one study specifically excluded those undergoing phototherapy (51).

The patient populations, recording lengths, and statistical reporting approaches of the five studies varied. Aarts and colleagues studied nineteen neonates and found that for thirteen, more than ninety percent of the time a HR within 5 bpm of the ECG standard could be derived (44). A diverse set of neonates between 25 and 42 weeks gestation, weighing 470 to 3810 grams, were recorded without changes to standard NICU lighting. Encouragingly, both a newborn being rocked in their mother's arms, as well as one receiving high frequency oscillation ventilation, could be successfully monitored. However, for nearly a third of patients, camera-derived HR was more inaccurate than the study cutoff for more than 10% of the time. The authors concluded that better hardware and algorithms were needed to improve robustness.

Even after excluding video segments in which their two reported preterm infants interacted with health professionals or parents, Villarroel and colleagues found non-contact HR values were >4 bpm different compared to ECG for approximately twenty percent of the recording time in their study (43). Over forty hours of footage in segments of varying lengths, from 53 minutes to 7.32 hours, was taken. Heart rate was extracted from the recordings using customised software. The authors concluded that the main barriers preventing increased accuracy of their device were threefold: major changes in lighting conditions, lack of visible skin area, and variation in the baby's activity patterns as small pre-term infants made irregular movements throughout the day.

In two of the non-contact photoplethysmography studies (42, 49), the mean difference and 95% limits of agreement between camera-derived and ECG HR were $\leq \pm 10$ bpm. However, Klaessens and colleagues only reported results from selected segments of their eight recordings during which the patient was still (49), and Scalise and colleagues discarded more than 40% of the expected datapoints likely due to webcam or ECG inaccuracy (42). Rather than excluding and minimising movement, Mestha and colleagues utilised an approach with a strong focus on motion compensation (51). Simultaneous capture of multiple regions of interest (areas of skin selected on the video of the patient), combined with an adaptive filter meant that poor signal quality due to movement in one or multiple areas was able to be detected. However, large motion resulting in loss of accurate monitoring occurred approximately 10% of the time for their half-hour recordings of eight term-born infants. During the remaining time, camera-derived HR was within 6 bpm of the ECG standard for $>95\%$ of the time. The authors conclude that this is close to a standard sufficient for clinical use, and that future work will involve validation on more subjects and improving low-light performance of the algorithm.

Reflectance pulse oximetry

Two studies, by Adu-Amankwa & Rais-Bahrami and Grubb and colleagues (45, 47) used reflectance pulse oximetry. Pulse oximetry waveforms were obtained in real-time, with HR from the waveforms calculated post-hoc. These studies demonstrated a comparatively high degree of accuracy with novel HR within 3 bpm of ECG more than 90% of the time, when data acquisition was stable. Adu-Amankwa & Rais-Bahrami's study of a wireless abdominal belt with this technology (45) trialled in the NICU included data from 25 neonates each recorded for ninety minutes. Only selections of at least three minutes duration wherein both monitors were displaying stable waveforms were compared for parity of peaks representing a beat. Whilst there was excellent beat-to-beat correlation between ECG and reflectance oximetry cardiac activity detected, these sections represent less than 20% of the total

recording time and may only be representative of periods of time when the subject was still.

A study of forehead reflectance pulse oximetry in the NICU (47) recruited 99 infants, making it the largest in this systematic review. Weight (gestational age) of participants ranged from 750 grams (26.9 weeks) to 4.9 kilograms (42 weeks). Recordings were evenly truncated to a length of twenty minutes to ensure a balance in contribution from each participant, and the reflectance pulse oximetry waveform was displayed in real-time (although selection of data for analysis occurred after recording).

Recordings from more than 20% of recruited children were discarded prior to data analysis due to technical problems. Nevertheless, the study reported promising results, especially in relation to their cohort of premature infants <32 weeks' gestation where the device limits of agreement with ECG were ± 12 bpm. Importantly however, paired data values were excluded when pulse oximetry leads were being adjusted and whenever the ECG trace was poor. Therefore, the proportion of total recording time during which reflectance pulse oximetry was adversely affected and unable to extract a reliable HR is unclear. The authors found that the greatest impact on accuracy arose from motion artefact. A clear direction for future improvements and research was articulated, including improved probe fixation to minimise motion artefact and excitingly a delivery room study in progress.

Sensor-based methods

Capacitive sensors in various forms have been used to assess newborn and infant heart rate. Atallah and colleagues embedded eight capacitive sensors into a neonatal cot mattress surrounded by a reference electrode made of conductive textile, all covered by a thin polyurethane protective cover (46). Fifteen premature infants were monitored for 75 hours with concurrent ECG; post-acquisition analysis using a complex constructed algorithm for deriving sensor HR using the two best processed sensor signal inputs found that an accurate HR could be determined less than half of the time, with poor subject-sensor coupling being a key impeding factor. In an effort to maximise coupling between the subject and sensor, Kato and colleagues used thin cotton underwear as the only insulator between the infants and their capacitive sensor surface, which was ingeniously made from a deformable fabric of nickel on copper plated polyester that covered the mattress surface (40). Four infants weighing between 3.5kg and 8kg with an age from ten to 133 days were studied. A key strength of the study was pressure mapping, which facilitated dividing the conducting fabric into three separate sensor areas that corresponded to predicted areas of better subject contact. A brief, qualitative description of results was provided; only one recording was described as successful. An overall comment was made that the

system had room for improvement and was unstable if the infant “was flopping or crying” (40). The authors reported that the detected waveform was distorted and that there was room for improvement in terms of their system’s practical use.

Piezoelectric sensors rely upon the mechanical stress exerted upon them to generate a polarization charge within the contained element which generates a proportional output signal (55). Their placement in a variety of locations has been used to detect the heart rate of preterm and term newborns. Nukaya and colleagues monitored a single 2840 gram 52-day old infant for sixty minutes using piezoelectric sensors affixed to 80mm polypropylene resin coasters placed underneath the four legs of a neonatal cot, recording movements including those due to heartbeat (41). A Pearson’s correlation coefficient of 0.91 between ECG and piezoelectric-derived HR was reported by Nukaya and colleagues, with periods of movement differentiated from periods of stillness by irregular, greater output from the piezoelectric sensors and verified by infant video recording (41). It was found that during these periods, heart rate could not be detected by any of the piezoelectric sensors, but that vibration caused by staff moving along the bedside did not cause significant interference with piezoelectric heart rate signal acquisition.

Wang and colleagues provide the only study results of a piezoelectric sensor for neonatal HR detection with real-time output compared to ECG (53). After preliminary studies to design an algorithm and an appropriate silicone base for their mattress-based synthetic film sensor strips (each 28 x 5 cm), five preterm infants weighing between 1532 and 2112 grams were studied for ten minutes each. An elegant wavelet multi-resolution decomposition was used to separate out pressure fluctuations due to respiratory efforts. An algorithm automatically selected and repeatedly re-evaluated the strongest of the four piezoelectric heart rate signals coming from each rectangular strip, which was logged and compared to ECG. The rate of incorrect heartbeat recording (either an inappropriate recorded beat or missed beat) was 8.24%, occurring primarily due to infant movement or weakness of the heartbeat vibration.

Sato and colleagues used a piezoelectric sensor attached to a small flexible plastic plate embedded within a towel-covered neonatal mattress (52). In this neonatal study, infants with a wide variety of diagnoses were included, such as chromosomal abnormality, atrial septal defect, patent ductus arteriosus, peripheral pulmonary artery stenosis, respiratory distress syndrome, transient tachypnoea of the newborn and pneumothorax. Three recruited newborns were receiving nasal continuous positive airway pressure, two were conventionally ventilated and two were on high frequency oscillation

ventilators. Recordings were between ten hours and nine days in length, sampled every two milliseconds. After excluding two recordings due to data quality issues, Sato and colleagues analysed one-minute segments from 27 remaining to reveal a correlation coefficient of 0.92 for piezoelectric-detected HR compared to simultaneous ECG (52). These short analysed segments were, however, selected from times in which the study participants were not moving. Analysis of prolonged recordings of the infants over several hours to days showed that HR was accurately detected by piezoelectric technology 82.6% of the time compared to 91.8% of the time with ECG. Breastfeeding, ventilation and spontaneous infant movement were listed as key sources of interference. Their piezoelectric sensor was considered easy-to-use, durable, easy to sterilise and safe, without a risk of causing skin irritation compared to conventional monitoring methods. They postulated that with development their system could be used as a backup cardiorespiratory monitor for a more secure monitor system, or as a main cardiorespiratory monitor for a healthier infant.

Other novel technologies

Only one study each used transcutaneous electromyography, laser Doppler vibrometry, and a digital stethoscope. Electromyography, the recording of the electrical activity of muscle tissue using electrodes attached to the skin, was tested by Kraaijenga and colleagues in a single centre study of 31 preterm infants with a gestational age between 26 and 32 weeks who were being treated with nasal continuous positive airway pressure or nasal oxygen. Although transcutaneous electromyography determined heart rate with a high degree of accuracy in comparison to conventional ECG (mean difference -0.3 bpm, 95% limits of agreement -5.3 to 4.7 bpm), study authors point out that transcutaneous electrodes used were similar to those for ECG; therefore it is likely that the technology offers limited advantage over current practice when considered for measurement of heart rate.

Marchionni and colleagues studied non-contact Doppler vibrometry HR monitoring using a single-point laser beam directed toward premature infants' anterior left chests to detect minute movements of their thoracic walls due to cardiac activity (54). Twenty infants (seven female) with a mean weight of 1111 grams were studied principally to test the technology for the assessment of heart rate. The laser beam was located 1.5 – 2m away from the subject and was unaffected by a transparent crib wall (26). Detected HR values were obtained through post-hoc, wavelet-based algorithm construction, with selection of parameters to best fit the gold standard data. Bland Altman analysis revealed that detected HR values had a mean difference (SD) of approximately 0 (8) bpm when compared to ECG values. The authors concluded that their study demonstrated some level of uncertainty with respect to laser

Doppler-acquired heart rate (which was quantified as 6% of the average heart rate), and that in the future it would likely be possible to reduce the dimensions, complexity and cost of such systems.

Digital stethoscope technology to monitor and record neonatal chest sounds in an electronic format developed with prototype smartphone software able to process data using algorithms to provide a visual display of heart rate in real-time was used to assess a diverse newborn and infant population in the neonatal unit. Fifty recordings were analysed from infants where 34% had respiratory support via an endotracheal tube, continuous positive airway pressure or heated humidified high-flow nasal cannulae and 24% had cardiac lesions. Digital stethoscope HR was rapidly acquired, with the median (IQR) time to first display being 2 (1–7) seconds. The HR was calculated and displayed in real-time, but was not highly accurate, with a mean difference (SD) of 7.4 (24) bpm (48). This inaccuracy and the need to exclude seven recordings was stated as being due to software algorithm and device design weaknesses. It was nevertheless concluded that accuracy was better than chest auscultation and umbilical cord palpation in the delivery room, setting the scene for a future study in this clinical environment.

Summary of Findings

We identified seven novel technologies for heart rate monitoring in neonates and infants. Each modality had its own limitations. Movement artefact in particular was a limitation mentioned in most of the studies reviewed. Ambient light was also a limitation in several of the studies assessing camera-based photoplethysmography. Fifteen studies were eligible for inclusion in the systematic review, with comparable published data summarised in Figure 3. An examination of the risks of bias and applicability of each study shows that patient selection methods and the practice of analysing index test results after obtaining results of the reference test were key restrictors of methodological quality.

DISCUSSION

Strengths and Limitations of the Review

We have conducted a comprehensive review of the published literature, following the systematic approach outlined in the QUADAS-2 methodology. We uniformly applied criteria for study inclusion. A key strength of our review is the cross-disciplinary nature of our search. We identified scientific papers from medical, biomedical and engineering journals.

The most salient limitations of our review arise from the nature of the included articles. Most of the

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included works describe small-scale, pilot studies of technology. Many of these can be accurately described as being in a developmental phase. Significant risk of bias affected methodological quality of these studies across multiple domains. Results were not reported in a standardised fashion across all studies, making comparisons of included works in order to identify the most promising novel technology difficult.

Applicability of Findings to the Review Question

Because we only included studies where novel technologies had been trialled on newborns or infants <6 months old in a neonatal unit in comparison to an established gold-standard, findings are considered applicable to the review question.

AUTHORS' CONCLUSIONS

Implications for Practice

The ongoing innovation of technological solutions for assessment of heart rate for unwell neonates and young infants is highly encouraging, with potential to change clinical practice. In order to gain acceptance in clinical practice novel devices will need to be accurate and precise when tested against a reference gold standard but also accessible in terms of cost and provide a user friendly interface for the practitioner in the context of performing clinical assessments during an acute resuscitation. Given the ubiquitous spread of smart device technology, digital stethoscope use pairing with such devices, if improved, may enable better assessment of heart rate globally including resource limited settings. Non-contact methods for HR assessment have the advantage of minimising noxious stimuli and infection pathways for vulnerable preterm infants. However, due to the limitations of the studies and trialled HR assessment methods described in this systematic review, the novel technologies cannot be recommended as being suitable for widespread clinical use at this stage.

Implications for Research

Several of the novel technologies, particularly photoplethysmography and capacitive sensors, suffered from poor signal accuracy due to movement of the neonate/infant (26, 43-45, 47, 49, 51, 54). Methods for minimising movement artefact have previously been developed to improve oximeter-based HR assessment in newborns (9). Given that multiple technologies mentioned above are reportedly being studied in the delivery room and resuscitation setting, it is clear that overcoming inaccuracy due to movement artefact is an area of high research importance for these novel HR monitoring technologies.

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Trial methodology and hence clinical applicability of future studies could be improved by inclusive patient selection criteria, larger sample sizes, standardised reporting of results with inclusion of all relevant data and real-time assessment of HR using the novel method. Future studies should also compare novel methods against each other, to ascertain the most promising technological approach.

DECLARATIONS OF INTEREST

The authors have no interests to declare.

LIST OF ABBREVIATIONS

bpm; beats per minute

ECG; electrocardiogram

HR; heart rate

Hz; hertz

IQR; interquartile range

NICU; neonatal intensive care unit

SD; standard deviation

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TABLES

Author, year	n patients	n recordings	n minutes analysed	n paired datapoints	R (Pearson)	mean difference	Limits of agreement (95% CI)
<i>Camera Photoplethysmography</i>						expressed in beats per minute	
Scalise,	7	56	28	33	0.94	-0.9	-9.7 7.9

Bernacchia, 2012								
Aarts, 2013	19	1	5	170		0.3	-5	5.5
Klaessens, 2014	7	8	-	8	0.96	0.8	-2.9	4.4
Mestha, 2014	8	8	215	12,900	-	2.5	-3.0	8.0
Villarroel, 2014	15	8	-	-	-	-	-	-
<i>Reflectance pulse oximetry</i>								
Adu-Amankwa, 2011								
	25	25	>375	-	-	-	-	-
Grubb, 2014	99	77	1,540	83,287	-	-0.1	-9.3	9.2
<i>Laser Doppler Vibrometry</i>								
Scalise, Marchionni, 2012								
	20	20	-	-	0.96	0.2	-	-
<i>Capacitive Sensors</i>								
Attallah, 2014								
	15	-	4,500	15,170	-	-	-	-
Kato, 2006	4	5	-	-	-	-	-	-
<i>Piezoelectric Sensors</i>								
Nukaya, 2014								
	1	1	60	-	0.91	-	-	-
Sato, 2010	29	27	27	-	0.97	-	-	-
Wang, 2007	5	5	50	-	-	-	-	-
<i>Digital Stethoscope</i>								
Kevat, 2015								
	57	57	50	3,972	-	7.4	-39.6	54.4
<i>Transcutaneous Electromyography</i>								
Kraaijenga, 2015								
	31	72	432	432	0.98	-0.3	-5.3	4.7

Table 1: Summary of data analysed from included studies

FIGURES LEGEND

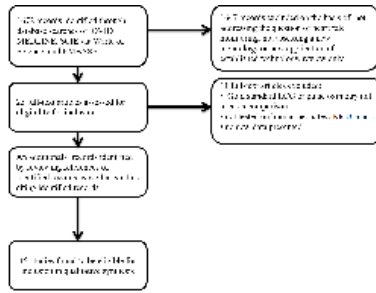
Figure 1: Search Strategy. Flow chart.

Figure 2: QUADAS-2 Tool Assessment. Structured assessment of methodological quality of included studies.

Figure 3: Comparison of Bland Altman Analyses from Studies. For each study with available data, mean difference (SD) between novel device and reference HR is presented.

Author, year	n patients	n recordings	n minutes analysed	n paired datapoints	R (Pearson)	mean difference	Limits of agreement (95% CI)	
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expressed in beats per minute								
Scalise, Bernacchia, 2012	7	56	28	33	0.94	-0.9	-9.7	7.9
Aarts, 2013	19	1	5	170		0.3	-5	5.5
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Villarroel, 2014	15	8	-	-	-	-	-	-
Reflectance pulse oximetry								
Adu-Amankwa, 2011	25	25	>375	-	-	-	-	-
Grubb, 2014	99	77	1,540	83,287	-	-0.1	-9.3	9.2
Laser Doppler Vibrometry								
Scalise, Marchionni, 2012	20	20	-	-	0.96	0.2	-	-
Capacitive and Load-cell Sensors								
Attallah, 2014	15	-	4,500	15,170	-	-	-	-
Kato, 2006	4	5	-	-	-	-	-	-
Piezoelectric Sensors								
Nukaya, 2014	1	1	60	-	0.91	-	-	-
Sato, 2010	29	27	27	-	0.97	-	-	-
Wang, 2007	5	5	50	-	-	-	-	-
Digital Stethoscope								
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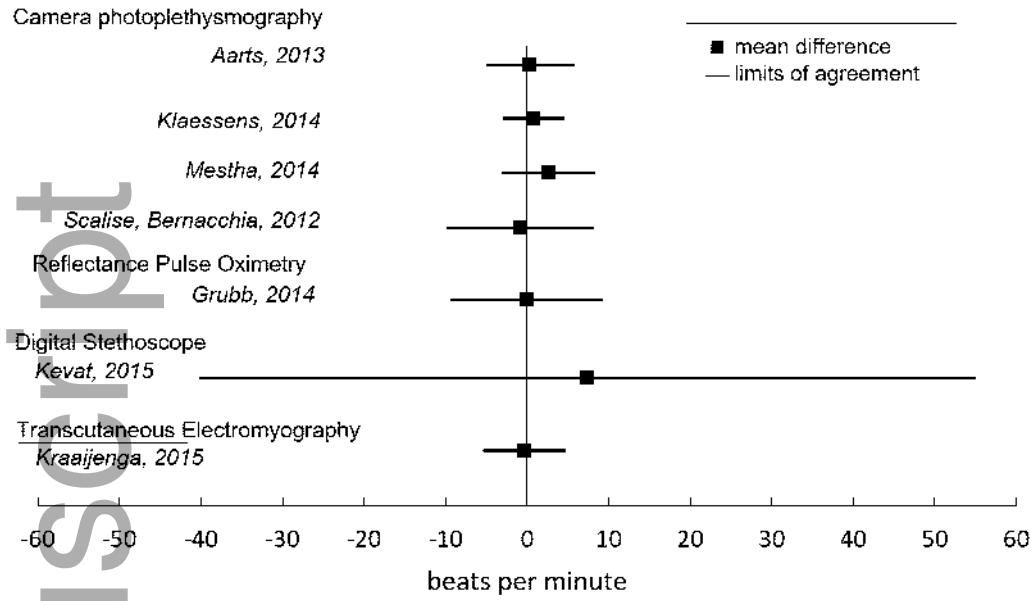
Table 1: Summary of data analysed from included studies



	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Std.	Flow and Timing	Patient Selection	Index Test	Reference Std.
<p>Key</p> <p>● - high</p> <p>● + low</p> <p>● ? unclear</p>							
<i>Camera-based photoplethysmography</i>							
Aarts, 2013	?	-	+	-	+	+	+
Klaessens, 2014	-	-	+	+	+	+	+
Mestha, 2014	+	-	?	+	+	+	+
Villarroel, 2014	?	-	+	-	-	+	+
Scalise, Bernacchia, 2012	?	-	+	+	+	+	+
<i>Reflectance pulse oximetry</i>							
Adu-Amankwa, 2011	?	-	+	?	?	+	+
Grubb, 2014	?	-	+	?	+	+	+
<i>Laser Doppler</i>							
Scalise, Marchionni, 2012	?	-	+	+	?	+	+
<i>Capacitive sensors</i>							
Attallah, 2014	?	-	+	?	-	+	+
Kato, 2006	-	+	+	+	+	+	+
<i>Piezoelectric sensors</i>							
Sato, 2010	?	-	+	+	+	+	+
Wang, 2007	?	?	+	+	-	+	+
Nukaya, 2014	-	-	+	+	-	+	+
<i>Digital Stethoscope</i>							
Kevat, 2015	-	-	+	+	?	+	+
<i>Transcutaneous electromyography</i>							
Kraaijenga, 2015	-	+	+	+	-	+	+

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Comparison of Bland Altman Analyses from Studies



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