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Wireless Monitoring Systems for Vital Signs in Neonates and Infants: a Systematic Review

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"The interest in wearable wireless monitoring systems has accelerated secondary to the ongoing COVID-19 pandemic. Moreover, the alarmingly high number of infections in the pediatric population underscores a gap in monitoring these vulnerable populations, particularly in the home setting."

Abstract:

The interest in wearable wireless monitoring systems has accelerated secondary to the ongoing COVID-19 pandemic. Moreover, the alarmingly high number of infections in the pediatric population underscores a gap in monitoring these vulnerable populations, particularly in the home setting. This systematic review aims to identify and assess currently available wearables used to monitor cardiopulmonary function in infants and neonates. The study, prospectively registered on PROSPERO (CRD42020200642), completed a search of PubMed 1946-, Embase 1947-, Cochrane Library, Scopus 1823-, and IEEE Explore 1872- in June 2020. A total of 2324 unique citations were identified, with 16 studies describing 17 unique devices meeting inclusion criteria. Types of devices included smart clothing, belts, and mechanical adhesives, each with unique battery designs, data collection, and transmission hardware. Only four of the 17 devices underwent rigorous comparative testing, and three demonstrated correlation with the standard of care monitoring systems. Low sensitivity and specificity were reported in two commercially available consumer devices compared to the standard of care monitoring systems. The risk of bias in the entire cohort was highly based on a modified ROBINS-I scale. Further development and rigorous wearable device testing are necessary for neonatal and infant deployment.

Keywords

Wearable, sensor, technology, pediatrics, neonates, critical care, cardiopulmonary disease

Introduction:

Wearable technologies, electronic devices worn directly on the body or attached to clothing that capture high-quality physiological information,(1) are an area of rapid development in healthcare. Recent challenges posed by COVID-19 to maintain high-quality, often distanced healthcare have only increased the relevance of wearable biosensors to monitor and quantify patients' physiological status of patients(2). Wearable monitoring devices have been used during the pandemic to facilitate remote care of infected patients, monitor clinical deterioration, and identify infections before symptom development.(3, 4) While there are several studies demonstrating the utility of wearables in adults, less is known in regards to wearables in the neonatal and infant population.(5-7) Given that SARS-CoV-2 infections in neonates and infants can present with a wide spectrum of clinical signs or symptoms and the lack of vaccine availability for this cohort, the use of wearables within the context of the current pandemic, has remained understudied in these younger patients.(8-13)

"Given the inherent vulnerability and distinct physiology of pediatric patients compared to adults, the potential utility of wearable devices for monitoring physiological parameters in this population extends beyond the pandemic. Wearable devices must overcome unique challenges related to skin fragility, anatomical differences, and differences in physiological ranges for heart rate and respiratory rate.(14-16)"

Given the inherent vulnerability and distinct physiology of pediatric patients compared to adults, the potential utility of wearable devices for monitoring physiological parameters in this population extends beyond the pandemic. Wearable devices must overcome unique challenges related to skin fragility, anatomical differences, and differences in physiological ranges for heart rate and respiratory rate.(14-16) Current monitoring methods require invasive and bulky devices that not only risk injury to neonatal skin (17, 18) but also preclude therapeutic parent-child skin-to-skin contact (19) and are not conducive for home use. Appropriately designed wearable biosensors have the potential to ameliorate these limitations and enable continuous, convenient physiological monitoring of neonates and infants. This systematic review assesses wearable devices that monitor cardiopulmonary function in neonates and infants by summarizing accuracy, performance, and usability.

Methods:

Search strategy and selection criteria

This systematic review assessed the accuracy and reliability of wearable devices for cardiopulmonary monitoring in neonates and infants available in the scientific literature. The protocol was prospectively registered on Prospero (CRD42020200642),(20) and reported according to PRISMA standards.(21) A medical librarian (M.B.) created search strategies for the themes of cardiovascular disease, infants, and wearable electronic devices. The search strategies were performed in PubMed (MEDLINE) 1946-, Embase (Elsevier) 1947-, the Cochrane Library (Wiley), Scopus (Elsevier) 1823-, and IEEE Explore (IEEE) 1872-. The search strategies for the Embase, Cochrane, Scopus, and IEEE databases were adapted from the MEDLINE search strategy. All databases were searched from inception with no date or language limits. Searches were completed by June 1, 2020. The full strategies are available in Appendix 3. All results were exported to Rayyan, and the automatic duplicate finder was applied.(22) The references of relevant studies were also reviewed to identify additional manuscripts.

"Inclusion criteria were the use and assessment of wearable technology in the neonatal or infant population. This includes subjects under two years of age, with neonates defined as birth to age less than one month and infants defined as age one month to less than two years per Food and Drug Administration guidelines. (23) "

Inclusion criteria were the use and assessment of wearable technology in the neonatal or infant population. This includes subjects under two years of age, with neonates defined as birth to age less than one month and infants defined as age one month to less than two years per Food and Drug Administration guidelines.(23) We also included programmable simulators for this age group for cardiopulmonary monitoring with the presentation of original data and publication in English. Animal studies, non-original studies, secondary research, abstracts, studies with only patient-reported outcomes, and studies using technology without investigation of its properties were excluded. Two reviewers (E.W., A.R.) screened all articles independently on the online Rayyan platform. First, a title and abstract screening were performed, followed by the full manuscript review of the selected abstracts. Disagreements were resolved by discussion between all reviewers.

Data analysis:

A standardized template for data extraction was developed and piloted with three articles in which two authors (E.W., A.R.) extracted relevant data. Both individual patient-level data and summary estimates were used. The template was modified according to the pilot assessment, and each author subsequently independently extracted data from the remaining articles. Each reviewer assessed all manuscripts for risk of bias using a modified ROBINS-I scale (available in Appendix 4), constructed with the assistance of the medical librarian (M.B.), which included grading of selection, performance, attrition, detection, and reporting bias.(24) The outcome measures reported by the studies were heterogeneous. Extracted variables included sensitivity, specificity, intraclass correlation coefficients, and mean difference. Discrepancies in the extraction results were discussed and resolved by both reviewers.

Results:

The search identified a total of 2323 unique citations. Four additional studies were identified through hand searching and review of references of included studies. After title and abstract review, 28 full-text articles were assessed for eligibility, and 16 studies describing 17 neonatal wearable devices were included in the final analysis (Figure 1). Three of the devices assessed were commercially available (Baby Vida, Owlet Smart Sock 2, and ANNE One), while the remaining 14 were in development as of 2020. Overall, 14 studies were engineering papers, and two were non-randomized studies of interventions. Additional information regarding the included studies is detailed in Table 1.

Device Designs

Body Placement

Given the intended utility of wearables as convenient, non-invasive devices for continuous monitoring, location, and placement of the device on the body are critical considerations in their design. This is a particular challenge in neonates and infants with smaller total body surface areas and often more fragile and irritable skin.(25) Most wearables in the cohort were designed for placement on the neonate's foot (three studies) or chest (three studies), or both (two studies) (Figure 2). Foot devices were wrapped around the foot and ankle, characterized as "socks," "booties," or skin-like wireless foot modules. Chest units varied from adhesive biosensors to chest belts. Six studies developed devices embedded in an article of clothing. Two devices were secured to the forehead, which the authors asserted would limit manipulation during clothing removal.(26) Generally, devices with both chest and limb components report more accurate device outputs.

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Battery

Power management is an important component of wearable device development given their intended use as long-term continuous monitoring tools,(27) and a significant portion of energy consumption occurs during raw data transmission from the device to external sites or the cloud.(28) Eight studies reported the use of a Bluetooth Low Energy (15) system to transmit collected data. Other technologies include near-field communication,(15) Teflon-associated microwires,(15) Zigbee technology,(29) and microcontroller transceivers.(30) To satisfy power requirements, most used commercially available batteries. However, innovation in battery technology and battery-free power sources are exciting and necessary for the evolution of future wearables(27). Chung et al. described several alternate power sources, including a modular bat-

Figure 1: Study selection (Prisma flowsheet)

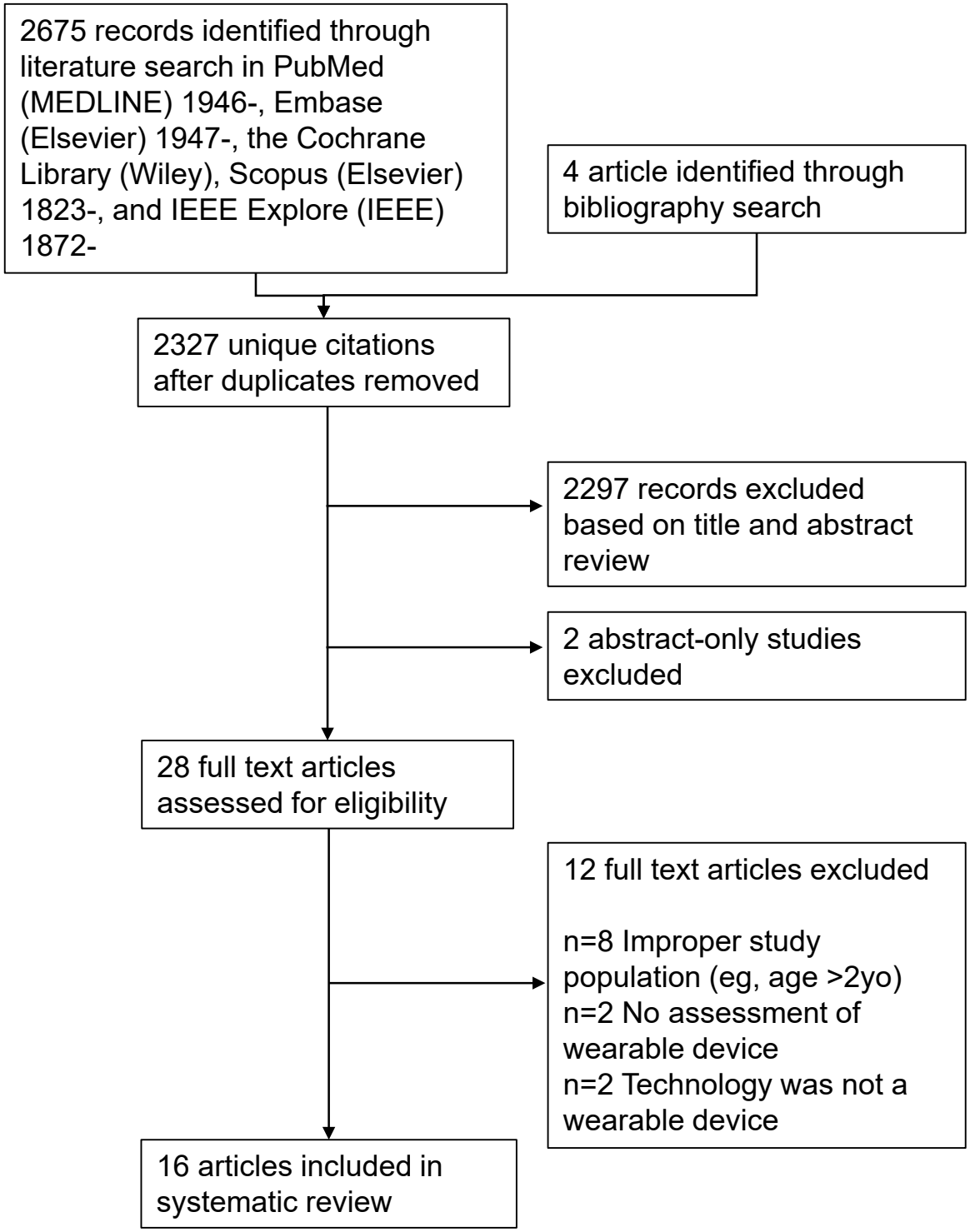

Table 1: Summary of Included Studies and Devices

Study	Study Type; Design	Wearable Device	Vital Signs Collected	Device Location	Device Design Technologies
Agezo et al, 2016	Conference Proceeding; Engineering Paper	Fabric onesie with Techniktex P180+B electrodes	Raw Data: ECG; Calculated Data: HR	Full body	Data Collection: TechnikTex P180+B[1] Data Transmission: RFID[2], Bluetooth Battery: no battery required
Bonafide et al, 2018	Letter; Non-randomized study of the effects of interventionS	Owlet Smart Sock 2 Baby Vida	Raw Data: pulse oximetry; Calculated Data: SpO_2, pulse rate	Foot & Ankle	Data Collection: Baby Vida device, Owlet Smart Sock Device Data Transmission: Bluetooth
Chen et al, 2010	Full Report; Engineering Paper	Smart jacket	Raw Data: ECG, SpO_2, body temperature	Full body	Data Collection: Medtex 130+B[3] textile electrodes by Shieldex and gold printed textile electrodes by TNO Science and Indusrtry; NTC Mon-A-Therm 90045 temperature sensor[4] Data Transmission: unspecified conductive textile wires
Chen et al, 2020	Full Report; Engineering Paper	Smart vest	Raw Data: ECG, motion, respiratory signals Calculated Data: HR, RR	Full body	Data Collection: Silver textile electrodes (Technik-tex P130 + B[5] and Berline RS of Shieldex Company[6]), PDMS-Graphene compound-based sensor[7], inertial measurement unit (IMU) sensors (MPU9250)[8] Data Transmission: Bluetooth Battery: 3.7V Li-battery and charging circuit
Chung et al, 2019	Full Report; Engineering Paper	Chest ECG device, foot PPG device	Raw Data: ECG, PPG, temperature; Calculated Data: HR, HR variability, RR, blood oxygenation, PAT	Chest; Foot	Data Collection: 2 wireless epidermal electronic system (EES) with chip-scale circuit components, metal mesh microstructures, small scale LEDs, temperature sensor; Data Transmission: near field communication
Chung et al, 2020	Letter; Engineering Paper	Chest unit, limb unit	Raw Data: acoustic signatures, PPG, movement/ changes in body orientation; Calculated Data: HR, RR, SpsO2, temperature, PAT, PTT	Chest; Limb on various peripheral locations	Data Collection: Wide-bandwidth 3-axial accelerometer (BMI160[9], Bosch Sensortec), clinical-grade temperature sensor (MAX30205[10], Maxim Integrated), ECG system consisting of two gold-plated electrodes, integrated pulse oximetry module (MAX30101[11], Maxim Integrated), temperature sensor (MAX30205[10], Maxim Integrated) Data Transmission: Bluetooth Low Energy System Battery: Several Configurations including modular battery unit coupled to device through pairs of magnets, battery-free that relies on wireless power transfer, wirelessly rechargeable lithium polymer battery
De et al, 2017	Full Report; Engineering Paper	Forehead belt	Raw Data: acceleration, HR, body temperature	Forehead	Data Collection: Silver textile electrodes (Technik-tex P130 + B[5] and Berline RS of Shieldex Company[6]), PDMS-Graphene compound-based sensor, inertial measurement unit (IMU) sensors (MPU9250[8]) Data Transmission: Data cable Battery: 3.7V Li-battery and charging circuit

Ferreira et al, 2016	Conference Proceeding; Engineering Paper	Chest belt	Raw Data: Accelerometry, Body temperature, ECG; Calculated Data: HR, RR, body position	Chest	Data Collection: iOT device with infrared thermopile sensor (TMP007[12]), LSM330DLC[13] inertial sensor, CC2530[14] microcontroller, AD8232[15] signal conditioning block Data Transmission: Zigbee technology to H Medical Interface, wireless USB adapter TL-WN725N[16]; Storage: cloud storage center Battery: TPS63060[17] battery
Inamori et al, 2020	Conference Proceeding; Engineering Paper	Forehead device	Raw Data: Reflected light intensity from LEDs; Calculated Data: HR, bilirubin concentration, SpO2	Forehead	Data Collection: 4 photodiodes with 4 wavelengths of LEDs, microcontroller unit for controlled timing of emissions Data Transmission: Bluetooth Low Energy Battery: Cointype cells
Leier et al, 2014	Conference Proceeding; Engineering Paper	Foot monitoring device	Raw Data: accelerometry, body temperature, PPG; Calculated Data: HR, RR, body posture and activity, SpO2	Foot	Data Collection: Three-axes accelerometer (BMA280[18]), optical sensors on flex cable, temperature sensor on flex cable Data Transmission: Bluetooth Low Energy, Micro-USB interface; Storage: On-board ferro-electric RAM memory module Battery: 400 mAH battery with micro-USB charging
Linti et al, 2006	Conference Proceeding; Engineering Paper	Sensory baby vest	Raw Data: ECG, delta resistance between thermistors, Garment moisture; Calculated Data: HR, RR, temperature, humidity/sweating	Full Body	Data Collection: Dry electrodes on garment with silicone rubber printed on textile substrate, silver particles, moisture sensors, miniature NTC thermistors[19] integrated into ribbon cable Data Transmission: AWG36[20]
Maitha et al, 2020	Full Report; Engineering Paper	Wireless vest	Raw Data: ECG, Respiratory signal, accelerometry; Calculated Data: HR, RR, body position	Full Body	Data Collection: 3 removable + replaceable patch electrodes, 3 axis accelerometer, force sensitive resistor; Data Transmission: Bluetooth Storage: SD card Battery: 2500 mAH battery + 3.3 V
Petrus et al, 2015	Full Report; Non-randomized study of the effects of interventions	Vest-based Floright ® system	Raw Data: Magnetic field signal; Calculated Data: HR	Full body	Data Collection: Magnetic dipole moment generated by vest + detected by antenna
Raj et al, 2018	Conference Proceeding; Engineering Paper	Wearable respiratory rate device	Raw Data: 3-axis accelerometer; Calculated Data: RR	Abdomen and chest	Data Collection: 3 axis accelerometer LIS2HH12[21] with 16-bit resolution Data Transmission: Bluetooth; Storage: None, streams raw data in analysis mode + transmits locally computed RR to gateway device which communicates with Cloud Battery: 3.7 V, 200 mAH Li-ion battery
Rimet et al, 2007	Conference Proceedings; Engineering Paper	BBA Bootee	Raw Data: pulse oximetry; Calculated Data: HR, position, SpO2	Foot	Data Collection: OEM III oximetry module[22], 3-axes accelerometer Data Transmission: Nordic ref. nRF9E5[23] Battery: 3.6 V battery + recharging circuity

Vora et al, 2017	Conference Proceeding; Engineering Paper	RFID Infant Monitor (Bellyband)	Raw Data: ECG, fabric strain gauge; Calculated Data: HR, RR	Abdomen and chest	Data Collection: electrodes for ECG, fabric strain gauge, RFID antenna Data Transmission: RFID tags Battery: no battery required

Legend: HR= heart rate, RR= respiratory rate, ECG= electrocardiogram, PPG=photoplethysmography, PAT=pulse arrival time, PTT=pulse transit time, RFID=radio frequency identification, ioT = internet of things, RAM= random access memory, SpO_2 = oxygen saturation

Terms: 1. TechnikTex P180+B: high conductive silver-plated knitted fabric, 2. RFID: radio frequency identification, 3. Medtex 130+B: silver coated textile electrodes by Shieldex, 4. NTC Mon-A-Therm 90045: temperature sensor, 5. TechnikTex P130+B: high conductive silver-plated knitted fabric, 6. Berline RS: high conductive silver-plated knitted fabric, 7. PDMS-Graphene compound-based sensor: polydimethylsiloxane-graphene, 8. MPU9250: a 9 degree-of-freedom (9-DoF) inertial measurement unit (IMU); small profile sensor houses an accelerometer and gyroscope, 9. BMI160: small, low power inertial power unit, 10. MAX30205: accurate temperature sensor with alarm/shutdown/interrupt output; has a high-resolution sigma-delta ADC (Analog-to-Digital Converter) that converts the temperature data to digital form, 11. MAX30101: high-sensitivity pulse oximeter and HR Sensor for fitness & healthcare, 12. TMP007: the latest thermopile sensor from TI, 13. LSM330DLC: a system-in-package featuring a 3D digital accelerometer and a 3D digital gyroscope, 14. CC2530: Zigbee and IEEE 802.15. 4 wireless microcontroller with 256kB Flash and 8kB RAM, 15. AD8232: an integrated signal conditioning block for ECG, 16. TL-WN725N: wireless USB adapter, 17. TPS6306x devices: provide a power supply solution for products powered by either three-cell up to six-cell alkaline, NiCd or NiMH battery, or a one-cell or dual-cell Li-Ion or Li-polymer battery, 18. BMA280 is an advanced, triaxial, low-g acceleration sensor with digital interfaces, aiming for low-power consumer electronics applications, 19. NTC thermistors: non-linear resistors, which alter their resistance characteristics with temperature; resistance of NTC will decrease as the temperature increases, 20. AWG36: flexible, Teflon-isolated microwires, 21. LIS2HH12: ultra-low-power high-performance three-axis linear accelerometer that is capable of measuring accelerations with output data rates from 10 Hz to 800 Hz, 22. OEM III Module provides a simple way to incorporate Nonin pulse oximetry technology, 23. Nordic ref. nRF9E5:microcontroller transceiver

tery unit that magnetically and electrically couples to their chest sensor called ANNE® One.(31) In addition, the study described the potential for a battery-free system that relies on wireless power transfer via a magnetically coupled harvesting unit configured to receive power from a transmission antenna.(16) Newly developed fabric onesie and Bellyband devices were battery-free, utilizing passive Radio Frequency Identification (RFID) technology for continuous energy supply.(32)

"Wearable devices often have four major modalities: (1) a biopotential-specific sensor unit, such as an electrocardiogram (ECG), (2) a motion sensor unit, such as an accelerometer or gyroscope, (3) an optical measurement unit, such as a photoplethysmograph, and (4) an environmental sensor unit, such as a video camera."

Device Outputs:

Wearable devices often have four major modalities: (1) a biopotential-specific sensor unit, such as an electrocardiogram (ECG), (2) a motion sensor unit, such as an accelerometer or gyroscope, (3) an optical measurement unit, such as a photoplethysmograph, and (4) an environmental sensor unit, such as a video camera. The devices included in this review contained variable combinations of these sensor modalities (Table 1). Of the 14 devices, 11 included a biopotential-specific sensor unit: six devices had ECG monitoring capabilities, and three contained pulse oximetry sensors. Seven of the 14 studies incorporated a motion sensor unit as a 3-axis-accelerometer. Three devices utilized photoplethysmography (PPG) sensors. Finally, five incorporated environmental sensors to measure body temperature and respiratory rate (16).

Given the breadth of possible cardiopulmonary function measures, final device outputs were not uniform across the devices. The simplest devices measured only respiratory rate. More advanced sensors reported an array of physiological parameters, including heart rate (H.R.), body temperature, and pulse oxygen saturation (SpO_2). H.R. was calculated through several methods, including the derivation from PPG, ECG, and reflected light intensities of the arterial pulse.(25) While PPG-derived HR is most accurate due to minimal confounding factors such as breathing patterns; all three methodologies are readily utilized and accepted.(33) R.R. was derived by pulse oximetry,(34) 3-axis-accelerometry,(35) fabric strain gauges,(32) magnetic field signal,(36) and ECG.(15, 16) Several devices reported unique capabilities, including sweat monitoring through collecting raw garment moisture volume(29) and ECG-derived pulse arrival time (PAT), which is a surrogate for continuous systolic blood pressure.(16)

Performance Metrics:

The primary outcome of interest was device accuracy and performance. However, there was significant heterogeneity in how results were reported across studies. Some studies reported sensitivity and specificity, while others reported alternate parameters, including mean differences and intraclass correlation coefficients. This variability can be attributed to the variety of device validation methodologies utilized by investigators and the different stages of development in which devices were tested.

Study Conditions:

While most publications recruited neonates and infants for testing, two studies used simulated models: an age-matched infant and a skin model to test a bellyband device and a onesie, respectively.(32, 37) Subgroups of neonates and infants also studied varied, with inclusion criteria as specific as infants with pulmonary disease(36) to as wide a group as all admitted premature neonates in the neonatal intensive care unit (NICU) and pediatric intensive care unit (PICU).(15, 16, 38, 39) Bonafide et al. utilized the broadest study population, which included infants with any cardiopulmonary condition requiring hospitalization at a large U.S. children's hospital.(34) When reported, the duration of device testing ranged widely from 18 minutes(40) to 230 hours.(31) Only two other studies carried out more than two hours of device validation, citing 30 and 2.5 hours of data, respectively.(16, 39) Study sizes were similarly disparate, varying from one subject(29, 30, 32, 37, 38, 41) to the largest cohort of 71 subjects.(31) There were several failures to report device validation methodology–one study did not report sample size,(25) and seven omitted descriptions of testing duration (Table 3). Device validation was overwhelmingly performed in the hospital or laboratory, with only one study conducting validation tests in the home.(15)

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Validated Devices:

In order to clinically validate new technologies, existing standard of care consensus systems must be used for product testing.(42, 43) In our cohort of studies, gold standard devices such as the IntelliVue MX800 bedside patient monitor and Masimo SpO_2 sensors were utilized as comparators in four of the 16 studies. Only these four studies can be validly assessed via their reported outcomes. Three of the studied devices demonstrated strong performances and close correlation with standard-of-care system outputs. Chung et al. developed and validated two separate monitoring platforms. In a 2019 Science paper, they introduced a binodal wearable system consisting of two electronic components mounted on the chest and foot, respectively. The system had H.R., R.R., and SpO_2 measuring capabilities validated in three NICU neonates. There was a reported mean difference of –0.17 beats per minute, 0.75 breaths per minute, and 1.02% for H.R., R.R., and SpO_2, respectively, when compared to the IntelliVue MX800. This wearable system also piloted PAT calculations via ECG and PPG raw data, although no correlative results with gold standard blood pressure measurements were reported. In the 2020 Nature Medicine article, the group described a newer iteration of their wearable system (ANNE® One) with more robust validation data. Compared to the IntelliVue MX800, the wireless sensor H.R. and SpO_2 measures showed a mean difference of -0·02 beats per minute and 0·11%, respectively, for a cohort of 20 neonates.(16) The calculated H.R. standard deviation (S.D.)

Study	Selection Bias		Performance Bias		Attrition Bias		Detection Bias	Reporting Bias	Overall Quality
	Consistent application of inclusion and exclusion criteria in selection of participants	Selection of representative group of participants with adequate sample size	Followed methods as outlined	Followed a method that could be used to validate the device	Reporting of all outcome data	Reporting of device validation data.	Consistent and comprehensive outcome measures	Complete, non-selective reporting of data	
Agezo et al, 2016	High	High	Low	Low	Unclear	Unclear	Low	High	Med risk of bias
Bonafide et al, 2018	Low	Low	Low	Low	High	Low	Low	Low	Low risk of bias
Chen et al, 2010	High	High	Low	Low	Low	Low	High	High	Med risk of bias
Chen et al, 2020	Low	Low	Low	Low	Low	Low	Low	Low	Low risk of bias
Chung et al, 2019	Low	Low	Low	Low	Low	Low	Low	Low	Low risk of bias
Chung et al, 2020	Low	High	Low	Low	Low	Low	Low	High	Low risk of bias
De et al, 2017	Low	High	Low	Low	High	Low	High	High	Med risk of bias
Ferreira et al, 2016	High	High	Low	Low	High	High	Low	High	High risk of bias
Inamori et al, 2020	High	High	Low	Low	High	High	Low	High	High risk of bias
Leier et al, 2014	High	High	Low	High	High	High	Unclear	High	High risk of bias
Linti et al, 2006	High	Unclear	Low	High	High	High	High	High	High risk of bias
Maitha et al, 2020	High	High	Low	High	Low	Unclear	Low	Low	Med risk of bias
Petrus et al, 2015	Low	High	Low	Low	Low	Low	Low	Low	Low risk of bias
Raj et al, 2018	Low	Low	Low	Low	Low	Low	Low	Low	Low risk of bias
Rimet et al, 2007	Low	Low	Low	Low	Low	Low	Low	Low	Low risk of bias
Vora et al, 2017	Unclear	Unclear	Low	Low	High	Low	Low	High	Med risk of bias

Table 2: *Quality and Bias Assessment of Included Studies*

Risk of bias was assessed using a modified ROBBINS criteria and 3 categorizations: low, high and unclear risk of bias. Overall quality was reported as med (medium), low, and high risk of bias.

Table 3: Performance and Accuracy of Wearable Devices

Study	Wearable Device	Relevant measures tested	Study Population	Cumulative Duration of Testing	Testing Condition	Comparator (*standard of care)	Main Findings
Agezo et al, 2016	Fabric onesie	Heart rate	1 skin dummy with cardio ECG stimulator	Unspecified	Lab	MediTrace foam electrodes	Output signal quality obtained from fabric onesie had 98.80% correlation with that from standard foam comparator.
Bonafide et al, 2018	Owlet Smart Sock 2	SpO_2	30 infants	60 hours	Hospital	Masimo Radical 7*	Sensitivity for hypoxemia was 88.8%. Specificity for hypoxemia was 85.7%. Sensitivity for bradycardia was 0.0%. Specificity for bradycardia was 100.0%.
	Baby Vida						Sensitivity for hypoxemia was 0.0%. Specificity for hypoxemia was 100.0%. Sensitivity for bradycardia was 0.0%. Specificity for bradycardia was 82.3%.
Chen et al, 2010	Smart jacket	Heart rate, SpO_2, temperature	1 premature infant	Unspecified	NICU	Solar® 8000M patient monitor	Temperature readings were within 0.1°C of Solar® 8000M. "Very good agreement" between smart jacket and Solar® 8000M derived HR and SpO_2.
Chen et al, 2020	Smart vest	ECG, heart rate, respiratory rate	15 neonates	150 minutes	NICU	Polysomnography (PSG)	ECG has "comparable signal quality and amplitude compared to PSG". HR Pearson correlation of r=0.967. RR Pearson correlation monitoring was r=0.969.
Chung et al, 2019	Dual sensor system including a chest and limb sensor.	Heart rate, respiratory rate, SpO_2	3 neonates	Unspecified	NICU	Intellevue MX800, Philips*	HR mean difference of –0.17 beats per minute. RR mean difference of 0.76 breaths per minute SpO_2 mean difference of 1.02%.
Chung et al, 2020	ANNE® One monitoring platform with two sensors including a chest and limb sensor.	Heart rate, SpO_2, temperature	20 neonates	25 hours	NICU, PICU	Intellevue MX800, Philips*; Giraffe Omnibed Incubator, GE (temp	HR mean difference of –0.02 beats per minute, SD of 2.08 bpm. SpO_2 mean difference of 0.11%, accuracy root mean square of 2.99% Temperature mean difference of 0.21°C, SD of 0.26°C.
		Respiratory rate	6 neonates	Unspecified (41 data points)	NICU, PICU	Direct physician observation	RR mean difference of 0.11, SD of 1.95 bpm.
		PAT/PTT	2 infants	4 hours	PICU	Arterial line*	PAT-derived SBP mean difference of 1.60 mmHg, SD of 7.99 mmHg. PTT-derived SBP mean difference of –0.04 mmHg, SD of 7.86 mmHg. (These results are within the ANSI/AA<MI SP10 standard for blood-pressure cuffs, which requires a mean different and SD of <5 mmHg and <8 mmHg.)

De et al, 2017	Forehead belt	Body temperature, ambient temperature, acceleration, heart rate	3 neonates	1.5 hours	Hospital	Unspecified	Temperatures, body acceleration and heart rates correlated exactly with existing wired system.
Ferreira et al, 2016	Chest belt	Heart rate, respiratory rate	1 infant	"Minutes"	Unspecified	Polar model T-34 heart rate chest strap	Chest belt and standard reference system "behave similarly in terms of heart rate measurement". Device able to detect all breaths when infant is on their back.
Inamori et al, 2020	Forehead device	Heart rate, SpO_2	Neonates	Unspecified	Unspecified	Unspecified	HR and SpO_2 results were "close to commercial monitor".
Leier et al, 2014	Foot monitoring device	Heart rate, respiratory rate, SpO_2	1 neonate	"Several hours"	Unspecified	None	No analysis of device accuracy.
Linti et al, 2006	Sensory baby vest	Heart rate, respiratory rate, temperature	1 simulation infant	Unspecified	Lab, hospital	None	No analysis of device accuracy.
Maitha et al, 2020	Wireless vest	Heart rate, respiratory rate, body position	2 infants	1121.2 seconds	Lab	None	Accelerometry data was qualitatively consistent with observed movement.
Petrus et al, 2015	Vest-based Floright ® system	Respiratory rate	19 healthy infants, 18 infants with lung disease	380 minutes	Hospital	Ultrasonic flowmeter (USFM)	RR mean difference of 0.71/min, with a 95% CI 0.24 – 1.17, p= 0.031.
Raj et al, 2018	Wearable respiratory rate device	Respiratory rate	30 neonates	Unspecified	Hospital	Clinician tabulated RR + video camera for backup/ cross certification	Device had a correlation coefficient (r) of 0.974 with physician tabulated values.
Rimet et al, 2007	BBA Bootee	Heart rate, SpO_2	71 neonates	230 hours	Hospital	Hewlett Packard Merlin with a Nellcor SpO_2 module*; Datascope Passport II with a Masimo SpO_2 module*	SpO_2 mean difference of -2.7%, SD of 2.1% and HR mean difference of -1bpm, SD of 9bpm when compared to the HP/ Nellcor unit. SpO_2 mean difference of 0.4%, SD of 1.6% and HR mean difference of -3bpm, SD 6bpm when compared to the Masimo unit.
Vora et al, 2017	RFID Infant Monitor (Bellyband)	Heart rate, respiratory rate	Simulation infant	Unspecified	Lab	NI myDAQ (data acquisition module)	Heart rate correlation was r=0.9976. Respiration monitor detected apnea within 10s of its onset.

Legend: SpO_2 = oxygen saturation, SD = standard deviation

Definitions: neonate = under 28 days old, infant = at or under 1 year old

of 2·08 beats per minute and SpO_2 accuracy root mean square of 2·99% fell within the regulatory guidelines of the Food and Drug Administration (FDA).(44) PAT- and pulse transit time (PTT)-derived systolic blood pressure were validated against arterial line monitoring and reported mean difference. S.D. similarly fell within American National Standards Institute and Association for the Advancement of Medical Instrumentation SP10 standards .(45) (15) The third validated device is the BBA Bootee described by Rimet et al. (31) This soft sandal-like device primarily reports H.R. and SpO_2 but also features an accelerometer which outputs infant motion data. In their study of 71 infants, they reported H.R. mean difference ± S.D. of -2·7% ± 2·1% (-1 bpm±9 bpm) compared with an FDA-approved Nellcor™ system and SpO_2 mean difference +/- SD of 0·4%±1·6% (-3bpm±6bpm) compared with the Masimo SET® pulse oximeter.

"The Owlet Smart Sock demonstrated a sensitivity and specificity for detection of hypoxemia of 88·8% and 85·7%, respectively. However, sensitivity and specificity for bradycardia detection were 0·0% and 100·0%."

Unvalidated Devices:

Although Bonafide et al. used standardized comparators in their investigation of two marketed devices, their results demonstrated the inaccuracy of technology. Thirty hours of the pulse oximeter and pulse measurements by the Owlet Smart Sock and Baby Vida were compared with the Masimo Radical 7 device, which features the Masimo rainbow SET® pulse oximeter.(34) The Owlet Smart Sock demonstrated a sensitivity and specificity for detection of hypoxemia of 88·8% and 85·7%, respectively. However, sensitivity and specificity for bradycardia detection were 0·0% and 100·0%. The Baby Vida sensitivity and specificity for hypoxemia were 0·0% and 100·0%, and for bradycardia, 0·0% and 82·3%, respectively. Unspecified or non-standard of care comparators were used in the remaining twelve studies. These comparators included video camera-captured respiratory and physician-observed respiratory rates, which were used to validate the respiratory rate monitoring device.(35) Validation of the RFID Bellyband reported a H.R. correlation of r=0·998 with a portable data acquisition device called N.I. myDAQ .(32) A commercially available yet clinically unvalidated was used to test a novel chest belt device,(30) and an ultrasonic flowmeter with facemask was compared to a newly developed vest system (36). Strong Pearson correlation coefficients (H.R. correlation of r=0·967 and R.R. correlation of r=0·969) were reported between the smart vest and an unspecified polysomnography unit.(39) In another study of a novel forehead belt, the comparator was described as the hospital's "existing wired system"; however, further detail regarding the make and model of the technology was omitted.(26) Three studies did not use a comparator or report device accuracy.(29, 40, 41) In several instances, studies reported using comparator measures but did not publish the comparison data between the wearable and the standard of care device.(25, 30) For example, the smart jacket described by Chen et al. was validated against a Solar® 8000M patient monitor; however, data points and statistical analysis were not reported.(38)

Quality Assessment:

The quality of each publication was assessed based on selection bias, performance bias, attrition, detection, and reporting bias based on the modified ROBINS-I scale, outlined in Table 2. Overall, six of the 16 studies had a high risk of selection bias due to inconsistent application of inclusion and exclusion criteria in participant selection, inadequate sample sizes, and unrepresentative participant groups. Three studies were at high risk of performance bias, given the failure to follow rigorous methods that could be used to validate the device. Additionally, seven studies had high attrition bias due to incomplete outcome data reporting, while four studies had high attrition bias due to a lack of device validation reporting. Most studies (12 of 16) had low detection bias, defined as bias in the outcome measurement outcome. Eight studies had high reporting bias due to selective data reporting.

"This review, including 16 studies, summarizes the evidence around the accuracy and performance of wearables for cardiopulmonary monitoring in neonates and infants. This is the first systematic review to explore the validity and reliability of wearable technologies for continuous monitoring in this population."

Discussion:

This review, including 16 studies, summarizes the evidence around the accuracy and performance of wearables for cardiopulmonary monitoring in neonates and infants. This is the first systematic review to explore the validity and reliability of wearable technologies for continuous monitoring in this population. Three novel technologies (the mechanical adhesive sensors of Chung et al.,(15, 16) and the BBA Bootee(31)) provided robust evidence of reliable performance with data outputs characterized by low mean differences against standard-of-care systems. Newer systems, published more recently than this review, suggest opportunities to assess both traditional vital signs such as heart rate and blood oxygenation as well as advanced measures such as cerebral hemodynamic monitoring.(46)

While the remaining 13 studies described the device designs with technical detail, clinical evaluation was limited; small sample sizes, poor comparators, and multiple instances of missing data compromised results. Short device testing durations were particularly notable, as the intention of wearables is long-term, continuous monitoring to capture rare catastrophic events rather than surveil intermittent point measurements of vital signs. This highlights the limitations of the current body of research on wearables in the infant and neonate population, with a need for larger, more rigorous investigations.

Furthermore, while wearable devices are most promising and often marketed for home monitoring neonates and infants (e.g., Owlet), only one was tested in a non-hospital or laboratory setting. While most studies described wearables newly developed by the authors, there is a need for external validation testing. For instance, Bonafide et al. investigated two marketed but non-FDA cleared devices: the Baby Vida and Owlet Smart Sock 2.(34) They showed that the Owlet Smart Sock inconsistently detected hypoxemia and the Baby Vida device failed to both detect hypoxemia and display accurate low pulse rates. Home-based monitoring for neonates and infants remains a major unmet clinical need, where wearable wireless devices have tremendous potential. A recent analysis of NICU Medicaid patients demonstrated a 37% one-

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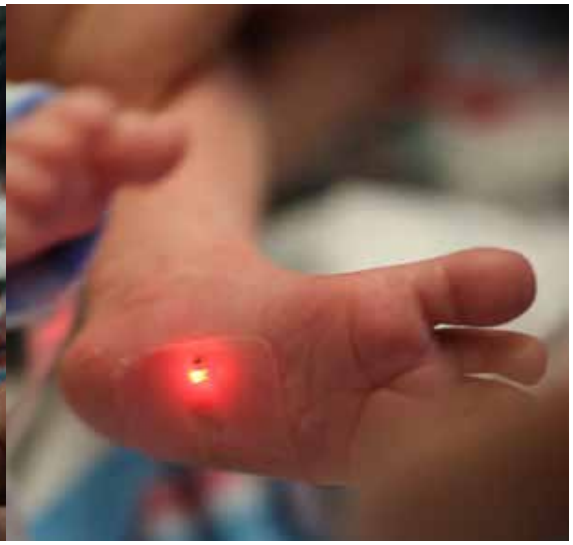

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year readmission rate, (47) suggesting inadequacies of discharge planning and home transition programs, which could be aided by implementing wearable home monitoring devices.

Notably, the current evidence for wearables use in neonates and infants has a low-GRADE rating.(48) In our overall quality assessment, 25% and 31% of included studies were systematically characterized by high and medium risk of bias, respectively. Data logging and processing and device sensitivity and specificity validation must be improved to assure the broad applicability of high-quality, evidence-based technologies in continuous cardiopulmonary monitoring. Fortunately, some of these efforts are ongoing, with some systems even achieving FDA clearance. For instance, the ANNE One system (Sibel Inc., Niles, IL), included in this review,(16, 49) and the Lifetouch biosensor (Isansys Lifecare Ltd, Oxfordshire, U.K.) (50) are FDA-cleared but currently limited to only adults. A recent 2022 publication showed that the ANNE One system compared favorably for heart rate, respiratory rate, SpO_2, and temperature against gold standard wired systems in n=84 neonates.(51) Notably, another medical device startup focused on global health, Neopenda, is also developing a wearable forehead device for neonatal monitoring in low-income settings.(52) Future work should focus on rigorous, well-conducted comparative trials of these new systems with gold standard wired monitoring systems followed by confirmatory studies in the home.

"Our review here suggests a tremendous unmet clinical need and a gap in evidence for novel wearable monitoring platforms for neonates and infants—too often, vulnerable populations such as these are overlooked when it comes to medical technology innovation."

Conclusion:

Our review here suggests a tremendous unmet clinical need and a gap in evidence for novel wearable monitoring platforms for neonates and infants—too often, vulnerable populations such as these are overlooked when it comes to medical technology innovation. In 2016, Congress enacted the 21st Century Cures Act with explicit incentives to drive forward pediatric device innovation. (53) Since then, the FDA has acted in conjunction with industry and other stakeholders to support pediatric device development through targeted meetings(54) and new initiatives (e.g., System of Hospitals for Innovation in Pediatrics(55)). The needs of neonates and infants for new monitoring solutions can only be met through coordinated collaboration between academics, entrepreneurs, industry, and regulators.

Figure 2: Wearable devices for cardiopulmonary monitoring in neonates and infants

Top: Textile-based devices

A. Foot monitor composed of a three-axis accelerometer, optical sensors, and temperature sensor(41)

B. Fabric onesie with two sewn-in ECG electrodes and RFID integrated connectors; ECG pulse signal obtained from onesie showing high correlation with a foam electrode(37)

Bottom: Patch-based devices

C. Skin interfaced biosensors designed for the limb and chest; Bland-Altman plots showing insignificant mean difference standards for H.R. and SpO_2(16)

D. Ultrathin, wireless ECG patch mounted on the chest with representation ECG and PPG waveform outputs from a healthy neonate(15)

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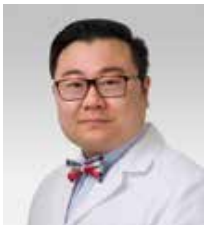

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