

Wireless skin sensors for physiological monitoring of infants in low-income and middle-income countries



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Globally, neonatal mortality remains unacceptably high. Physiological monitoring is foundational to the care of these vulnerable patients to assess neonatal cardiopulmonary status, guide medical intervention, and determine readiness for safe discharge. However, most existing physiological monitoring systems require multiple electrodes and sensors, which are linked to wires tethered to wall-mounted display units, to adhere to the skin. For neonates, these systems can cause skin injury, prevent kangaroo mother care, and complicate basic clinical care. Novel, wireless, and biointegrated sensors provide opportunities to enhance monitoring capabilities, reduce iatrogenic injuries, and promote family-centric care. Early validation data have shown performance equivalent to (and sometimes exceeding) standard-of-care monitoring systems in premature neonates cared for in high-income countries. The reusable nature of these sensors and compatibility with low-cost mobile phones have the future potential to enable substantially lower monitoring costs compared with existing systems. Deployment at scale, in low-income countries, holds the promise of substantial improvements in neonatal outcomes.

Introduction

The 2030 UN Sustainable Development Goals call for a reduction in preventable neonatal deaths from 2.7 to 1.2 million per year (<12 per 1000 livebirths) in low-income and middle-income countries (LMICs).¹ To achieve this goal, greater attention towards the major modifiable drivers of neonatal death is required—prematurity (35%), intrapartum complications (14%) such as birth asphyxia, and infection (14%) including sepsis, pneumonia, and meningitis. Moreover, acuity matters. A third of all global neonatal deaths occur during the first day of life and three-quarters within the first week of life.² Complications related to prematurity, intrapartum events, and infection lead to predictable physiological changes in heart rate, respiratory rate, blood pressure, temperature, and blood oxygenation (SpO₂) quantifiable by physiological monitoring systems. However, existing neonatal monitoring systems have undergone little innovation over the past five decades—nearly all requiring a multitude of rigid sensors and accessories affixed to a neonate's skin with strong adhesives or tape and are wired to large, bulky, and expensive base units.³ Current monitors from adult systems have been minimally adapted for use in neonates.⁴ Specific consideration is required for comprehensive neonatal monitoring in LMICs. Innovation in physiological monitoring systems has the potential to improve neonatal care in the intrapartum and early post-partum periods by addressing several key unmet clinical needs: wirelessly capturing both comprehensive and advanced physiological measurements of clinical relevance,⁴ reducing iatrogenic skin injuries,^{5,6} facilitating therapeutic kangaroo mother care⁷ and family-centric care,⁸ and alerting clinicians strategically⁹ to deliver lifesaving interventions.

The promise of so-called big data and artificial intelligence rely on high-quality inputs. Although existing physiological monitoring systems produce rich data streams continuously, these data have been underutilised in critical care for clinical decision making support.^{10,11}

The opportunities to link physiological data with electronic health records, imaging reports, and laboratory values have the potential to yield powerful algorithms to signal actionable diagnoses and predict future deterioration. Examples relevant to neonatal health include predictive algorithms for neonatal sepsis or intrapartum complications for both neonates and women in labour.¹² The HeRO system (Medical Predictive Science Corporation, Charlottesville, VA, USA) is a commercially available monitoring accessory that provides an early warning of neonatal deterioration.¹³ However, the promise of predictive algorithms and meaningful clinical decision support is hindered by several challenges with existing monitoring platforms. Access to raw data waveforms are difficult to obtain and often viewed by manufacturers as proprietary—for instance, the HeRO platform is limited to only the electrocardiogram (ECG) data stream without validation in the LMIC setting.^{10,14} Without access to this data, the development of deeper insights from the physiological outputs for clinical decision making support is challenging for data scientists. Second, substantial challenges in interoperability are present across physiological monitoring systems produced by different manufacturers.^{15,16} These challenges create fragmented data and inhibit data synthesis across platforms. Third, the large amount of generated data creates storage and management challenges.¹⁷ Finally, the existing commercially available systems that enable signal access from monitors (eg, BedMasterEx, Excel Medical Electronics; ViNES, Baxter; and Bernoulli Data Collection System, Capsule Technologies) might be too expensive or complicated in the LMIC setting where information technology (IT) infrastructure is scarce.

New sensor systems that advance the opportunity for clinical decision support and future predictive algorithms could directly address these issues. Our research group has developed systems that provide open access to all raw data files with automated signal quality indicators for each second of data output, allowing for

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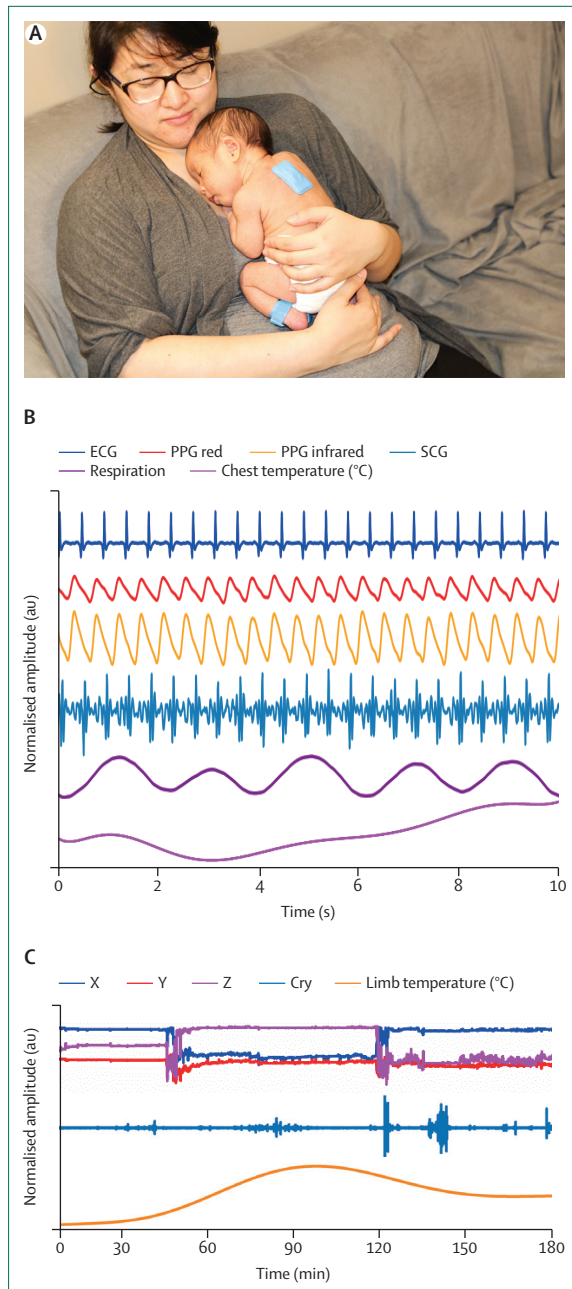


Figure 1: Comprehensive physiological outputs from wireless skin sensors (A) Placement of biointegrated sensors facilitate continuous physiological monitoring during kangaroo mother care. (B) The data streams from these sensors offer a comprehensive and continuous view of neonatal physiological status. (C) Advanced measurements, such as automated body position classification, dual temperature sensing, and crying time, offer new clinically relevant insights not typically collected in even the most advanced tertiary-level neonatal ICUs. Cry=cry time. ECG=electrocardiogram. ICU=intensive care unit. PPG red=photoplethysmographic red LED outputs. PPG IR=photoplethysmographic infrared LED outputs. SCG=seismocardiography. X=x-axis accelerometry. Y=y-axis accelerometry. Z=z-axis accelerometry.

future algorithm discovery that eliminates the need for time-consuming data cleaning, and preprocessing procedures. Expanded, high-fidelity data streams beyond

ECG, including measurements of temperature, seismocardiography, photoplethysmography, accelerometry, and arterial stiffness as a surrogate for systolic blood pressure, could enable more sensitive, specific, and predictive algorithms for neonatal health once validated in the LMIC setting. These algorithms could then be built into intuitive clinical decision making interfaces to facilitate timely interventions that reduce neonatal morbidity and mortality.

In the near-term, initial alarming could be established in which clinician-set thresholds of respiratory rate, heart rate, SpO₂, and temperature could trigger an alert on the mobile tablet or be pushed to a user's smartphone. These systems could also yield advanced indices that incorporate multiple physiological data streams in a single metric; for instance, the outputs of this system could display a Triage Early Warning Score as an input to the South African Triage Scale.¹⁸ With future clinical trials, validation, and regulatory approval, these systems have the potential to offer advanced capabilities ranging from broader prediction of clinical deterioration to more specific issues, such as the need for mechanical ventilation or nutritional support. When deployed at scale across large populations, these sensors could serve as a component of a broader epidemiological surveillance system for disease.

With alerts and clinical decision support, careful consideration will be required around overdiagnosis and alarming. Alarm fatigue is a serious patient safety concern related to physiological monitoring systems that can reduce productivity in cases of false alarms and desensitisation to alarms in genuine clinical emergencies.¹⁹ In LMICs, alarm fatigue is particularly dangerous given the low availability of medical professionals. Future efforts to reduce alarm fatigue should include managing the duration required to trigger an alarm on the basis of bradycardia, apnoea, or desaturation, and reducing non-actionable alarms for neonates.²⁰

A new class of monitoring technologies: wireless, skin-integrated sensors

Broadly, our research group has pioneered the development of a wide range of miniaturised, flexible, and biointegrated electronics for physiological monitoring and onbody biochemical sensing.^{21–24} From this body of work, we reported the development of a new wireless monitoring system with features explicitly designed for neonatal care, including electronic components connected via serpentine traces that allow for bending, stretching, and folding, and create small and thin form factors, embedded within medical grade silicone to ensure biocompatibility (figure 1A).³⁴ The innovative design provides high-quality measurement capabilities and data management while also ensuring skin safety. Central to this monitoring system are two soft, skin-like, and fully wireless sensors mounted centrally and peripherally that provide high-resolution intensive care unit (ICU) grade measurements

of heart rate via ECG, respiratory rate, SpO₂, and central and peripheral temperature (figure 1B). In addition to these core vital signs, the system continuously provides advanced measurements of high clinical utility that are not typically collected in even tertiary level neonatal ICUs in high-income countries. These capabilities include continuous measurements of arterial stiffness via determination of pulse wave velocity as a surrogate for systolic blood pressure, acousto-mechanic signatures of the heart via seismocardiography, neonatal vocalisations such as cry time, swallowing, and automated body position classifications for kangaroo mother care (figure 1C). Although these measurements are not typically collected in neonatal ICUs, they add value by providing additional information about the status and stability of the neonate. In regards to neonatal vocalisation, capturing these data might offer future opportunities to quantify neonatal distress, pain, or hunger in an automated fashion.^{25–27} Capturing the respiratory rate and respiratory phase with swallowing in a single data stream might permit continuous tracking of a neonate's ability to suck, swallow, and breathe to guide feeding interventions.²⁸ The ability to assess surrogates of blood pressure continuously via the skin offers alternative placement of invasive arterial lines, which are often not feasible in LMICs. Furthermore, invasive arterial lines can cause serious neonatal complications, such as vascular thrombosis, occlusion, infection, rupture, bleeding, and even death.^{29,30}

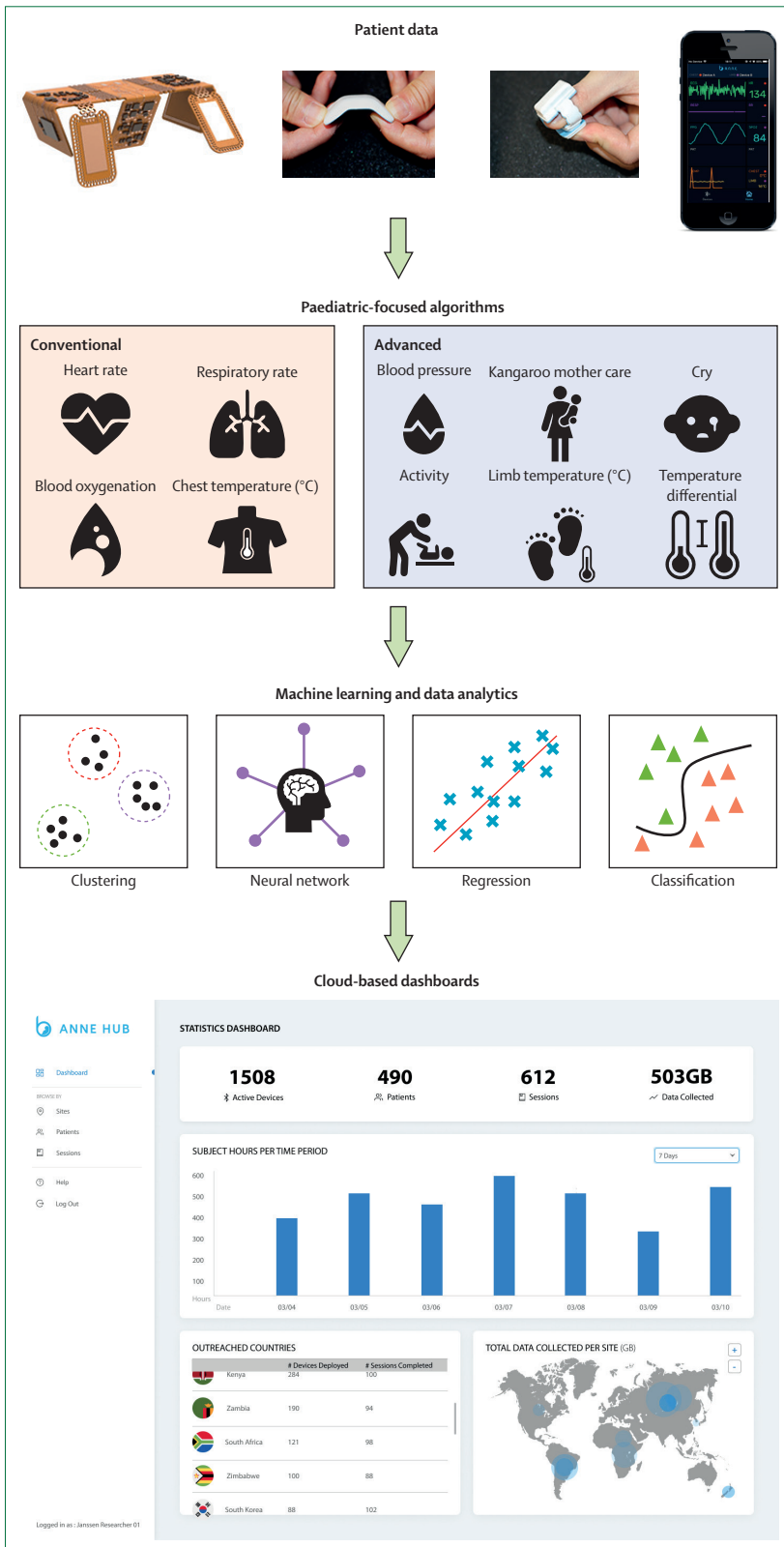
In addition to enhanced measurement and data management capabilities, the low profile, soft, and flexible nature of these skin-integrated sensors offers form factor adaptations designed for neonates. For instance, extremely low birthweight neonates are less than 1 kg with a small body surface area.³¹ In the smallest premature neonates in neonatal ICUs, 15% of the entire body surface area can be traumatised daily.³² Compared with adults, the skin of premature neonates is up to 60% thinner with substantially lower mechanical strength.³³ As such, the incidence of skin breakdown and iatrogenic injury due to medical devices and associated adhesives in hospitalised neonates ranges from 31% to 45%.^{5,34} Skin-integrated sensors achieving form factors as small as 4.4 cm × 2.4 cm and as thin as 1 mm in versions fully wirelessly powered allow continuous monitoring in this vulnerable population. The inherently thin, soft mechanical properties of these sensors allow for skin coupling to premature neonates without strong adhesives. The most advanced versions adhere to the skin via electrostatic van der Waals forces alone. Other versions with embedded batteries use a thin, conductive hydrogel coupling layer to record ECG while providing gentle adhesion to the skin. The soft and flexible nature of these sensors, coupled with their fully wireless operation, substantially reduces normal and shear stresses at the skin interface associated with natural motion or routine clinical care. The simple act of electrode removal poses the greatest risk of skin injury via epidermal stripping,⁵

often leading to ulceration and infection. The thinnest versions of these soft, flexible sensors impart forces an entire order of magnitude (approximately 10 times) lower at steady-state peeling rates compared with standard neonatal ICU adhesives and medical tape. Overall, the mechanical softness of these sensors offers effective moduli of 4 kPa of which neonatal skin is 70 MPa.³⁵ In over 50 critically ill neonates and paediatric patients receiving care in LMICs, a promising safety profile was noted, with no reports of skin injuries.

Although wireless functionality has permeated consumer electronics, traditional vital sign monitors require multiple wired cables tethering the patient to wall-mounted base units to display data. These systems are not completely without harm. Beyond the nuisance of wires and cables, tethering patients increases immobility (and hence the risk of venous thrombosis), sleep disturbance, functional decline, and delirium.^{16,36,37} For premature neonates—particularly in LMICs—wireless functionality offers substantial diagnostic and therapeutic benefits. In our own studies and feedback from neonatal nurses and parents, monitoring cables represent a physical barrier to kangaroo mother care, a crucial intervention in neonates that can be lifesaving in low birthweight infants.³⁸ A 2014 Cochrane review found that kangaroo mother care reduces all-cause mortality by 40%, hospital-based infection by 65%, and

Panel 1: Key features of the wireless skin sensors, advantages to neonates, and applicability to low-income and middle-income countries

- Full vital signs monitoring capabilities, which allows for comprehensive sensing of modifiable drivers of early neonatal mortality, and reduces the number of required vendors and manufacturers in low-income and middle-income countries (LMICs)
- Continuous, non-invasive measurements of arterial stiffness as a surrogate to systolic blood pressure, which potentially reduce the frequency or length of the arterial line, reducing the associated neonatal morbidity and mortality of conventional monitoring systems, and offers crucial information non-invasively in the absence of medical expertise or resources for arterial line placements in neonates in LMICs
- Soft, flexible electronics that bend, twist, and stretch with natural motion, which are compatible with the ultra-fragile skin of premature neonates, reducing the risk of infection that antibiotics and wound care expertise are not able to treat in LMICs
- Wireless streaming, which facilitates kangaroo mother care for neonates and allows for a single health-care provider to be able to monitor many patients at a central nursing station, reducing the need for high-cost incubators in LMICs
- Real-time analytics, which allows for point-of-care decision making for neonates and enables transportability across a wide range of care settings from rural clinics to high acuity hospitals in LMICs
- Reusable with up to 1 week of battery life, which reduces nursing burden in understaffed clinical settings, and reduces the need for high-cost consumables in LMICs
- Compatible with a wide range of mobile devices, which allows for continuous, real-time data display with immediate interoperability and with an existing user interface that is familiar to staff, reducing the cost of initial capital equipment purchase, cost of installation, and cost and complexity of maintenance
- Cloud integration of data outputs, which facilitates telehealth monitoring, and allows for population-level monitoring in LMICs



hypothermia by 72%, and there was a clinically significant increase in weight, length, and head circumference growth for neonates.³⁸ Facilitating kangaroo mother care without sacrificing continuous vital data, wireless sensing enables the tracking of kangaroo mother care through automating body position determination. Quantifying the benefit by assessing heart rate, blood pressure, respiratory rate, SpO₂, and temperature responses could reinforce the practice in all care settings.

In LMICs, the availability of specialised medical staff to care for each neonate can be scarce. The fact that new monitoring technologies should not increase provider burden in the installation and operation of the system and the risk of alarm fatigue is crucial. Versions of skin-integrated sensors that are wirelessly powered without the need of a battery through an embedded magnetic loop antenna allow for simultaneous wireless data transmission and power delivery through a single link with mattress-embedded antennae. Manufacturable and rugged versions of these sensors with embedded batteries can operate for up to 1 week, reducing the need for unnecessary removal to recharge. Alarm fatigue also represents a major challenge. A nurse can spend up to 20 min per day managing alarms from existing tethered systems, detracting from essential aspects of patient care.^{37,39} The soft, flexible nature of the sensors allows for secure skin coupling even with motion-enhancing signal acquisition quality for both optical (eg, pulse oximetry) and electro-potential (eg, ECG) sensing to reduce the likelihood of false alarms. The features and applicability of the system to LMICs have been summarised in panel 1. To date, our systems have been tested in tertiary-level neonatal ICUs and paediatric ICUs in the USA and Europe, and in low-income countries, such as Kenya and South Africa.

Making data available and useful

Data management of system outputs is essential to the successful implementation of new technologies in both LMICs. Existing physiological monitoring systems are limited by restricted access to the raw physiological signals, low interoperability, proprietary software, and non-standardised data files.¹⁶ These limitations reduce the utility of data generated and create barriers to implementation in LMICs. For instance, substantial IT infrastructure with dedicated technical staff is required to operate standard-of-care monitors in high-income countries. New, advanced wireless sensor

Figure 2: Cloud computing, machine learning, and advanced data analytics allows for future predictive algorithms of clinical outcomes for neonates

The data flow allows for wireless skin sensors to leverage existing mobile devices to stream data for continuous derivation of both conventional and advanced physiological monitoring outputs; the application of advanced machine learning and data analytics coupled to outside data sources enable predictive algorithms; cloud synchronisation permits remote monitoring and population-level surveillance.

systems with compatibility to mobile tablets offer a pragmatic path forward for data management. In our own ground deployments in Zambia of adult versions of our soft flexible sensors, a modest upfront set-up was required to establish a local data server that communicates directly with mobile devices and the cloud. The tablets used to display data from the skin-integrated sensors have existing WiFi capabilities allowing for a local area network to transmit encrypted patient data to a local server in near real time. The local server then pushes physiological data collected from patients securely to the cloud for broader access and systems-level monitoring. Access to the data can be granted to anyone with the appropriate credentials and internet access, circumventing the need for complex IT infrastructure or specialised staff to set up, operate, and sustain the system (figure 2).

Cost considerations

Although the African medical device market continues to grow at a 6·3% annual compounded rate with an expected market size of US\$7 billion by 2023, there remains high price sensitivity, with the greatest need in low-cost medical devices.⁴⁰ As essential equipment, physiological monitoring systems are affected by price pressures from an upfront capital equipment and a consumables cost perspective. Rather than depending on custom, expensive, and proprietary display units, these skin-integrated sensors can communicate securely via encrypted low-power Bluetooth to wide-range mobile devices for continuous real-time analytics, data display, and point-of-care operation. This ability offers several advantages relevant to LMICs. First, mobile smartphones—specifically low cost (<\$100) Android devices—are growing in popularity in LMICs. Of sub-Saharan Africans younger than 35 years, 77% own a smartphone.^{41,42} Compatibility with these devices reduces cost and offers an intuitive interface that health-care workers or even patients are already familiar with. Key limitations of medical technology designed for high-income countries deployed in LMICs include the complexity for repairs, reduced support for older hardware versions, and scarcity of spare parts.^{43,44} In an analysis of inventory reports across hospitals in 16 LMICs, nearly 40% of all donated medical equipment was unusable.⁴⁵ For popular smartphones, there is an existing service and hardware infrastructure.

The reusable, rechargeable, and highly manufacturable nature of these skin-integrated sensors coupled with the wide availability of low-cost Android smartphones could offer substantial cost reductions (5400%) compared with existing systems. Given that many LMICs have little access to basic monitoring equipment, the low upfront and daily use cost of these skin-integrated sensors could facilitate uptake and scalability even in the most under-resourced settings. Future high-volume manufacturing that leverages local production and distribution could further decrease costs.

Panel 2: Examples of the consequences and solutions of real-world inputs from the new monitoring system, from low-income and middle-income countries

- Women in labour in non-climate-controlled environments showed higher rates of sweating, which resulted in decreased electrocardiogram signal quality, but the use of ultrasound gel improved signal quality throughout labour
- Higher proportion of patients with darker skin pigmentation resulted in decreased signal quality on blood oxygenation (SpO₂) but a new firmware version update allowed for improved pulse oximeter function
- Scarce experience with pulse oximeter placement resulted in decreased signal quality on SpO₂ but new training modules and example videos were introduced to improve staff self sufficiency
- Tablet brightness disturbed mothers and infants who were not used to electronic systems operating continuously but a software user interface update with a low-light night mode reduced patient sleep disturbance
- Patient-driven concern of the health consequences of wireless signal transmission resulted in a decrease in patient consent and increase in nursing concern; therefore, patient-centric material describing the low risk of health-related sequelae of Bluetooth energy was written
- High volumes of data outputs reduced immediate feedback, which resulted in concern of poor data capture without adequate surveillance; however, daily automated data quality checks were sent via secure email to hospital administrators and research staff
- Rolling blackouts interrupted data transmission to the cloud but this problem was solved by the implementation of reserve battery power supplies
- Inconsistent internet access interrupted data transmission to the cloud but was solved by the implementation of two internet service providers that acted as redundancies

Implementation and ethical considerations of systems deployment in LMICs

Real-world deployment of these wireless skin sensors yields essential inputs from both clinical staff and patients in LMICs. Our active engagements with Save the Children and the Bill & Melinda Gates Foundation include deployments in four LMICs (Zambia, Kenya, Ghana, and India) with an expected scale of more than 15 000 pregnant women and up to 500 neonates by mid-2021.⁴⁶ Existing feedback from our first 1000 patients yielded a diversity of important inputs. Examples of user-driven inputs from LMICs and the resulting engineering modifications that are essential to successful deployment and scale are summarised in panel 2. Without question, scaling up these systems will reveal new technical and clinical challenges. Further field testing with continuous inputs from local investigators, health-care providers, and patients is necessary to capture rare failure modes, ensure acceptance of the system, and receive additional feedback for improvements.

Regulatory approval is required in each country of operation for clinical deployment of these systems at a broad scale. Typically, physiological monitoring systems are considered Class II (moderate risk) medical devices by the US Food and Drug Administration (FDA) and Class IIB by the EU. The performance and accuracy of these systems including alarming and apnoea detection before regulatory approval is

well established with only minimal requirements for human testing.^{47,48} However, approval for use in neonatal and paediatric critical care settings will probably require additional and larger clinical trials. Furthermore, predictive algorithms and clinical-decision support alerts require additional regulatory approval before use.

With any new technology deployed in LMICs, there are important safety and ethical considerations. Burns to neonates related to traditional wired pulse oximeters, electrodes, and phototherapy blankets have been reported.⁴⁹ Although the wireless, battery-powered sensors offer some advantages, there is an inherent risk of burn injury due to the proximity of the electronics and battery to the skin. Thus, engineering designs must account for the need for enhanced levels of safety that might not be relevant for passive wired electrodes. Mitigation features can include power safety circuits that automatically detect overheating, which then automatically switches off the device, and thermally insulated material layers that prevent burns. From an ethical perspective, these devices must meet all applicable international safety standards before deployment to these vulnerable populations in LMICs. Given that many neonatal deaths occur in home settings, additional efforts must be made to evaluate the feasibility and clinical benefits of these systems in non-hospital-based care. All studies investigating the use of these devices must be approved under local institutional review boards with parents providing informed consent. Future opportunities include monitoring labour and pregnancy to better understand the physiological drivers of premature birth.

Panel 3: Advantages and disadvantages of existing approaches to neonatal monitoring

- Soft, flexible, and wireless electronics: wireless nature enables skin-to-skin contact, has comprehensive measurement capabilities with validation against clinical gold standards, reduces skin injury risk, and there is advanced measurement capabilities that enable future clinical insights, but has a safety risk related to batteries and electronics exposed to the skin
- Consumer baby monitors: widely available, low cost due to economies of scale, and often integrated with existing smartphones, but they have an unclear measurement accuracy and performance, and reduced measurement capabilities
- Smart garments: potential for reduced skin injury risk and nursing burden, but they have limited validation, require a base unit to transmit data and power the garment, and have unclear measurement accuracy and performance
- Camera-based solutions: poses zero skin injury risk, but they have a high upfront cost, unclear measurement accuracy and performance, limitations in emergency situations, and are susceptible to ambient lighting conditions

Alternative technology development efforts in neonatal monitoring

Beyond efforts reported here of soft, flexible electronics, substantial progress in the development of smartphone integrated sensors marketed as advanced baby monitors has been made. The most prominent example is the Owlet (Owlet Baby Care, UT, US)—a wireless device positioned on a neonate's foot that measures heart rate and SpO₂. Although systems such as the Owlet Smart Sock have had substantial success on a commercial scale,⁵⁰ independent analysis raises questions about the system's accuracy at detecting neonatal hypoxaemia and bradycardia compared with FDA-cleared systems.^{51–53} Furthermore, home monitoring of cardiorespiratory function in neonates has not successfully prevented sudden unexpected deaths in infants.⁵⁴ Other examples include MonBaby, a small Bluetooth enabled rigid device, that tracks body motion and respiratory motion. Procter and Gamble announced a partnership with their nappy brand, Pampers, and Verily Life Sciences, a health-care focused subsidiary of Alphabet, to launch a device (Lumi) affixed to a neonate's nappy to track the baby's movement and sleep. Draeger Medical—a well established medical technology company that produces advanced neonatal monitoring systems, neonatal incubators, and ventilators—has also launched a home baby monitoring solution in Europe called Dream Guard. These products are marketed as baby monitors without regulatory approval. Although the scale and popularity of these systems offer expanded access and broader big data opportunities, the clinical use and accuracy of these systems remain unclear as they straddle a grey zone between a medical device and consumer baby monitor.

In addition to consumer-focused neonatal monitors, there have been other attempts to improve neonatal monitoring in the clinical setting, including the neonatal ICU. Early efforts have focused on contactless sensing with video and computer vision algorithms.^{55,56} The advantages of contactless sensing include the elimination of the risk of skin injury from medical adhesives and the potential for long-term cost reduction. However, video-based physiological monitoring in neonates requires further validation and testing, particularly in the context of clinical care situations in which the field of view of a camera might easily be obstructed due to medical procedures, ambient lighting conditions, and privacy concerns. The ability to capture SpO₂ consistently and accurately remains a challenge for video-based approaches. Another area of active research is the development of electronic textiles in which physiological sensing capabilities are embedded within clothing fabrics to reduce skin irritation and the need for adhesives. A key technical challenge is modifying traditional, non-conductive fabrics (eg, nylon, polyester, and cotton) into sufficiently conductive materials, or embedding electronic meshes within fabrics⁵⁷ to replace the need for electrodes to adhere to the skin. Although

Search strategy and selection criteria

The search strategies were launched in PubMed (MEDLINE), Embase (Elsevier), Cochrane Library (Wiley), and Scopus (Elsevier) from Jan 1, 2000, to July 31, 2020 with search terms "wearable*", "sensor**", "monitor**" AND "neonate* OR pediatric* OR infant* OR children*". Only papers published in English were reviewed. Additional natural language searches were done in search engines to supplement the review and our own files. The final reference list was generated on the basis of originality and relevance to the broad scope of this Viewpoint.

early work has been published showing the feasibility of neonatal monitoring with garment-based sensors, technologies of this type are at an early stage.^{58,59} Smart garments also require base units directly connected to the fabric for battery power, signal processing, and data transmission. With the scarce access to low-cost and dependable neonatal monitoring in LMICs, any efforts in technology development should be encouraged and tested rigorously. From non-contactless video monitoring to flexible electronics, specific use cases based on the acuity of care and various technology approaches will have different advantages, disadvantages, and opportunities (panel 3).

Conclusion

Soft, flexible, and skin-interfaced sensors are at the early stages of broad clinical adoption and deployment. Regulatory approval is necessary and large-scale deployments will assess whether these technologies offer clinical benefit over existing options. However, commercially deployed physiological sensors remain largely focused on adult populations in high-income countries for non-critical care applications (eg, outpatient cardiac monitoring).¹² The most pressing clinical need might be among neonates in LMICs who are acutely and critically ill. Although the world has made important advances to reduce neonatal mortality over the last decade, much progress is needed to achieve the 2030 UN Sustainable Development Goals for neonatal mortality.⁶⁰ Expanding access to high-quality physiological monitoring technologies, which is widely available in high-income countries, might facilitate medical decision making in LMICs and reduce morbidity and mortality for vulnerable neonates. Through continued intentional collaboration between engineers, data scientists, nurses, health-care providers, philanthropists, and patients' families, new skin-integrated systems offer the promise of raising the standard of neonatal monitoring by improving outcomes and humanising care worldwide.

Contributors

SX and JAR conceived the study and drafted the manuscript. AYR composed the figures and edited the manuscript. JSAS drafted the manuscript and provided critical reviews of the manuscript. BV, MPC, and ASG provided critical edits to the revised manuscripts and added additional insights on the field requirements of these technologies.

Declaration of interests

SX and JAR report stock ownership in Sibel Health, a private enterprise commercialising soft flexible sensors for neonatal monitoring. SX, JAR, and AYR disclose inventorship in patents (PCT/US2019/059131, PCT/US2019/059156, PCT/US2019/059190, US Patent Application 16/670,161) related to wireless sensors assigned to Northwestern University and licensed to Sibel Health. All other authors declare no competing interests.

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References

- 1 UN. Transforming our world: the 2030 agenda for sustainable development. New York, NY: United Nations, 2015.
- 2 Sankar MJ, Natarajan CK, Das RR, Agarwal R, Chandrasekaran A, Paul VK. When do newborns die? A systematic review of timing of overall and cause-specific neonatal deaths in developing countries. *J Perinatol* 2016; **36** (suppl 1): S1–11.
- 3 Chung HU, Kim BH, Lee JY, et al. Binodal, wireless epidermal electronic systems with in-sensor analytics for neonatal intensive care. *Science* 2019; **363**: eaau0780.
- 4 Chung HU, Rwei AY, Hourlier-Fargette A, et al. Skin-interfaced biosensors for advanced wireless physiological monitoring in neonatal and pediatric intensive-care units. *Nat Med* 2020; **26**: 418–29.
- 5 Lund C. Medical adhesives in the NICU. *Newborn Infant Nurs Rev* 2014; **14**: 160–65.
- 6 Broom M, Dunk AM, Mohamed ALE. Predicting neonatal skin injury: the first step to reducing skin injuries in neonates. *Health Serv Insights* 2019; **12**: 1–10.
- 7 Chan GJ, Labar AS, Wall S, Atun R. Kangaroo mother care: a systematic review of barriers and enablers. *Bull World Health Organ* 2016; **94**: 130–41J.
- 8 O'Brien K, Robson K, Bracht M, et al. Effectiveness of family integrated care in neonatal intensive care units on infant and parent outcomes: a multicentre, multinational, cluster-randomised controlled trial. *Lancet Child Adolesc Health* 2018; **2**: 245–54.
- 9 Poncette AS, Spies C, Mosch L, et al. Clinical requirements of future patient monitoring in the intensive care unit: qualitative study. *JMIR Med Inform* 2019; **7**: e13064.
- 10 Chase JG, Preiser JC, Dickson JL, et al. Next-generation, personalised, model-based critical care medicine: a state-of-the-art review of in silico virtual patient models, methods, and cohorts, and how to validation them. *Biomed Eng Online* 2018; **17**: 24.
- 11 Ordóñez P, Desjardins M, Feltes C, Lehmann CU, Fackler J. Visualizing multivariate time series data to detect specific medical conditions. *AMIA Annu Symp Proc* 2008; **2008**: 530–34.
- 12 Xu S, Jayaraman A, Rogers JA. Skin sensors are the future of health care. *Nature* 2019; **571**: 319–21.
- 13 Fairchild KD, Lake DE, Kattwinkel J, et al. Vital signs and their cross-correlation in sepsis and NEC: a study of 1,065 very-low-birth-weight infants in two NICUs. *Pediatr Res* 2017; **81**: 315–21.
- 14 Wetzel RC. First get the data, then do the science! *Pediatr Crit Care Med* 2018; **19**: 382–83.
- 15 Holmgren AJ, Patel V, Adler-Milstein J. Progress in interoperability: measuring US hospitals' engagement in sharing patient data. *Health Aff (Millwood)* 2017; **36**: 1820–27.
- 16 Lehne M, Sass J, Essenwanger A, Schepers J, Thun S. Why digital medicine depends on interoperability. *NPJ Digit Med* 2019; **2**: 79.
- 17 Goodwin AJ, Eytan D, Greer RW, et al. A practical approach to storage and retrieval of high-frequency physiological signals. *Physiol Meas* 2020; **41**: 035008.
- 18 Rominski S, Bell SA, Oduro G, Ampong P, Oteng R, Donkor P. The implementation of the South African Triage Score (SATS) in an urban teaching hospital, Ghana. *Afr J Emerg Med* 2014; **4**: 71–75.
- 19 Graham KC, Cvach M. Monitor alarm fatigue: standardizing use of physiological monitors and decreasing nuisance alarms. *Am J Crit Care* 2010; **19**: 28–34.

- 20 Joshi R, van Pul C, Atallah L, Feijs L, Van Huffel S, Andriessen P. Pattern discovery in critical alarms originating from neonates under intensive care. *Physiol Meas* 2016; **37**: 564–79.
- 21 Koh A, Kang D, Xue Y, et al. A soft, wearable microfluidic device for the capture, storage, and colorimetric sensing of sweat. *Sci Transl Med* 2016; **8**: 366ra165.
- 22 Kim J, Gutruf P, Chiarelli AM, et al. Miniaturized battery-free wireless systems for wearable pulse oximetry. *Adv Funct Mater* 2017; **27**: 1604373.
- 23 Heo SY, Kim J, Gutruf P, et al. Wireless, battery-free, flexible, miniaturized dosimeters monitor exposure to solar radiation and to light for phototherapy. *Sci Transl Med* 2018; **10**: eaau1643.
- 24 Kim DH, Lu N, Ma R, et al. Epidermal electronics. *Science* 2011; **333**: 838–43.
- 25 Peña-Bautista C, Escrig R, Lara I, García-Blanco A, Cháfer-Pericás C, Vento M. Non-invasive monitoring of stress biomarkers in the newborn period. *Semin Fetal Neonatal Med* 2019; **24**: 101002.
- 26 Pasero C. Pain assessment in infants and young children: neonates. *Am J Nurs* 2002; **102**: 61–64.
- 27 Esposito G, Hiroi N, Scattoni ML. Cry, baby, cry: expression of distress as a biomarker and modulator in autism spectrum disorder. *Int J Neuropsychopharmacol* 2017; **20**: 498–503.
- 28 Reynolds EW, Grider D, Bell CS. Swallow-breath interaction and phase of respiration with swallow during non-nutritive suck in infants affected by neonatal abstinence syndrome. *Front Pediatr* 2017; **5**: 214.
- 29 Joseph R, Chong A, Teh M, Wee A, Tan KL. Thrombotic complication of umbilical arterial catheterization and its sequelae. *Ann Acad Med Singap* 1985; **14**: 576–82.
- 30 Gross BA, Orbach DB. Addressing challenges in 4 F and 5 F arterial access for neurointerventional procedures in infants and young children. *J Neurointerv Surg* 2014; **6**: 308–13.
- 31 Doyle LW, Faber B, Callanan C, Ford GW, Davis NM. Extremely low birth weight and body size in early adulthood. *Arch Dis Child* 2004; **89**: 347–50.
- 32 Rutter N. The immature skin. *Br Med Bull* 1988; **44**: 957–70.
- 33 Lund CH, Tucker JA. Adhesion and newborn skin. In: Hoath SB, Maibach HI, eds. *Neonatal skin: structure and function*, 2nd edn. New York, NY: Marcel Dekker, 2003: 299–324.
- 34 McLane KM, Bookout K, McCord S, McCain J, Jefferson LS. The 2003 national pediatric pressure ulcer and skin breakdown prevalence survey: a multisite study. *J Wound Ostomy Continence Nurs* 2004; **31**: 168–78.
- 35 Vogel HG. Age dependence of mechanical and biochemical properties of human skin. Part I: stress-strain experiments, skin thickness and biochemical analysis. *Bioeng Skin* 1987; **3**: 67–91.
- 36 Brown CJ, Friedkin RJ, Inouye SK. Prevalence and outcomes of low mobility in hospitalized older patients. *J Am Geriatr Soc* 2004; **52**: 1263–70.
- 37 Chen S, Zakaria S. Behind the monitor—the trouble with telemetry: a teachable moment. *JAMA Intern Med* 2015; **175**: 894.
- 38 Conde-Agudelo A, Diaz-Rossello JL. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. *Cochrane Database Syst Rev* 2016; **8**: CD002771.
- 39 Dressler R, Dryer MM, Coletti C, Mahoney D, Doorey AJ. Altering overuse of cardiac telemetry in non-intensive care unit settings by hardwiring the use of American Heart Association guidelines. *JAMA Intern Med* 2014; **174**: 1852–54.
- 40 Market Research Future. Africa Medical Devices Market Report – Forecast 2023. <https://www.marketresearchfuture.com/reports/africa-medical-devices-market-2845> (accessed Nov 30, 2020).
- 41 Cascals A. How China benefits from Africa's smartphone boom. 2019. <https://www.dw.com/en/how-china-benefits-from-africas-smartphone-boom/a-51016346> (accessed Nov 26, 2020).
- 42 Ghandi D. Figure of the week: gap in universal mobile phone and internet access in Africa. Africa in Focus. 2019. <https://www.brookings.edu/blog/africa-in-focus/2019/04/12/figure-of-the-week-gap-in-universal-mobile-phone-and-internet-access-in-africa/> (accessed Nov 26, 2020).
- 43 Miesen M. The inadequacy of donating medical devices to Africa. Without spare parts or trained technicians, they stop working almost immediately. Sept 20, 2013. <https://www.theatlantic.com/international/archive/2013/09/the-inadequacy-of-donating-medical-devices-to-africa/279855/> (accessed Nov 26, 2020).
- 44 WHO. Medical device donations: considerations for solicitation and provision. WHO medical device technical series. Geneva: World Health Organization, 2011.
- 45 Perry L, Malkin R. Effectiveness of medical equipment donations to improve health systems: how much medical equipment is broken in the developing world? *Med Biol Eng Comput* 2011; **49**: 719–22.
- 46 Morris A. Wireless, skin-mounted sensors monitor babies, pregnant women in the developing world. March 11, 2020. <https://news.northwestern.edu/stories/2020/03/wireless-skin-mounted-sensors-monitor-babies-pregnant-women-in-the-developing-world-2/> (accessed Sept 23, 2020).
- 47 US Food and Drug Administration. Guidance for Industry: cardiac monitor guidance (including cardiotachometer and rate alarm). Washington, DC: US Department of Health and Human Services, 1998.
- 48 US Food and Drug Administration. Pulse oximeters—premarket notification submissions [510(k)s]: guidance for industry and Food and Drug Administration staff. FDA. Washington, DC: US Department of Health and Human Services, 2013.
- 49 Rimdeika R, Bagdonas R. Major full thickness skin burn injuries in premature neonate twins. *Burns* 2005; **31**: 76–84.
- 50 Dangerfield MI, Ward K, Davidson L, Adamian M. Initial experience and usage patterns with the owlet smart sock monitor in 47,495 newborns. *Glob Pediatr Health* 2017; **4**: 1–8.
- 51 Bonafide CP, Localio AR, Ferro DF, et al. Accuracy of pulse oximetry-based home baby monitors. *JAMA* 2018; **320**: 717–19.
- 52 Bonafide CP, Jamison DT, Foglia EE. The emerging market of smartphone-integrated infant physiologic monitors. *JAMA* 2017; **317**: 353–54.
- 53 Malik A, Ehsan Z. Media review: the Owlet Smart Sock—a “must have” for the baby registry? *J Clin Sleep Med* 2020; **16**: 839–40.
- 54 Moon RY. SIDS and other sleep-related infant deaths: evidence base for 2016 updated recommendations for a safe infant sleeping environment. *Pediatrics* 2016; **138**: e20162940.
- 55 Villarroel M, Chaichulee S, Jorge J, et al. Non-contact physiological monitoring of preterm infants in the neonatal intensive care unit. *NPJ Digit Med* 2019; **2**: 128.
- 56 Aarts LA, Jeanne V, Cleary JP, et al. Non-contact heart rate monitoring utilizing camera photoplethysmography in the neonatal intensive care unit—a pilot study. *Early Hum Dev* 2013; **89**: 943–48.
- 57 Kim DH, Kim YS, Wu J, et al. Ultrathin silicon circuits with strain-isolation layers and mesh layouts for high-performance electronics on fabric, vinyl, leather, and paper. *Adv Mater* 2009; **21**: 3703–07.
- 58 Bouwstra S, Chen W, Feijs L, Oetomo S. Smart jacket design for neonatal monitoring with wearable sensors. Sixth International Workshop on Wearable and Implantable Body Sensor Networks; Berkeley, CA, USA; June 3–5, 2009 (abstr).
- 59 Joyce K. Smart textiles: transforming the practice of medicalisation and health care. *Sociol Health Illn* 2019; **41** (suppl 1): 147–61.
- 60 Hug L, Alexander M, You D, Alkema L. National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis. *Lancet Glob Health* 2019; **7**: e710–20.

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