HHS Public Access

Author manuscript

JACC Adv. Author manuscript; available in PMC 2023 May 05.

Published in final edited form as:

JACC Adv. 2023 March ; 2(2): . doi:10.1016/j.jacadv.2023.100267.

Wearable Biosensors in Congenital Heart Disease:

Needs to Advance the Field

Animesh Tandon, MD, MS[a,b,c,d], **Hoang H. Nguyen, MD, MS**[e], **Sravani Avula, MD**[e], **Dhruv R. Seshadri, PHD**[f], **Akash Patel, MD**[a], **Munes Fares, MD**[e], **Orkun Baloglu, MD**[b,g], **Shahnawaz Amdani, MD**[a,b], **Roozbeh Jafari, PhD**[h], **Omer T. Inan, PhD**[i], **Colin K. Drummond, PhD**[d]

[a]Department of Pediatric Cardiology, Pediatric Institute, Cleveland Clinic Children's, Cleveland, Ohio, USA

[b]Cleveland Clinic Children's Center for Artificial Intelligence (C4AI), Cleveland Clinic Children's, Cleveland, Ohio, USA

[c]Department of Biomedical Engineering, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, USA

[d]Department of Biomedical Engineering, Case School of Engineering at Case Western Reserve University, Cleveland, Ohio, USA

[e]Division of Cardiology, Department of Pediatrics, UT Southwestern Medical Center, Dallas, Texas, USA

[f]Department of Orthopaedics, University Hospitals Cleveland Medical Center, Cleveland, Ohio, USA

[g]Department of Critical Care, Pediatric Institute, Cleveland Clinic Children's, Cleveland, Ohio, USA

[h]Departments of Biomedical Engineering, Computer Science and Electrical Engineering, Texas A&M University, College Station, Texas, USA

[i]School of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, Georgia, USA.

Abstract

Traditional measures of clinical status and physiology have generally been based in health care settings, episodic, short in duration, and performed at rest. Wearable biosensors provide an opportunity to obtain continuous non-invasive physiologic data from patients with congenital heart disease (CHD) in the real-world setting, over longer durations, and across varying levels of activity. However, there are significant technical limitations to the use of wearable biosensors in CHD. Here, we review current applications of wearable biosensors in CHD; how clinical

ADDRESS FOR CORRESPONDENCE: Dr Animesh Tandon, Cleveland Clinic Children's, 9500 Euclid Avenue M41, Cleveland, Ohio 44195, USA. tandona2@ccf.org. Twitter: @ATandonMD.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

and research uses of wearable biosensors must consider various CHD physiologies; the technical challenges in developing wearable biosensors for CHD; and special considerations for digital biomarkers in CHD.

Keywords

artificial intelligence; congenital heart disease; wearables; wearable biosensors

Traditional measures of clinical status and physiology including lab tests, imaging studies, and vital sign monitoring have generally been performed in clinic or hospital settings, and are usually episodic, short in duration, and performed at rest. Recently, focus has shifted toward more continuous and at-home care delivery,[1] accelerated by the COVID-19 pandemic. Wearable biosensors, a subset of biometric monitoring technologies[2] and digital health tools,[3] provide an opportunity to obtain wearable-derived, non-invasive continuous physiologic data from patients in the real-world setting, over longer durations, and across varying levels of activity, stress, and time of day, enabling the development of digital biomarkers.[3] Wearable biosensors have already been adopted in cardiovascular care in adults ranging from diagnosing and monitoring heart rhythm abnormalities to reduction in heart failure admissions,[4] and when used primarily at the consumer level, have formed the cornerstone of the "quantified self."[5] However, the use of wearable biosensors has been limited for patients with congenital heart disease (CHD).

The goal of this review is to discuss the development and use of wearable biosensors in CHD, highlighting technical and physiologic challenges and suggesting potential strategies to overcome those challenges. We also review current applications of wearable biosensors in CHD; how clinical and research uses of wearable biosensors must consider various CHD physiologies; the technical challenges in developing wearable biosensors for CHD; and special considerations for digital biomarkers in CHD.

CURRENT USE OF WEARABLE BIOSENSORS IN CONGENITAL HEART DISEASE

Remote patient monitoring, as a concept, is well-established in pediatric cardiology. Recent publications outline the use of tele-electrocardiography and remote telehealth visits for CHD,[6,7] and of home monitoring programs using remote intermittent data collection and frequent telehealth and in-person visits for interstage single ventricle patients.[8] The goal of these programs is to understand the physiology of the patient at any given time, so the natural extension would be to understand perturbations of that physiology on a continuous basis. However, little is known about how to use wearable biosensors to obtain continuous physiologic data from patients with CHD, and what to do with those data once generated. Based on clinical experience and industry studies, it is known that patients and caregivers are using wearable biosensors to monitor themselves or their children with CHD.[9] Anecdotally, the most common uses appear to include tracking heart rate, activity/step counts, arrhythmia burden, and oxygen saturation (example biosensor form factors and measurements outlined in the Central Illustration).[10] This is in addition to the commonly-used short- and mid-term

heart rate and arrhythmia tracking done clinically through the use of Holter monitors and patch-style rhythm monitors.[11] Unfortunately, there are no current standards of care for the use of wearable biosensors, especially pulse oximeters, in CHD (excluding Holter monitors), nor real standards in adult cardiology either.[4] Further, many of these biosensors lack peer-reviewed or published analytical validation data[12] in infants, children, or adults with CHD.[10] There have been small studies looking at heart rate in children and adults with CHD showing reasonable accuracy,[13,14] small studies of portable (but not wireless) pulse oximeters for cyanotic infants showing that both the hospital and the wearable pulse oximeters were inaccurate at low saturation levels,[15] and a number of studies focused on step counts.[16–18] To our knowledge, at present there are no Food and Drug Administration–cleared wireless, wearable pulse oximeters or heart rate monitors for infants for use at home.

Other wearable biosensors that measure parameters beyond traditional vital signs like heart rate and oxygen saturation are being developed as well, usually adapted from technologies made for adults. For instance, seismocardiography, which measures chest vibrations,[19] and electrical volumetry, which measures chest impedance,[20] have been recently tested in cardiac output measurement in patients with CHD. However, these technologies have not yet reached technical feasibility for clinical use.

CLINICAL AND RESEARCH USE OF WEARABLE BIOSENSORS MUST CONSIDER THE DIFFERENT PHYSIOLOGIES OF CHD

OVERALL FRAMEWORK.

The use of wearable biosensors in CHD, whether clinical or research, must be informed by the clinical scenario and designed to be fit-for-purpose[2] by considering:

What types of continuous physiologic data might provide the appropriate insights for a specific patient, given their current physiologic state? (Table 1)

What are the relevant clinical outcomes, or even “current standard”[2] in-clinic or in-hospital measures, to which to compare the wearable data?

What data analysis may be needed to transform the wearable physiologic data? And, especially in the clinical setting, what interventions could be taken based on these analyses?

For some physiologies described below, the goal for monitoring with wearable biosensors may not be to predict or identify acute events, but to have earlier recognition of a more chronic decline (such as ventricular or liver function).

The example of adult heart failure management is instructive, demonstrating how wearable biosensors may replace invasive hemodynamic measurements. In the CHAMPION (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients) study,[21] the goal was to reduce heart failure readmission by using an implanted pressure sensor to determine pulmonary artery pressure. The managing cardiologists titrated diuretics based directly on pulmonary artery pressure, and using this additional hemodynamic data, there was a 37% reduction in heart-failure-

related hospitalization in the treatment group. In comparison, the LINK-HF (Multisensor Non-invasive Remote Monitoring for Prediction of Heart Failure Exacerbation) study[22] used a non-invasive wearable biosensor to try to accomplish the same goal. Retrospectively, they used a wearable biosensor applied to the chest that collects continuous electrocardiographic (ECG) waveform, continuous 3-axis accelerometry, skin impedance, skin temperature, and information on activity and posture. Derived data include heart rate, heart rate variability, arrhythmia burden, respiratory rate, gross activity, walking, sleep, body tilt, and body posture. Researchers used the first 72 hours after discharge to generate a baseline physiologic model for a given patient, then their system generated a score about how abnormal the biomarkers were compared to this baseline. In this study, their algorithm generated an alert a median of 6.5 days before heart failure hospitalization. These studies provide examples for using multiple physiologic parameters and advanced analytics to relate non-invasive continuous physiologic data to either directly to measurable parameters like pulmonary artery pressure, clinical outcomes, or other actionable insights in CHD as well.

Below, we describe 3 clinical scenarios where wearable biosensors may provide additional insights from patients with CHD in the real world, and some technical considerations in each of these populations.

INTERSTAGE SINGLE VENTRICLE HEART DISEASE.

Patients with functional single ventricle heart disease who are between stage I and stage II of palliation have a unique physiology where a shunt directly connects the systemic and pulmonary circulations, which run in parallel instead of in series. These patients are extremely vulnerable to sudden changes in pulmonary and systemic vascular resistance, and at risk for shunt thrombosis, arrhythmias, and other complications, which may be evident in oxygen saturation and heart rate changes. Because of this instability, interstage patients are at high risk of cardiovascular collapse and death.[23] The causes of mortality are not always clear and mortality is often unpredictable, as evidenced by the fact that over half the deaths occur at home or in the emergency room.[24] Unfortunately, identifying effective interventions for interstage patients has proven difficult. The current standard of care monitoring for interstage patients includes weekly clinic visits, daily pulse oximetry and weight checks at home, and significant family education, and the implementation of this intense monitoring may have decreased overall mortality.[23,25] Collection and analysis of wearable-derived continuous physiologic data could help define what the true baseline oxygen saturations and heart rates are for a specific interstage patient, and then identification of anomalies in these data could provide early warning of these high-risk scenarios, allowing timely intervention and improved outcomes (Figure 1).

Analysis of time-series data are already showing promise in the pediatric cardiac intensive care unit setting for interstage patients. Recently, prediction of oncoming cardiorespiratory deterioration within 1 to 2 hours could be achieved using a combination of waveform ECG data, chest impedance, vascular pressures, heart rate, respiratory rate, oxygen saturation, ST-segment changes, and blood pressure.[26] This risk index algorithm was able to predict deterioration with an area under the curve of 0.96, and set a threshold that yielded a true positive rate of 45% with a false positive rate of 0.2%. In the future, it may be possible

to apply this approach to continuous physiologic data in the outpatient setting, akin to the LINK-HF study described above.[22]

PATIENTS BEFORE AND AFTER A MAJOR INTERVENTION.

A critical question in many forms of CHD is the optimal timing of major interventions. For instance, the standard surgical interventions for tetralogy of Fallot (TOF) in infancy often lead to pulmonary regurgitation and residual right ventricular (RV) outflow tract obstruction, which over time can lead to RV and left ventricular (LV) failure in 25% of adults. Many patients with repaired tetralogy of Fallot will have to undergo pulmonary valve replacement (PVR) to address these sequelae. The current standard of care for monitoring patients with tetralogy of Fallot is annual echocardiograms when patients are young, cardiac magnetic resonance imagings when they get older, ECGs and Holter monitors as needed, annual stress tests, and routine semiannual to annual clinic visits.[27]

Current recommendations pertaining to timing of PVR rely on heart failure symptoms, sustained tachyarrhythmias related to volume overload, exercise intolerance, and cardiac magnetic resonance imaging criteria.[28] However, timing of PVR and predicting outcomes after PVR continue to be debated among congenital cardiologists because these “traditional” cutoffs have limited sensitivity and specificity: 30% to 40% of patients do not show positive ventricular remodeling after PVR.[29] Moreover, most of these metrics are intermittent and based on in-hospital testing, with only patient-reported symptoms representing continuous, outside the hospital, real-life indicators.

Wearable sensors could assist in identifying the best time for PVR in multiple ways. First, they could be used to quantify arrhythmia burden with wearables that are easier or longer-lasting than Holter monitors, similar to atrial fibrillation detection in adults via smartwatch.[30] Wearable continuous physiologic data could also be used to correlate to in-hospital test results; in adults, smartwatch data have been used to correlate to peak VO_2.[31,32] Further, novel correlations could be calculated from wearable continuous physiologic data to cardiovascular magnetic resonance parameters like using 1-lead ECG to predict low ejection fraction, as in adults (Figure 2).[33] Finally, novel metrics could be derived from combining step count, activity, heart rate, and other data from the wearable biosensor to assess functional status. Similar frameworks could be used to look for physiologic changes before and after PVR as well, or extended to other scenarios including before and after aortic valve replacement, ventricular assist device for heart failure, initiation of new medications or physical activity regimens, or act as the basis of N-of-1 studies.[34]

There are currently significant limitations to implementing these in clinical practice. Most importantly, most wearable biosensors do not have analytical validation for CHD populations, due to smaller patient numbers, heterogeneity of disease states, and lack of correlation of wearable continuous physiologic data metrics to current-standard metrics in children, though these are all problems that can be addressed in future studies.

THE SLOWLY DETERIORATING PATIENT.

A more challenging scenario for wearable biosensors in CHD is in patients with slowly progressive declines. As immediate outcomes after surgical repairs for CHD continue

to improve, there is now a shift in focus toward identifying long-term sequelae in this cohort,[35] especially for children with single ventricle CHD. Such patients often begin their journey with either a systemic RV or a left ventricle and eventually get palliated to a Fontan, after which they continue to be in a state of chronic venous hypertension and low cardiac output.[35,36] The effects of being in such a chronically decompensated state starts to become obvious with age, as demonstrated by the development of chronic liver and kidney disease, abnormal lymphatic flow leading to protein-losing enteropathy or plastic bronchitis, significant growth or pubertal failure, exercise/functional limitation, frailty and neurologic impairment from their multiple bypass runs, and ischemic/embolic strokes.[35,36] Because of the indolent course and decades-long timeframe for decline, it is difficult to identify those with failing Fontan physiology who may benefit from advanced heart failure therapies. There is broad practice variation in referral for advanced heart failure therapies[37] and the patients are often referred too late,[38] which suggests an opportunity for wearable biosensors to gather more salient continuous physiologic data to assess functional status (eg, step or activity counters), physiologic changes (eg, reduced heart rate variability, which has been shown to correlate to both systolic and diastolic function in the general adult population)[39]; degree of heart failure (eg, using seismocardiography, which can differentiate compensated vs decompensated heart failure[40]); and prediction of heart failure hospitalizations (eg, by performing a LINK-HF-like study in Fontans) (Figure 3).

Beyond readmission, continuous physiologic data may allow us to differentiate the sub-phenotypes of Fontan failure (reduced or preserved ejection fraction, abnormal lymphatics, and normal heart[41]) and be able to follow their physiology over time to identify each individual patient's arc. Non-invasive estimation of pulmonary arterial pressures may help identify diastolic dysfunction and pulmonary maladaptation to exercise/activity that is difficult to identify on routine echocardiographic monitoring or at rest. For patients with abnormal lymphatics, with either plastic bronchitis or protein-losing enteropathy, a biosensor that can monitor respiratory rate, quantify lung congestion, and thoracic and abdominal impedance may allow identification of worsening thoraco-abdominal fluid collection prior to overt observance of casts (in plastic bronchitis) or diarrhea/growth failure (in protein-losing enteropathy). The challenge in this slow burn scenario is that the time from complication onset to eventual "hard outcomes," ie, death or transplant, may take years. Studying higher risk cohorts, such as those with systemic RVs, at least 10 years post Fontan may seem attractive as this cohort is probably closer to a hard outcome but may be too late to catch the early signs of Fontan failure. At the same time, early institution of wearables and collection of multi-point parameters may give us information overload with little actionable data. As a community, we must determine who should we target (age, systemic ventricular morphology, duration since Fontan), which wearable biosensor to use (ideally that give a comprehensive non-invasive assessment of multiple organs), and what end points we should measure to improve outcomes.

CHALLENGES IN THE DEVELOPMENT OF WEARABLE BIOSENSORS FOR CHD

There are key challenges in the development of wearable biosensors for CHD. There is broad anatomic and physiologic heterogeneity in CHD, requiring biosensor analytical validation and accuracy across a broad range of values. For instance, healthy athletic teens may have heart rates near 40 beats/min, while infants with supraventricular tachycardia can have heart rates above 220 beats/min. In patients with complete mixing lesions like single ventricle heart disease, TOF with pulmonary atresia, truncus arteriosus, etc, oxygen saturations in the 75% to 85% range are expected and desired, but others can have chronically low saturations in the 60% range. Respiratory rates of children in distress can reach 40 breaths/min or more. These represent a far broader range of standard vital sign values than are needed for most adults, posing a challenge for device analytical validation.

Related to this underlying physiologic heterogeneity is a lack of “normal” values for specific populations. Even in healthy children the normal vital sign values change significantly over time due to somatic growth and age[42]; in patients with CHD, these values likely change even more due to surgical and transcatheter interventions and disease progressions/exacerbations, and what is normal for a patient with TOF is unlikely to be the normal for a patient with Fontan circulation. Even for something as simple as step count, the “normal” values are unclear, as they may vary by season[16] and disease severity.[43] And for emerging parameters like seismocardiography and ballistocardiography, or combined features from multiple modalities of wearable sensors, like pulse transit time and pulse arrival time, there are no clear studies of normal values in children or those with CHD. Defining population normal or patient baseline values are likely necessary to allow actionable interpretations of continuous physiologic data. Combined, the broad range of possible vital sign values, and lack of defined normal values, suggest that patient- and scenario-specific biosensor design and testing will be required.

DIGITAL BIOMARKERS FOR CONGENITAL HEART DISEASE

The phrase “digital biomarker” emerged from the intersection of the separate, but related, fields of biomarkers and digital health technologies,[3] and was recently defined by a Food and Drug Administration working group as “a characteristic or set of characteristics, collected from digital health technologies, that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions.”[3,44] During their life, patients with CHD already generate multiple types of data including physical exam, imaging, biochemical lab values, exercise stress, and patient reports of symptoms, and clinicians must make patient management decisions based on these varied kinds of data. Wearable biosensors will provide the opportunity to incorporate continuous physiologic data as well.

Fundamentally, a clinician might use a digital (or other type of) biomarker to drive clinical decision-making if it has been validated and shows improved prognostic capability, ability to integrate multiple types of or time-series data, or otherwise somehow surpass “traditional” metrics. At this time, few if any digital biomarkers are used to drive clinical decision-making

in CHD because, given the hardware limitations described above, data to perform clinical validation[12] was not available. However, this work is beginning in other fields, such as using wrist-worn wearable accelerometry data to detect treatment-related changes in resting tremor and bradykinesia,[45] using wearable-derived mobility metrics as digital endpoints in clinical trials for heart failure,[46] showing that continuous physiologic data from wearables relate to B-type natriuretic peptide and other biochemical biomarkers in ischemic heart disease,[47] and using wearable-based atrial fibrillation detection for “pill-in-pocket” targeted anticoagulation,[48,49] extending prior work from implantable sensors.[50]

It is likely that artificial intelligence and machine learning (AI/ML) techniques will facilitate the development of digital biomarkers, as in adult use cases. AI/ML are being used to reduce noise and artifacts in continuous physiologic data,[51] and can be used to determine which features/metrics are important in predicting outcomes. For instance, one study described 29 metrics of heart rate variability[52]—which one should be analyzed? In terms of clinical utility, AI/ML has been used to combine multiple continuous physiologic data streams to define a “normal state” for a given patient, and then generate alerts based on deviations from that physiologic normal: to predict heart failure readmission in adults (LINK-HF)[22]; to predict mortality in the pediatric intensive care unit[53]; and to predict in-hospital cardiorespiratory events for interstage single ventricle patients.[26]

One key limitation for implementation of digital biomarkers in CHD is that the event rate is often considerably lower than, for instance, the readmission rate in adult heart failure, especially over short time frames. The low pretest probability must be considered when creating cutoff for alerts, which is especially important when considering use in the outpatient setting, where, by definition, patients should be lower risk. One instructive example is that of sudden infant death syndrome, which has been the target for many baby monitors.[54] In the CHIME (Collaborative Home Infant Monitoring Evaluation) studies, cardiorespiratory monitoring was used to detect risk for sudden infant death syndrome and showed that apnea and bradycardia that met alarm thresholds were quite common, even in healthy term infants.[55] These studies were part of the basis for the American Academy of Pediatrics to recommend against the use of home monitoring for sudden infant death syndrome.[56] Obviously, those with CHD are at higher risk of adverse clinical events than healthy infants, so the tradeoff between false positives and false negatives must be considered: in interstage patients, for instance, a false positive may lead to an unnecessary hospital admission, vs a false negative leading to death at home. Other practical issues with too much or too little data, data overfitting, modeling noise, and algorithm selectivity for the intended purpose of the sensor measurement also impede translation to clinical practice.

These instructive examples show that using physiologic data with AI/ML analyses can generate clinically meaningful alerts for patients in high-risk timeframes overall, and as continuous physiologic data from patients with CHD become more common, we expect that similar analyses could be run in selected high-risk populations in the outpatient setting. Given the relative rarity of CHD, achieving this goal will likely require multicenter studies with high-quality biosensors.

LEGAL AND ETHICAL IMPLICATIONS

The use of wearable biosensors, especially in the outpatient setting, raises several legal and ethical concerns, many of which are outside the scope of this review. For instance, the use of smartwatches to detect atrial fibrillation in adults may pose ethical concerns in that the lack of evidence and high false-positive rate can lead to harm, though improvements in the algorithms may mitigate these concerns in the future.[57] There have already been lawsuits related to type I and II errors in detection of atrial fibrillation with wearable biosensors. As noted already, devices being designed only for adults continue to leave children and other vulnerable populations out.[58] Privacy and data ownership concerns only become magnified more when dealing with children, as do the ethical implications of AI/ML biases.[59]

CONCLUSIONS

Wearable biosensors present an excellent mechanism to obtain continuous physiologic data and continue the transition of care from in-hospital to at-home for patients with CHD. However, the development of wearable biosensors for patients with CHD faces significant technical and theoretical challenges. However, the potential gains for patients with CHD from these technologies is immense, and thus teams of physicians, engineers, and data scientists should continue to pursue developing meaningful digital biomarkers in real-world settings. It is an exciting time to dream of how wearable biosensors will enable us to provide better care for patients with CHD.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Tandon acknowledges the support from the Thrasher Foundation Early Career Research Award, Brett Boyer Foundation, Children's Health Innovation Grant, Cleveland Clinic Caregiver Catalyst Grant, UT Southwestern Cary Council/DocStars/Southwestern Medical Foundation, and UT Southwestern Center for Translational Medicine Swim with the Sharks Grant; and he is a consultant for Synergen Technology Labs, LLC and Siemens Healthineers. Dr Jafari has filed a patent related to blood pressure and this patent is licensed to SpectroBeat LLC. The associated patent application is US 2020/0138303 with the title "System and method for cuffless blood pressure monitoring". Dr Inan is a co-founder, board member, and Chief Scientific Officer for Cardiosense Inc, and Scientific Advisor for Physiowave, Inc. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ABBREVIATIONS AND ACRONYMS

AI/ML	artificial intelligence/machine learning
CHD	congenital heart disease
ECG	electrocardiographic
PVR	pulmonary valve replacement
RV	right ventricle
TOF	tetralogy of Fallot

REFERENCES

1. Joynt Maddox K, Bleser WK, Crook HL, et al. Advancing value-based models for heart failure: a call to action from the value in healthcare initiative's value-based models learning collaborative. Circ Cardiovasc Qual Outcomes. 2020;13:e006483. [PubMed: 32393125]
2. Coravos A, Goldsack JC, Karlin DR, et al. Digital medicine: a primer on measurement. Digit Biomark. 2019;3:31–71. [PubMed: 32095767]
3. Vasudevan S, Saha A, Tarver ME, Patel B. Digital biomarkers: convergence of digital health technologies and biomarkers. NPJ Digit Med. 2022;5:36. [PubMed: 35338234]
4. Bayoumy K, Gaber M, Elshafeey A, et al. Smart wearable devices in cardiovascular care: where we are and how to move forward. Nat Rev Cardiol. 2021;18:581–599. [PubMed: 33664502]
5. Feng S, Mantymaki M, Dhir A, Salmela H. How self-tracking and the quantified self promote health and well-being: systematic review. J Med Internet Res. 2021;23:e25171. [PubMed: 34546176]
6. Satou GM, Rheuban K, Alverson D, et al. Telemedicine in pediatric cardiology: a scientific statement from the American Heart Association. Circulation. 2017;135:e648–e678. [PubMed: 28193604]
7. Chowdhury D, Hope KD, Arthur LC, et al. Telehealth for pediatric cardiology practitioners in the time of COVID-19. Pediatr Cardiol. 2020;41:1081–1091. [PubMed: 32656626]
8. Rudd NA, Ghanayem NS, Hill GD, et al. Interstage home monitoring for infants with single ventricle heart disease: education and management: a scientific statement from the American Heart Association. J Am Heart Assoc. 2020;9:e014548. [PubMed: 32777961]
9. 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;4:2333794X17742751.
10. Roelle L, Conner T, Avari Silva JN. Direct to Consumer Wearables For Children: Who, What, When and How? American College of Cardiology: Latest in Cardiology; 2022.
11. Schultz KE, Lui GK, McElhinney DB, et al. Extended cardiac ambulatory rhythm monitoring in adults with congenital heart disease: arrhythmia detection and impact of extended monitoring. Congenit Heart Dis. 2019;14:410–418. [PubMed: 30604934]
12. Goldsack JC, Coravos A, Bakker JP, et al. Verification, analytical validation, and clinical validation (V3): the foundation of determining fit-for-purpose for Biometric Monitoring Technologies (BioMeTs). NPJ Digit Med. 2020;3:55. [PubMed: 32337371]
13. Kobel M, Kalden P, Michaelis A, et al. Accuracy of the apple watch iECG in children with and without congenital heart disease. Pediatr Cardiol. 2022;43:191–196. [PubMed: 34468775]
14. Striepe S, Michaelis A, Markel F, et al. Use of the Apple Watch iECG in adult congenital heart disease patients. Indian Pacing Electrophysiol J. 2022;22:131–136. [PubMed: 35121144]
15. Harris BU, Stewart S, Verma A, et al. Accuracy of a portable pulse oximeter in monitoring hypoxemic infants with cyanotic heart disease. Cardiol Young. 2019;29:1025–1029. [PubMed: 31304897]
16. Kuan MTY, Voss C, Lopez J, Hemphill NM, Harris KC. Children with congenital heart disease exhibit seasonal variation in physical activity. PLoS One. 2020;15:e0241187. [PubMed: 33151936]
17. Voss C, Duncombe SL, Dean PH, de Souza AM, Harris KC. Physical activity and sedentary behavior in children with congenital heart disease. J Am Heart Assoc. 2017;6:e004665. [PubMed: 28264859]
18. Voss C, Gardner RF, Dean PH, Harris KC. Validity of commercial activity trackers in children with congenital heart disease. Can J Cardiol. 2017;33:799–805. [PubMed: 28347581]
19. Ganti VG, Gazi AH, An S, et al. Wearable seismocardiography-based assessment of stroke volume in congenital heart disease. J Am Heart Assoc. 2022;11:e026067. [PubMed: 36102243]
20. Egbe AC, Wajih Ullah M, Afzal A, et al. Feasibility, reproducibility and accuracy of electrical velocimetry for cardiac output assessment in congenital heart disease. Int J Cardiol Heart Vasc. 2020;26:100464. [PubMed: 31956694]
21. Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. Lancet. 2011;377:658–666. [PubMed: 21315441]

22. Stehlik J, Schmalfuss C, Bozkurt B, et al. Continuous wearable monitoring analytics predict heart failure hospitalization: the LINK-HF multicenter study. Circ Heart Fail. 2020;13:e006513. [PubMed: 32093506]

23. Ghanayem NS, Allen KR, Tabbutt S, et al. Interstage mortality after the norwood procedure: results of the multicenter single ventricle reconstruction trial. J Thorac Cardiovasc Surg. 2012;144:896–906. [PubMed: 22795436]

24. Schidlow DN, Gauvreau K, Patel M, Uzark K, Brown DW. Site of interstage care, resource utilization, and interstage mortality: a report from the NPC-QIC registry. Pediatr Cardiol. 2015;36:126–131. [PubMed: 25107545]

25. Oster ME, Ehrlich A, King E, et al. Association of interstage home monitoring with mortality, readmissions, and weight gain: a multicenter study from the National Pediatric Cardiology Quality Improvement Collaborative. Circulation. 2015;132:502–508. [PubMed: 26260497]

26. Rusin CG, Acosta SI, Vu EL, Ahmed M, Brady KM, Penny DJ. Automated prediction of cardiorespiratory deterioration in patients with single ventricle. J Am Coll Cardiol. 2021;77:3184–3192. [PubMed: 34167643]

27. Valente AM, Cook S, Festa P, et al. Multimodality imaging guidelines for patients with repaired tetralogy of fallot: a report from the American Society of Echocardiography: developed in collaboration with the Society for Cardiovascular Magnetic Resonance and the Society for Pediatric Radiology. J Am Soc Echocardiogr. 2014;27:111–141. [PubMed: 24468055]

28. Geva T Indications for pulmonary valve replacement in repaired tetralogy of fallot: the quest continues. Circulation. 2013;128:1855–1857. [PubMed: 24065609]

29. Heng EL, Gatzoulis MA, Uebing A, et al. Immediate and midterm cardiac remodeling after surgical pulmonary valve replacement in adults with repaired tetralogy of fallot: a prospective cardiovascular magnetic resonance and clinical study. Circulation. 2017;136:1703–1713. [PubMed: 29084778]

30. Wasserlauf J, You C, Patel R, Valys A, Albert D, Passman R. Smartwatch performance for the detection and quantification of atrial fibrillation. Circ Arrhythm Electrophysiol. 2019;12:e006834. [PubMed: 31113234]

31. Duking P, Van Hooren B, Sperlich B. Assessment of peak oxygen uptake with a smartwatch and its usefulness for training of runners. Int J Sports Med. 2022;43:642–647. [PubMed: 35094376]

32. Jones L, Tan L, Carey-Jones S, et al. Can wearable technology be used to approximate cardiopulmonary exercise testing metrics? Perioper Med (Lond). 2021;10:9. [PubMed: 33722305]

33. Attia ZI, Harmon DM, Dugan J, et al. Prospective evaluation of smartwatch-enabled detection of left ventricular dysfunction. Nat Med. 2022;28:2497–2503. [PubMed: 36376461]

34. Marcus GM, Modrow MF, Schmid CH, et al. Individualized studies of triggers of paroxysmal atrial fibrillation: the I-STOP-AFib randomized clinical trial. JAMA Cardiol. 2021;7:167–174.

35. Rychik J, Atz AM, Celermajer DS, et al. Evaluation and management of the child and adult with Fontan circulation: a scientific statement from the American Heart Association. Circulation. 2019;140:e234–e284. 10.1161/CIR.0000000000000696

36. Rychik J. The relentless effects of the Fontan paradox. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2016;19:37–43. [PubMed: 27060041]

37. Sadat-Hossieny S, Karamlou T, Marino BS, et al. Contemporary provider management practices and attitudes toward referral for advanced heart failure therapies in Fontan patients across North America. J Card Fail. 2022;28:576–587. [PubMed: 34991953]

38. Chen S, Shezad MF, Lorts A, et al. Outcomes after initial heart failure consultation in Fontan patients. J Heart Lung Transplant. 2022;41:S94.

39. Arshi B, Geurts S, Tilly MJ, et al. Heart rate variability is associated with left ventricular systolic, diastolic function and incident heart failure in the general population. BMC Med. 2022;20:91. [PubMed: 35189879]

40. Inan OT, Baran Pouyan M, Javaid AQ, et al. Novel wearable seismocardiography and machine learning algorithms can assess clinical status of heart failure patients. Circ Heart Fail. 2018;11:e004313. [PubMed: 29330154]

41. Book WM, Gerardin J, Saraf A, Valente AM, Rodriguez F 3rd. Clinical phenotypes of Fontan failure: implications for management. Congenit Heart Dis. 2016;11:296–308. [PubMed: 27226033]
42. Fleming S, Thompson M, Stevens R, et al. Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. Lancet. 2011;377:1011–1018. [PubMed: 21411136]
43. Brudy L, Hock J, Hacker AL, et al. Children with congenital heart disease are active but need to keep moving: a cross-sectional study using wrist-worn physical activity trackers. J Pediatr. 2020;217:13–19. [PubMed: 31740142]
44. Center for Drug Evaluation and Research. Patient-Focused Drug Development: Collecting Comprehensive and Representative Input. 2018. Accessed February 2023. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-collecting-comprehensive-and-representative-input
45. Mahadevan N, Demanuele C, Zhang H, et al. Development of digital biomarkers for resting tremor and bradykinesia using a wrist-worn wearable device. NPJ Digit Med. 2020;3:5. [PubMed: 31970290]
46. Kramer F, Butler J, Shah SJ, et al. Real-life multimarker monitoring in patients with heart failure: continuous remote monitoring of mobility and patient-reported outcomes as digital end points in future heart-failure trials. Digit Biomark. 2020;4:45–59. [PubMed: 33083685]
47. Shufelt CL, Kim A, Joung S, et al. Biometric and psychometric remote monitoring and cardiovascular risk biomarkers in ischemic heart disease. J Am Heart Assoc. 2020;9:e016023. [PubMed: 32896202]
48. Passman R. “Pill-in-Pocket” anticoagulation for atrial fibrillation: fiction, fact, or foolish? Circulation. 2021;143:2211–2213. [PubMed: 34097452]
49. American Heart Association. Leading Science, Research and Technology Leaders Join Forces to Accelerate REACT-AF Trial. 2022. Accessed February 2023. https://newsroom.heart.org/news/leading-science-research-and-technology-leaders-join-forces-to-accelerate-react-af-trial
50. Passman R, Leong-Sit P, Andrei AC, et al. Targeted anticoagulation for atrial fibrillation guided by continuous rhythm assessment with an insertable cardiac monitor: the rhythm evaluation for anticoagulation with continuous monitoring (REACT.COM) pilot study. J Cardiovasc Electrophysiol. 2016;27:264–270. [PubMed: 26511221]
51. Cui F, Yue Y, Zhang Y, Zhang Z, Zhou HS. Advancing biosensors with machine learning. ACS Sens. 2020;5:3346–3364. [PubMed: 33185417]
52. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. Front Public Health. 2017;5:258. [PubMed: 29034226]
53. Aczon MD, Ledbetter DR, Laksana E, Ho LV, Wetzel RC. Continuous prediction of mortality in the PICU: a recurrent neural network model in a single-center dataset. Pediatr Crit Care Med. 2021;22:519–529. [PubMed: 33710076]
54. Food and Drug Administration. Baby Products with SIDS Prevention Claims. 2019. Accessed February 2023. https://www.fda.gov/medical-devices/products-and-medical-procedures/baby-products-sids-prevention-claims
55. Ramanathan R, Corwin MJ, Hunt CE, et al. Cardiorespiratory events recorded on home monitors: comparison of healthy infants with those at increased risk for SIDS. JAMA. 2001;285:2199–2207. [PubMed: 11325321]
56. TASK FORCE ON SUDDEN INFANT DEATH SYNDROME. SIDS and other sleep-related infant deaths: updated 2016 recommendations for a safe infant sleeping environment. Pediatrics. 2016;138:e20162940. [PubMed: 27940805]
57. Predel C, Steger F. Ethical challenges with smartwatch-based screening for atrial fibrillation: putting users at risk for marketing purposes? Front Cardiovasc Med. 2020;7:615927. [PubMed: 33521064]
58. Canali S, Schiaffonati V, Aliverti A. Challenges and recommendations for wearable devices in digital health: data quality, interoperability, health equity, fairness. PLoS Digit Health. 2022;1:e0000104. [PubMed: 36812619]

59. Boch S, Sezgin E, Lin Linwood S. Ethical artificial intelligence in paediatrics. Lancet Child Adolesc Health. 2022;6:833–835. [PubMed: 36084667]

HIGHLIGHTS

- Wearable biosensors provide an opportunity to improve patient care in congenital heart disease by enabling the collection of continuous physiologic data in a wide variety of environments.
- Artificial intelligence and machine learning will be the key to converting wearable biosensor data to actionable insights.
- Due to the wide heterogeneity in congenital heart disease physiology, special considerations should be taken in wearable biosensor design, testing, and implementation.

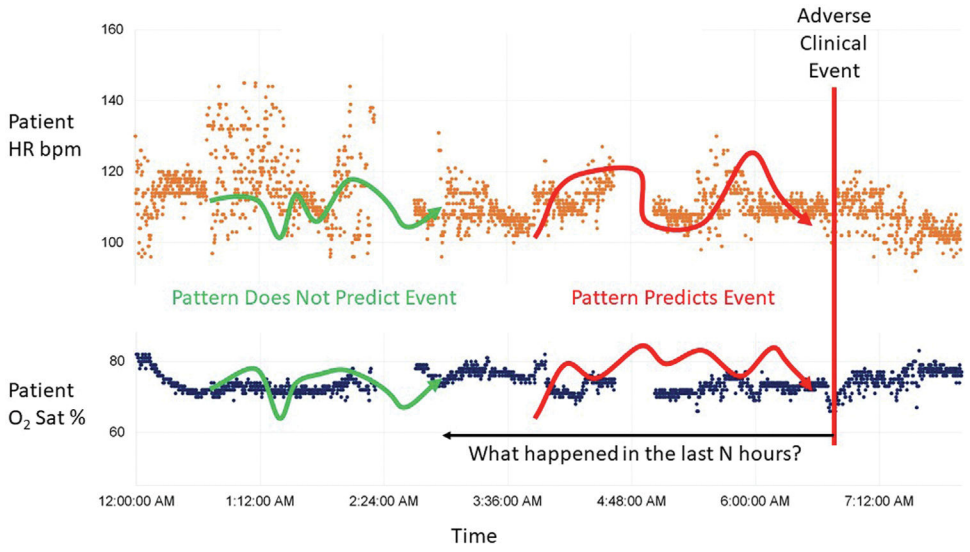


FIGURE 1. Potential Uses for Wearable Biosensors in Interstage Home Monitoring

For patients with single ventricle heart disease who are in the interstage period, one potential use case for wearable biosensors is to use the continuous physiologic data from the wearables to detect pattern changes in vital signs as precursors to adverse clinical events. Given that oxygen saturation and heart rate are salient vitals in this population, analyzing those data may be a good starting point, but novel metrics may be useful in the future as well. Shown here are data from a hypothetical interstage patient using a wearable continuous pulse oximeter.

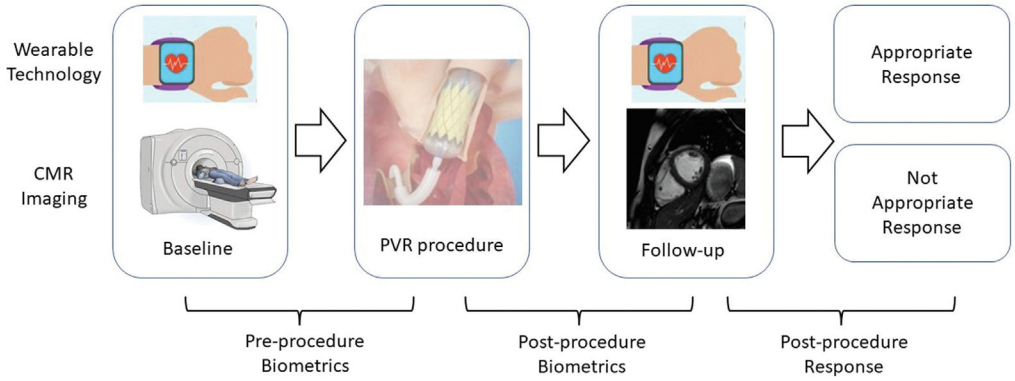


FIGURE 2. Potential Uses for Wearable Biosensors Before and After Major Interventions

In some congenital heart disease populations, timing of major interventions, such as pulmonary valve replacement in repaired tetralogy of Fallot, remains unclear. Wearable biosensors may provide a method of assessing physiologic response to pulmonary valve replacement, by comparing to current standard metrics like CMR, or by development of novel digital biomarkers. CMR = cardiovascular magnetic resonance; PVR = pulmonary valve replacement.

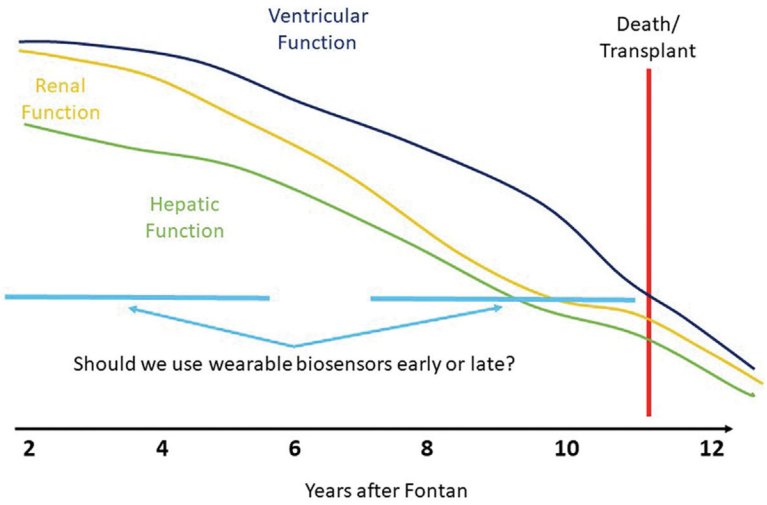
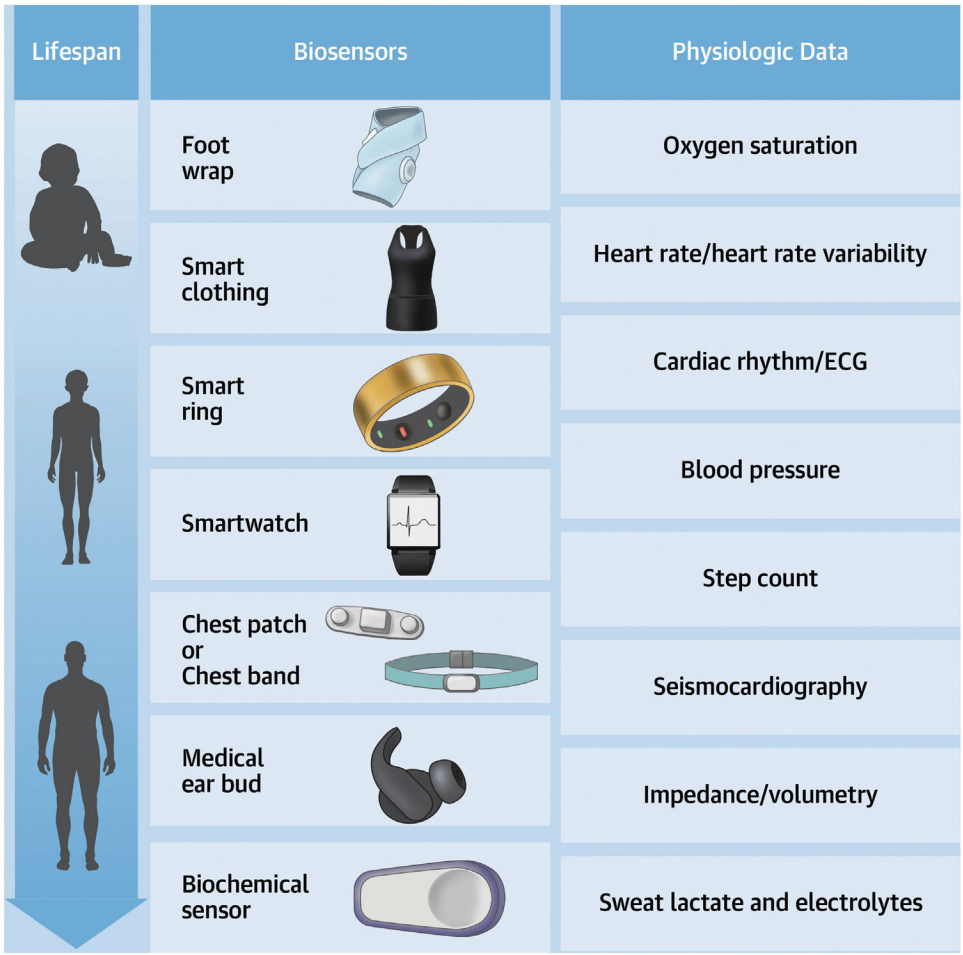


FIGURE 3. Potential Uses for Wearable Biosensors in the Slowly Deteriorating Patient

A fundamental challenge in using wearable biosensors to track patients with slow declines, like those with a Fontan circulation, is identifying the best time to use wearables to generate continuous physiologic data. Is it better to try to catch early, subtle declines, or capture continuous physiologic data closer to clinical adverse events, where the outcome is clearer, but interventions may be too late?



CENTRAL ILLUSTRATION. Current and Future Use Cases for Wearable Biosensors in Congenital Heart Disease

This figure outlines different form factors of wearable biosensors that are being or may be used for patients with congenital heart disease across the age spectrum and the physiologic data that are currently collected by wearable biosensors. Given the broad anthropometric, developmental, and physiologic changes that patients with congenital heart disease undergo throughout their lives, different form factors are needed to collect applicable physiologic data.

Table 1

Physiologic Measurements Collected by Wearable Biosensors and Their Potential Clinical Uses

Measurements Collected	Potential Clinical Scenarios
Oxygen saturation	• Interstage single ventricles: home monitoring • Cyanotic heart disease: home monitoring
Heart rate/Heart rate variability	• Interstage single ventricle: home monitoring • Chronic CHD: before and after interventions or medication initiation • Failing Fontans: tracking decline • Patients with arrhythmias: burden and response to medications • Heart failure: outcome prediction • High-risk patients: monitoring and prescribing exercise
Blood pressure	• Coarctation: hypertension monitoring, medication titration
Cardiac rhythm/ECG	• Interstage single ventricle: event prediction and home monitoring • Fontans: tracking arrhythmia burden • Repaired tetralogy of Fallot: atrial and ventricular tachycardia monitoring • Patients with arrhythmias: burden and response to medications • Long QT: mediation titration
Step count	• All populations: activity monitoring, including exercise for high-risk patients • Cardiac rehabilitation: exercise prescription monitoring
Impedance/volumetry	• Interstage single ventricle: cardiac output monitoring, volume status • Fontans: cardiac output monitoring • Pulmonary overcirculation: volume status
Biochemical sensors	• Interstage single ventricle: sweat lactate monitoring • Failing Fontan: sweat lactate monitoring • Patients with arrhythmias: electrolyte balance

CHD = congenital heart disease; ECG = electrocardiogram.