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Mobile Health Monitoring of Cardiac Status

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Abstract

Cardiovascular diseases (CVDs) are responsible for more deaths than any other cause, with coronary heart disease and stroke accounting for two-thirds of those deaths. Morbidity and mortality due to CVD are largely preventable, through either primary prevention of disease or secondary prevention of cardiac events. Monitoring cardiac status in healthy and diseased cardiovascular systems has the potential to dramatically reduce cardiac illness and injury. Smart technology in concert with mobile health platforms is creating an environment where timely prevention of and response to cardiac events are becoming a reality.

INTRODUCTION

Cardiovascular diseases (CVDs) account for the largest percent of preventable morbidity and mortality worldwide (1). Primary prevention of CVD includes lifestyle change and risk reduction whereas secondary prevention of CVD includes these measures and regular clinical visits to monitor therapy. At the population level, prevention includes placement of emergency equipment such as automated external defibrillators (AEDs) in population centers (e.g., arenas, airports) and reducing environmental risk factors. In patients with known CVD and risk of sudden cardiac death, implanted devices such as internal cardiac defibrillators and pacemakers serve a secondary preventive and life-preserving role. All of these strategies are dependent on monitoring individuals to prevent cardiovascular events before they happen. Advances in monitoring and data handling have increased our ability to monitor lifestyle behavior and physiology and respond quickly to irregularities in physiological biomarkers to reduce morbidity and mortality. This review summarizes current strategies for mobile cardiac health monitoring of individuals with and without CVD and emphasizes novel strategies that have the potential to improve the monitoring and handling of data on cardiac status collected using mobile devices.

Preventing onset of disease through lifestyle management and responding quickly to cardiac events are paramount to public health efforts. Finding ways to promote lifestyle behavior changes for primary prevention of CVD has been a focus of cardiovascular medicine for some time. Assessing cardiorespiratory fitness (CRF) and physical activity level (PAL) as vital signs has become common in clinical practice; increasing CRF and PAL has been shown to have a significant impact on the prevention of CVD (2, 3). Companies have been successful in monitoring PAL, giving individuals a tool for tracking and estimating CRF. A quick response to cardiac events, e.g., to sudden cardiac arrest (SCA), has been shown to dramatically improve outcome (4). For every minute that passes after onset of SCA without CPR (cardiopulmonary resuscitation) and defibrillation, the chances of survival decrease by 7–10% (5). The placement of AEDs in public places (e.g., airports) has been observed to increase the rate of survival after an SCA event due to the speed with which bystanders may provide AED therapy compared to an emergency response team (6). Similarly, an implantable cardioverter-defibrillator (ICD) serves the same purpose for patients with known risk for SCA, with the added ability to monitor rhythm ahead of an event and transmit the data to a medical provider. An ever-increasing number of devices, including wearables, are passively collecting health data to monitor cardiac status, especially heart rate (HR) but also electrocardiogram (ECG) data and other related biomarkers.

TRADITIONAL METHODS FOR MONITORING CARDIAC STATUS

Accurate assessment of CRF and PAL has been traditionally done with expensive medical equipment and trained expert analysts. The standard for assessing CRF is the cardiopulmonary exercise test (CPET), in which individuals exercise from resting conditions to peak intensity while their respiratory gases (carbon dioxide and oxygen) are monitored. CPET is very time consuming and the metabolic cart that is used for respiratory gas measurement is very expensive and requires specialized training to operate and interpret the results. However, the results of CPET give the individual a precise assessment of his or her maximum ability to consume oxygen, which is the strongest predictor of CRF.

Other assessments of CRF have been developed, including timed walking and running tests, step tests, and algorithms that include several of these and other biological metrics. An individual's PAL is strongly correlated to CRF, and several methods have been developed for the assessment of PAL to estimate CRF. Pedometers and accelerometers are devices that may be worn on the body to track steps and acceleration, respectively. These methods have been used for some time

and offer less expensive and time consuming, albeit limited, insights into PAL and CRF. Hickey & Freedson (7) have reviewed these types of devices and their utility in CVD prevention and treatment. It is extremely challenging to convey health information and counsel and motivate individuals to engage in CVD risk–lowering behaviors through traditional methods (e.g., face-to-face counseling) (8).

The development and popularity of wearable monitors with integrated accelerometers and other sensors have led to an environment in which metrics of cardiac function can be monitored almost constantly from personal smart devices. For example, studies combining step measurement and text messaging to cell phones have observed that using wearable monitors as a feedback mechanism between clinicians and patients has the potential to induce health behavior changes while avoiding common barriers related to transportation and scheduling (9–12). In American Heart Association and European Society of Cardiology statements, Burke et al. (13) and Frederix et al. (14) noted that mobile health (mHealth) and mobile technologies can overcome these limitations in targeting behavior change by improving communication of patient self-management with healthcare providers in real time and in a natural setting.

Many of these data have led to the creation of risk scores that may be calculated based on some user-generated input data. Cardiovascular risk calculators such as the Stroke Riskometer™ (15), MARS (mobile application rating scale) (16), and atherosclerotic cardiovascular disease risk assessment tool (17) have been digitized and are available as applications (apps) from the American College of Cardiology (**https://www.cardiosmart.org/Tools**), among others. Fitness-based scores such as PAI (personal activity intelligence) have also been developed and are available as apps that offer users a fitness score calculated from metrics such as age, sex, and resting and maximum HR (17, 18). These risk and fitness assessment tools are easily integrated into mHealth platforms with wearable monitors as the interface, allowing data to be communicated to and between patients and clinicians.

DEVICES AND SYSTEMS FOR MOBILE CARDIAC HEALTH MONITORING

Development of Wearable Monitors

Wearable monitors for the recording of physiological metrics have been used for some time in sports science and medicine. Step counting has been performed since Roman times (19), but the first mention of counting steps as a health behavior occurred in the 1960s, when the Yamasa company developed the Manpo-kei ("10,000 steps meter") device for the monitoring of PAL (19). This was believed at the time to be the number of steps necessary to prevent coronary artery disease. Accelerometers were first investigated in the 1950s to measure gait velocity and acceleration, and in the 1970s technological advances allowed for the measurement of human motion in more detail (20). Chest straps for HR monitoring have been used for exercise testing and prescription in health and disease since the early 1980s (21, 22), and motion-detecting monitors (i.e., pedometers and accelerometers) have been in use since the 1970s for monitoring human movement (23–25). Excellent historical reviews of these earlier-generation PAL recording devices in sports and medicine have been conducted by Freedson et al. (26) in 2012 and Bassett et al. (19) in 2017. Cardiovascular implantable electronic devices include ICDs, pacemakers (PMs), cardiac resynchronization therapy (CRT) devices, implantable loop recorders, and implantable hemodynamic monitors (27). These devices, which monitor cardiac function remotely and can provide therapy to a malfunctioning heart, are exemplary in their abilities to monitor pathology and directly influence cardiac health. Mirowski and Mower developed ICD technology in the 1960s using dogs as experimental subjects, and the first implantation in a human was in Johns Hopkins Hospital in 1980. Currently

in the United States, more than 100,000 people are implanted with an ICD every year. Remote monitoring of implanted cardiac devices allows the data stored in the device to be transferred remotely from the home to a central database. The implanted device is equipped with an antenna that uses radiofrequency signals to communicate with the home monitor. The data are then sent from the home monitor to a secure data server using a telephone line or wirelessly (28). This type of remote monitoring of ICDs, CRT devices, and PMs, along with clinic visits, has been observed to improve outcomes compared to clinic visits alone (28).

Current wearable monitors have great potential for collecting data and interactions between the device, the wearer, and the healthcare system. Currently there are devices that can measure behavioral metrics such as movement and physiological parameters such as HR, ECG, oxygen saturation, blood pressure, skin temperature, and respiration rate (29, 30). Commonly found as a wrist-based product, most HR monitors use an optical technique known as photoplethysmography (PPG) to assess HR (31). Although there are some known issues with PPG signals, especially due to the location and the properties of the subject's skin at measurement (including individual skin structure, blood oxygen saturation, blood flow rate, skin temperatures, and the measuring environment), advances in preprocessing have greatly improved quality, although may not be at the level of chest straps (32, 33). Passive and continuous monitoring of HR has become very popular by an ever-expanding consumer-based market that includes devices such as Apple Watch, Fitbit Charge 2, Microsoft Band 2, and Garmin Forerunner 235, among many others (34). Recently, studies have shown that commercially available products have acceptable accuracy in estimating HR but fail to deliver accurate energy expenditure (EE) and CRF estimates (35). It seems that several algorithms for EE may not be incorporating HR and that there is large interindividual variability in activity-specific EE (35). A recent study of wearable smart HR and activity monitors found that tracking with these devices was well tolerated in a cardiovascular patient population, with high adherence (90%) and low attrition (0.09% decrease per day) over a period of 90 days (36).

Data Storage and Connectivity/Networking of Cardiac Monitors

Technological advances and a consumer-driven market have spurred the use of wearable monitors for a variety of purposes (37). In response to the increased adoption of these monitors by both physicians and consumers, an unprecedented volume and variety of patient-generated health data (PGHD) consisting of physiological and behavioral information are now available (38). These include more traditional cardiovascular biomarkers (e.g., HR and EE) and advanced biomarker tracking (e.g., detection of arrhythmia) but also include novel markers, including mobile body temperature monitoring (TempTraq), crowdsourcing air quality (Air Louisville), and guiding the blind through mobile devices (Aria). Advances in data storage and connectivity have allowed physiological and other data to be transferred from wearable monitors to platforms, e.g., for sharing exercise data within online running communities (e.g., Strava; **https://www.strava.com**) or sharing data with clinical professionals for monitoring HR and rhythm.

To communicate and visualize data remotely, monitors must link to external devices such as smartphones for the collection and visualization of data. This has allowed for prompt two-way communication (e.g., for coaches and clinicians), empowering users through a data-driven approach. The World Health Organization defines mHealth as "medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices" (39, p. 14). mHealth consists of apps in which wearable monitors connect to a clinical network to increase connectivity for patients, especially to their healthcare providers. The interoperability of mHealth data has been enabled on iOS and Android devices by the HealthKit and Google Fit interfaces, respectively. These application

programming interfaces (APIs) provide a central health data repository where the user can specify exactly which apps can read and write health fields such as steps, systolic blood pressure, or even electronic medical records (EMRs). In 2015, Epic Systems Corporation, which houses over half of all US medical records, announced an integration with HealthKit whereby their personal health record app MyChart could read HealthKit data from a patient's phone and record the data in the patient's EMR (40). This system was used to collect data from virtual weigh-ins in a study about the influence of social incentives on weight loss (41), as well as to track blood glucose in pediatric diabetes patients at Stanford Children's Hospital (42). Oschner Health has implemented a HeathKit-to-Epic system to provide digital tracking of hypertension, doubling the percentage of usual-care patients that achieve target blood pressure control (43). In the case of heart failure, Oschner has reduced readmissions by 44% by following patients with wireless scales and reacting clinically by adjusting oral diuretics or scheduling same-day appointments (44). Oschner's solutions not only transmit PGHD but also include sites where patients can get help setting up their devices, automated reminders when readings are not made, and teams that are constantly looking at the PGHD and reacting clinically (45).

Toolkits for Mobile Health Applications

Simply transferring health data is not sufficient for apps; some medical conditions also require apps that can administer surveys to collect patient-reported outcomes, present educational materials, and provide reminders, such as for medications. In the mid-2010s, corporate and academic efforts spurred the creation of the software libraries ResearchKit, ResearchStack, ResearchSuite, and SageResearch, which provide key functionalities needed to make mHealth studies as native apps on devices running iOS and Android and findable via Apple's App Store and Google's Play Store. These studies typically begin with self-directed eligibility questions, followed by an electronic consent typically using a patient-centered consent framework, which couples animations to titles, short descriptions, optional videos, and a "learn more" feature (46). The core app sections seen in these studies include (*a*) an activity list that triggers surveys and active tasks, in which data are collected from phone sensors; (*b*) a dashboard, which presents information back to participants; (*c*) a learn section, with educational content and links; and (*d*) a profile screen, with options such as data export and withdraw. In the background, these apps can passively collect data from motion APIs (such as CoreMotion to get a seven-day activity assessment) and health data stores such as HealthKit and Google Fit, which may be populated by a variety of wearable monitors, apps, and medical record sources in fields such as steps, HR, blood pressure, and health record. Some manufacturers, like Fitbit, do not support these common health data platforms and require either specific code in order to integrate with their APIs or a third-party app in order to sync the data. In 2016, Apple released the CareKit framework for mHealth apps that can start with clinical encounters. Patients can track their care plans (with activities such as taking a medication, changing a wound dressing, or meditating) with the Care Card module, monitor their progress through surveys and device data with the Symptoms and Measurement Tracker, see the relationship between treatment and progress with the Insight Dashboard, and share their data with care teams with the Connect module.

With government, academic, and commercial groups creating platforms to enable nontechnical investigators to build cross-platform study apps, the number of mHealth trials is expected to proliferate (47). These platforms rely on web forms that allow the surveys in the app to be customized. They also enable data to be collected from wearable monitors, although this is typically restricted to devices that can write to HealthKit. One such platform, MyCap (**https://www.projectmycap.org**), offers customized web-based interfaces that interact with REDCap to capture research

outcomes on mobile devices. Another platform, Thread (**https://www.threadresearch.com**), offers multiple remote patient research approaches, integrating traditional research tools into mobile platforms with the goal of performing clinical research while minimizing the burden of clinical visits. Medable (**https://www.medable.com**) offers a HIPAA (Health Insurance Portability and Accountability Act)-compliant backend as a service and has created no-code-required solutions to create ResearchKit (Axon) and CareKit (Synapse) apps. Similar platforms are offered by Overlap Health (**https://www.overlaphealth.com/**) and Zendra Health (**https://www.zendrahealth.com**). The US Food and Drug Administration's (FDA) Sentinel Initiative has sponsored the development of the similarly featured MyStudies App (**https://www.fda.gov/drugs/science-and-research-drugs/fdas-mystudies-application-app**), which is capable of being fully compliant with Title 21 21 of the Code of Federal Regulations, Part 11, and is being used to collect data in several live clinical trials. Pattern Health (**https://pattern.health/**) offers a platform that has dashboards not only for researchers to design their studies but also for clinical and care team members to track participants.

TRANSLATION: MONITORING CARDIAC STATUS IN PRACTICE

Monitoring Cardiac Status for Prevention

Monitoring patients to prevent future injury and/or illness has many different applications. Traditional monitoring for secondary prevention includes the monitoring of anyone with cardiovascular disease with the aim of preventing further events. These efforts are typically as part of cardiac rehabilitation (CR) and cardiac maintenance programs. Other efforts are related to monitoring special populations, including those who may not be able to travel; passive monitoring for population-sized studies on heart rhythm; real-time monitoring of patients on continuous left ventricular assist device (LVAD) therapy; and integrating monitors in population-scale mHealth preventive health programs.

Cardiac rehabilitation and cardiac maintenance programs. CR and cardiac maintenance programs have led the way in implementing mHealth to increase healthcare utilization and improve outcomes. These programs are effective but underutilized in the secondary prevention of CVD, and increasing utilization is an important goal in healthcare (48–51). The Million Hearts® initiative (**https://www.millionhearts.hhs.gov**) from the CDC (Centers for Disease Control and Prevention) is an educational initiative designed to prevent at least one million heart attacks and strokes over five years (2017–2021) by increasing participation in CR from 20% to 70%, which is projected to save around 25,000 lives (48). The main barriers to participation in CR and cardiac maintenance programs are transportation and scheduling problems (9, 10, 12, 52). Wearable monitors integrated with mHealth platforms could increase utilization and improve monitoring, making CR available to more patients by alleviating these barriers (53). One of the strategies to achieve these goals is to use text messaging and feedback from wearable monitors, which are simple interventions that have been shown in a study by Lounsbury et al. (54) to increase CR attendance by 10%. In this study, researchers offered patients entering CR the opportunity to receive three to five text messages per week containing information about their heart health and asking patients about their body weight, minutes of exercise, blood pressure, and adherence to medication. The study showed 10% higher participation in the text message group than in the group receiving traditional CR (61.5% versus 50%, $p = 0.01$), and among those who completed the study, the text message group completed significantly more sessions (31.4 versus 25.3, $p = 0.01$). Considering the simplicity of the trial, these data convincingly support the potential of mHealth communications to change health behaviors.

Remote monitoring for home-based prevention of cardiovascular disease. Dansky et al. (55) observed that remote monitoring of 284 heart failure patients led to improvements in rehospitalization, symptoms related to sodium and fluid intake, and medication effectiveness, but not in PAL status at 60 days after discharge. The observed improvements did not persist after 120 days. The authors suggested that the observed nonsignificant trend at 120 days may be significant given a larger sample size. The authors concluded that timely feedback through the monitors supported appropriate behaviors and timely medical intervention to manage heart failure; however, in-person physical therapy may be needed to improve PAL. Using a similar methodology, Green et al. (56) applied remote monitoring to 778 patients with hypertension with the goal of improving blood pressure. Interestingly, although the group receiving monitoring and web training only had improved blood pressure at 12 months, adding web-based pharmacist care led to significant improvements in blood pressure compared to both usual care and the group receiving monitoring and web training without web-based pharmacist care.

In 2015, 51 studies of remote monitoring in primary and secondary CVD prevention (9 with analyzable CVD outcome data) were subject to a systematic review and meta-analysis (57). Studies with follow-ups at 2–24 months showed a net benefit of remote monitoring of overall CVD outcomes compared to usual care. The authors suggested that these observations were especially linked to improvements among higher-risk populations or those targeting secondary CVD prevention. There were also improvements in weight loss, body mass index, blood pressure, and LDL (low-density lipoprotein) cholesterol for CVD in studies on primary prevention. Taken together, initiatives that led to improvements in risk factors for CVD seen in primary prevention studies did not translate to secondary prevention, and initiatives resulting in significant reductions in CVD events in secondary prevention studies did not translate to primary prevention. Considering that CVD events are more likely to occur in secondary prevention than in primary prevention, these findings support further investigation of specific remote monitoring for different CVD populations.

The Better Effectiveness After Transition–Heart Failure (BEAT-HF) randomized clinical trial remotely monitored for readmission at 180 days and 30 days, all-cause mortality at 30 and 180 days, and quality of life at 30 and 180 days in more than 715 patients with heart failure over two years. As with other large trials on remote monitoring, the BEAT-HF trial did not find any significant effect on all-cause hospital readmission within the first 30 or 180 days (58). However, there was a significant effect on quality of life at 180 days.

Other novel remote monitors in cardiovascular disease prevention in special populations. Older populations with CVD have special challenges in successfully performing in-clinic therapy programs and visits. Pedone et al. (59) evaluated a simple combined monitoring/telephone support model on 50 patients whose average age was 80 years. The mobile devices included a sphygmomanometer (A&D Engineering, San Jose, CA), a scale (A&D Engineering), and a pulse oximeter (Nonin Medical, Inc., Plymouth, MN), and patients were able to use an office hour telephone-based clinical support system. Compared to controls, patients participating in the program were half as likely to experience all-cause mortality and hospital readmission at 180 days. The authors attributed the success of the trial to (*a*) having a geriatrician leading the intervention and (*b*) immediate ambulatory response to abnormalities in remotely monitored data. These were also important factors that have limited other studies in which remote monitoring alone supplementing usual care has not been effective (60, 61).

In contrast to the abovementioned observations, Cakmak et al. (62) conducted a pilot feasibility study aimed at creating personalized models from passive smartphone data to identify changes in heart failure severity. The authors followed 10 patients with heart failure over one year,

producing over 680 million samples of physical movement data, 9,000 geographic location updates, and 11,000 individual social networking events. From this passive data algorithms could predict an established measure of quality of life with 83% accuracy. Passively monitoring the clinical status of patients with heart failure accurately would give clinicians a useful tool for rapid response to deteriorating health of heart failure patients.

Lastly, in another study (63), a passive remote device with a piezoelectric sensor under a mattress was used to monitor breathing, heart pumping, and body movements of patients who had been hospitalized for heart failure. In total, 29 patients were passively recorded for 640 nights, and the devices were tolerated by 97% of the patients. Patients who were readmitted for heart failure had a significantly different piezoelectrically assessed respiratory rate, movement rate, and number of hours with rapid shallow breathing, as well as amount of time spent in bed.

In conclusion, several studies have assessed a variety of technologies to remotely monitor cardiac status as primary and secondary prevention. Using a combination of passive monitoring and quick clinical response system to abnormalities in the remotely monitored signal may be the most effective way to improve clinical outcomes and decrease adverse cardiac events.

Monitoring of Heart Rhythm (Arrhythmias)

Newer HR wearable monitors are capable of ongoing passive measurements such as HR variability metrics, daily activity measures, and sleep analysis (34). Cardiogram is an app that collects and analyzes such data to detect clinical events such as atrial fibrillation (AF) (64). In addition to optically based HR methods, other methods of analyzing HR have been developed. AliveCor's KardiaBand (**https://store.alivecor.com/products/kardiaband**) is a clinical-grade ECG wearable monitor that is integrated into the Apple Watch band, providing access to 30-s single-lead ECG readings. More recently, Series 4 and newer versions of the Apple Watch have ECGs built into the watch itself. Patch-based wearable monitors have risen in popularity, especially in clinical care environments. However, a physician prescription is needed for ECG monitors that focus on latent arrhythmia detection, such as iRhythm's Zio patch (65) and Cardiac Insight's Cardea SOLO (**https://www.cardiacinsightinc.com/cardea-solo**). Furthermore, although the accuracy of the algorithms is improving, electrophysiologist-trained physicians are also still necessary to read the ECG reports from these patches. Wrist-based wearable monitors are also starting to make advances in the detection of cardiac arrhythmia, both through integrated ECG and PPG. Especially in AF, there are devices that have shown accuracy that is comparable to analysis by expert electrophysiologists. FibriCheck by Qompium (Hasselt, Belgium) is the first medically certified (class IIa) smartphone arrhythmia monitoring app for diagnosing heart rhythm disorders (**https://fibricheck.com**). It was used in two separate prospective nonrandomized studies and showed equivalency against ECG with a positive correlation ($r_s = 0.993$, with a root-mean-square error of 23.04 ms and a normalized root-mean-square error of 0.012) between the peak-to-peak intervals from FibriCheck and the R-R intervals from the wearable ECG monitor (66, 67). AliveCor's heart monitor device (**http://www.alivecor.com**) derives a single-lead (lead I) ECG signal from two sensors and three algorithms. The approach has reported a sensitivity of 98% and a specificity of 97% for detecting AF compared to traditional 12-lead ECG read by a trained cardiologist (68, 69).

Efforts are currently underway to test the utility of this wearable monitor in an intervention affecting clinical outcomes in a real-world setting; the iHEART (iPhone helping to evaluate AF rhythm through technology) study is a randomized controlled trial that will enroll 300 participants with AF to receive a smartphone with an ECG app and motivational text messages or usual cardiac care (70). The investigators will assess clinical outcomes, quality of life, quality-adjusted life-years,

and disease-specific knowledge after six months to test the efficacy of the mHealth program. Other technologies are currently being investigated using the PPG signal of a smartphone to detect atrial arrhythmia.

Chan et al. (71) tested the ability of the standalone smartphone Cardiio Rhythm (Cardiio, Inc., Cambridge, MA) PPG app to detect AF in patients with high risk of AF. Patients were assessed with a single-lead ECG, then had three PPG waveforms measured by pressing a fingertip against the smartphone camera and assessed by an app running on the smartphone. The Cardiio Rhythm PPG app assessed AF in this population of 1,013 subjects (28 with AF) with a sensitivity and specificity of 92.9% [95% confidence interval (CI) of 77–99%] and 97.7% [95% CI 97–99%], respectively (71). Although these preliminary data are promising, real-world data (e.g., out of the clinic, free-ranging) are still lacking, and caution must be used when assessing data from these devices (72).

Another clinical population at high risk for cardiac arrhythmia and clinical deterioration are patients with congenital heart disease. Patients with congenital heart disease also require frequent follow-ups to assess clinical status and progression of disease. Koole et al. (73) investigated whether remote monitoring could enable swift therapeutic response and detect new diagnosis in 109 patients with congenital heart disease. They monitored for recurrences and new diagnosis of arrhythmia, hypertension, and heart failure and evaluated adherence and patient experience using questionnaires. As with other studies, remote monitoring was supplemented with a clinical staff that would contact the patients directly if necessary. After completing a median follow-up time per patient of 12 months, the authors were able to respond quickly to the targeted symptoms, and the program was well accepted by the patients and practitioners. In total, 77% of patients who started with weekly assessments were able to continue with an adherence rate greater than 70%. In this and other patient groups who are at high risk of arrhythmia and require frequent follow-ups, this type of program may decrease disease progression and risk of adverse cardiac events.

With the ubiquity of smart watches, the ability to monitor arrhythmia using the smartwatch PPG in these devices may offer an enormous opportunity to prevent adverse cardiac events on a large scale. Koshy et al. (74) evaluated the rhythm of 102 hospitalized patients each for 30 minutes with continuous ECG and simultaneous smartwatch HR monitoring. Both devices showed good agreement to ECG in sinus rhythm and atrial flutter but underestimated HR in AF, leading to the observation that although the devices may underestimate HR in AF at low HR (<100 bpm), tachycardic readings on wearable devices occurring at rest may be suggestive of an underlying atrial arrhythmia.

In patients with a history of AF, early detection after cardioversion or ablation is important for guidance of therapy. Rozen et al. (75) investigated the diagnostic accuracy of an mHealth app in 98 patients pre- and postcardioversion. The Cardiio Rhythm mobile app uses an iPhone camera to take multiple finger pulse recordings; in the current study three 20-s measurements were performed before and after cardioversion, and rhythms were designated as AF if two out of three measurements were sufficiently irregular. Compared to a 12-lead ECG interpreted by two cardiologists and one senior electrophysiologist, the app correctly identified the presenting rhythm in 93% (89/96) and 92% (80/87) of the patients and pre- and postcardioversion, respectively. Although the study was limited to a population with known AF at the time of presentation, the study shows a high accuracy of detecting AF versus sinus rhythm in a controlled environment where the accurate assessment of rhythm has high clinical importance (75).

In a population study on the ability of a smartwatch to passively detect AF, Tison et al. (64) enrolled 9,750 participants (347 with AF) to develop the detection algorithm and 51 patients with AF undergoing cardioversion who served as an external validation cohort. Heuristic pretraining was used to train a deep neural network based on approximations of R-R interval and validated against

12-lead ECG. The neural network was trained on more than 139 million HR measurements and had a sensitivity and specificity of 98% and 90%, respectively, against external validation and 68% for both against self-report. This shows proof of concept that combining PPG and deep neural network seems to be fairly precise compared to 12-lead ECG (64).

Recently Perez et al. (76) reported the Apple Heart Study, , which is by far the largest study to assess arrhythmia detection using a wearable monitor and therefore adds substantially to the literature. The study intermittently and passively collected PPG data from optical sensors of the Apple Watch from 419,297 participants over eight months. The device classifies pulses as either regular or irregular based on a proprietary algorithm that bases regularity on interpeak intervals plotted on a Poincaré plot and degree of dispersion. Applying these methods, 0.52% of participants received an irregular pulse notification. One of the limitations of the study was a relative inability to detect paroxysmal and infrequent AF on a subsequent ECG patch due to its transient nature. This is reflected in the fact that 34% of those who received notifications from the watch had AF on subsequent ECG patch. Unfortunately, the return rate of patches from those who received notifications for follow-up was only 450 out of 2,161 (21%). Very few participants were notified by the watch of an irregular pulse; of those notified, about a third had AF as assessed by ECG patch, and concordance of AF between the positive notifications and the patch was 84% (95% CI 76–92%) (76). The low adherence to follow-up was also reflective of earlier studies on remote monitoring; therefore, much work still needs to be done to increase participation in order for these programs to be successful in improving health and preventing cardiac disease and injury.

Finally, there are some published cases of mHealth technology correctly detecting AF in individuals with an ICD. Doshi et al. reported the case of a 57-year-old golfer with a history of cardiomyopathy who had an ICD placed and wore a smartwatch (77). While golfing the individual received a haptic signal meant to alert the user of AF. This episode of AF was confirmed the next day through scheduled ICD device interrogation, during which it was confirmed that the individual experienced AF which had spontaneously converted back to sinus rhythm. Overbeek et al. (78) reported a case in which an upper-middle-aged female was diagnosed with complete heart block after being continuously alerted by her Apple Watch for several hours of a low HR. The individual presented with a baseline HR of 37 bpm and ECG displayed complete heart block, for which a dual-chamber PM was implanted. These real-life examples show the potential benefits of widespread use of wearable technology in detecting life-threatening cardiac arrhythmias.

Monitoring Cardiac Status with Left Ventricular Assist Device Support

Patients with LVADs need permanent support until the device can be removed due to eventual recovery or transplant. As well as their regularly scheduled appointments for heart failure, they also need to closely monitor the device itself for cleanliness and function.

Although technology for remote monitoring has been available for the last decade with the HeartAssist 5® system [MicroMed Cardiovascular, Inc., Houston, TX (79)], continual monitoring of parameters from the two most frequently implanted LVAD pump systems, HeartMate II/III (Thoratec Corp., Pleasanton, CA) and HeartWare (Heartware Int., Framingham, MA), is not currently possible. Although the necessary interfaces are already integrated in the devices, they have not been cleared for telemonitoring due to the prohibition of remote treatment, the detectability of medical services, and liability issues (on the part of the treating physicians, but also on that of the manufacturers regarding technical defects) (80–83). For these devices to be effective, the LVAD should be interfaced, and either through mHealth tools or a patient–clinician interface, blood pressure, heart rhythm, coagulation, and other parameters (e.g., photos of infection and PAL) should be continually available to clinicians (83).

The largest telemonitoring cohort of LVAD patients was recently reported by Hohmann et al. (84). Eleven patients who had either the HeartAssist 5 or aVAD (ReliantHeart, Inc., Houston, TX) LVAD with telemonitoring were included and followed for a median follow-up time of 2,438 patient-days. Pump performance indexes of outflow graft blood flow, pump speed, and power consumption were transmitted on 15-min running average values over a cellular network to medical personnel. Participants had remote monitoring on top of routine in-clinic office visits. Remote transmission of system information was successful 74% of the time, illustrating a major limitation of using cellular networks. However, the study was successful in demonstrating timely recognition of clinically important abnormalities, which alleviated the need for complicated LVAD exchanges and hospital admissions. Furthermore, the authors reported that they were able to interpret waveforms from the monitors to evaluate arrhythmias, volume depletion, suction events, and aortic valve opening. There are still few LVADs with remote monitoring capability, but the advances in technology and increase in number of patients living longer with heart failure and device support seem to warrant more research in the effect of LVAD monitors in improving outcomes and reducing the cost of ongoing LVAD therapy (85).

Large-Scale Monitoring of Cardiac Status Using mHealth Strategies

Using some of these abovementioned strategies, there has been progress toward viable mHealth systems to population-level preventive health. The goal of these strategies is to inform and measure the effect of therapy and interventions.

The MyHeart Counts Cardiovascular Health Study (**https://itunes.apple.com/us/app/myheart-counts/id972189947?mt=80**) is a smartphone-based mobile cardiovascular health research study that was launched alongside ResearchKit (**Figure 1**). The study uses mHealth capabilities of smartphones and HealthKit-enabled wearable monitors (currently watches but the platform can accommodate any device that can transmit data wirelessly) to assess daily activity measures (with and without heart disease), fitness, and, through questionnaires, cardiovascular risk factors. The study has collected activity and cardiovascular health data on thousands of participants (>58,700 have enrolled) and has provided much more quantitative data on the type, duration, and intensity of daily activities based on accelerometry recorded from the phone core motion processor. Results from phase I of the study were published in January 2017 (86). Primarily, 82% of those enrolled uploaded data to the wearable monitors and 42% completed four of the seven days of motion data collection. Although efforts need to be made to increase participation in such programs, the results show that large-scale data can be gathered in real time from mobile devices, stored securely, transferred, deidentified, and shared securely. For example, the largest dataset for 6-minute walk test (6MWT) performance was collected using the platform in a matter of weeks by replacing a manual distance measurement with a participant-initiated test that used GPS, accelerometry, and pedometers. Patients only needed to press a button on their smartphone and a 6MWT was initiated, and the user was prompted to start walking and stop after six minutes. The data were automatically calculated, saved, and transmitted without any effort from the user, and the data could be seen and analyzed on the smartphone or another remote device. This was able to not only measure distance but also provide additional information such as gait. The second phase of the study introduced a randomized controlled clinical trial (**https://clinicaltrials.gov** identifier NCT03090321) of four different physical activity prompts and their effect on increasing PAL in the study population as measured by change in step count, which was measured by the phone's motion coprocessor or a wearable monitor like the Apple Watch that can write to HealthKit (86–88). Data from the subset of MyHeart Counts participants who opted to share broadly are available on a data portal to broadly defined qualified researchers (87).

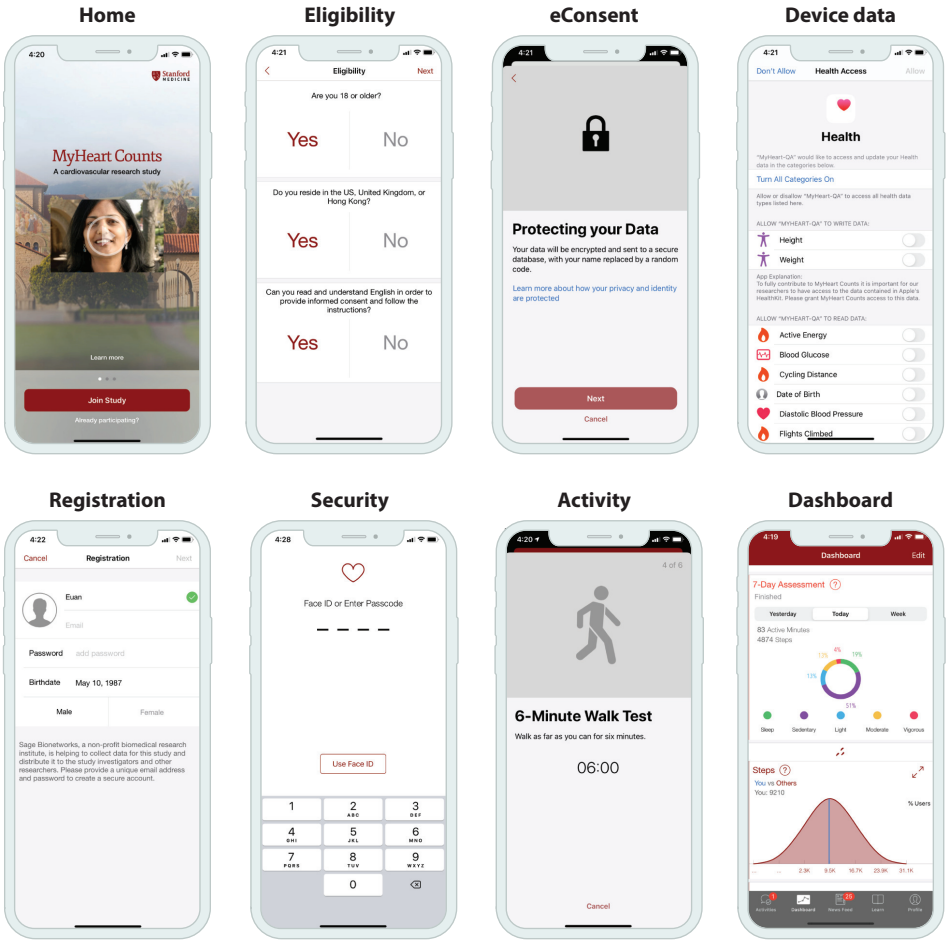

Figure 1

Anatomy of a mobile health clinical study mobile application (app) showing screens from the mobile app used in the MyHeart Counts Cardiovascular Health Study.

Advances in the collection and interpretation of complex cardiac biomarkers have made efforts to apply data collected on cardiac health a reality. Ongoing investigations such as Verily/Alphabet's Project Baseline (**https://www.projectbaseline.com**) and the NIH's All of Us (**https://allofus.nih.gov**) are currently collecting self-reported data, data recorded by mobile devices or other sensors, EMRs, biospecimens, and data recorded by medical devices from a very large sample (>1 million individuals) to discover paths toward delivering precision medicine (89, 90).

FUTURE APPLICATIONS OF WEARABLE MONITORS IN HEALTH AND FITNESS

Over the last 20 years, wearable monitors have become ubiquitous in Western society, and developers are constantly producing novel ways to use these devices in health and fitness. Recently, the Centers for Medicare and Medicaid Services issued guidance to enable reimbursement to healthcare providers for certain remote patient monitoring and telehealth services (91).

Although the applications of monitoring and intervening via mHealth platforms are showing promise and will surely change the landscape of medicine and science in sports and exercise in the future, research in wearable monitoring is trending toward using them as tools of precision medicine. Future studies will discover algorithms for how data from these monitors may be predictive of a person's molecular state. Lim et al. (92) studied 233 normal volunteers for relationships between biomarkers taken from wearable monitors and CVD risk. Resting HR measured by wearable monitors was shown to have strong associations to CVD risk factors and was comparable to HR measured clinically. It was shown that several steps measured by wearable monitors were negatively correlated to markers of cardiac disease. The upper quartile of PAL was predictive of exercise-induced (physiological) cardiac remodeling and the identification of sphingolipid species, which are associated with physical activity and insulin resistance, as well as other diseases (93). Furthermore, the authors used a combination of metrics from wearable monitors to stratify the cohort into behavioral clusters with distinct characteristics, which could be useful in further research into the relationships between an ever-growing number of biomarkers available from wearable monitors and health status. These would be useful for early detection of changes in an individual's personal cardiovascular and metabolic disease (CVMD) risk profile, potentially resulting in more timely detection and intervention of CVMDs. Furthermore, there is an ever-increasing amount of biomarker data related to cardiovascular illness available to integrate into mHealth platforms, such as data from an ankle swelling sensor to remotely monitor edema (94); a toilet seat cover that monitors blood pressure, stroke volume, and blood oxygenation (95); and several devices for the measurement of pulse wave velocity (96). All of these novel tools may be integrated in the future into a smart medical home (**Figure 2**) that could potentially provide automated notification to a healthcare team, including the exact location of the patient in case of a medical emergency (97).

Remote monitoring systems will need to translate into programs that can show clinical impacts on patient care and merit reimbursement. Leaders here include Oschner Health System, as mentioned above, as well as Livongo and Omada Health (**https://www.omadahealth.com**), who, after first having transformed the diabetes prevention program into a digital health program, now offer solutions in weight loss and the cardiovascular space (98, 99). Importantly, these and other mHealth programs need to be evaluated thoroughly before they can be translated and eventually applied in a preventive or clinical population environment. However, the future of mHealth in an environment of precision medicine may include combining a large number of biomarkers from wearable monitors with the ability to stratify populations into risk categories. This would allow for more precise interventions based on these biomarkers during early disease.

As with all new technologies, issues related to data quality, standardization of methods and output, protection of personal health information, and cost will need to be addressed. Specifically, it is very difficult to assess wearable monitors and create standards in an environment where the technology is advancing faster than the community at large can validate them.

To address the need for standards and regulation of mHealth data, the European Union has created the General Data Protection Regulation (GDPR), which mandates that wearable users be made aware of what data are being accessed and of any transfer of personal data to other apps or entities (100). GDPR implements restrictions on the amount of data collected, the accessibility and necessity of data required, the level of processing, and the storage times. Under GDPR, a data privacy impact assessment (DPIA) is required for enterprise adoption, which would allow for the sharing of data via cloud computing. The DPIA is a process to help identify and minimize the data protection risks pertaining to the use of wearables (100).

Within the United States, the FDA normally does not regulate low-risk products that promote a healthy lifestyle including fitness bands and smartwatches (101). It is important to note a

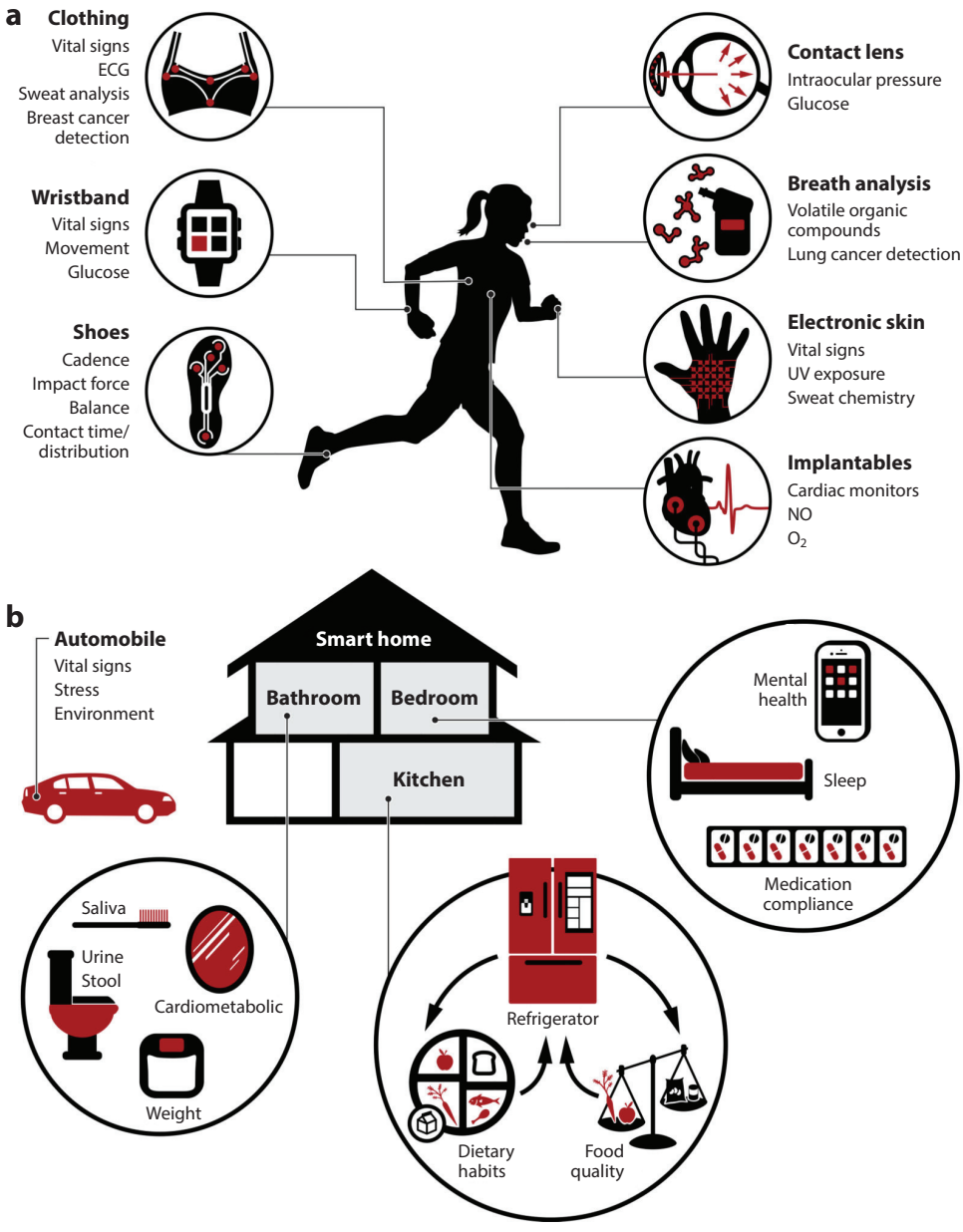

Figure 2

A pictorial representation of wearable (*a*) and home-based (*b*) devices that can measure physiological, behavioral, and environmental health data. Abbreviation: ECG, electrocardiogram. Figure adapted with permission from Reference 109; copyright 2018 by the authors, some rights reserved; exclusive licensee American Association for the Advancement of Science.

difference in the FDA's regulations. The most advanced regulatory status is FDA approval, which is done only for class III products—technologies that might have higher risk but also higher benefits. For example, AliveCor's Kardia and QardioCore, both class III devices, have been granted approval by the FDA, while Apple Watch, a class II product, has only been granted FDA clearance. This distinction of different classes represents a move forward by the FDA to provide regulatory oversight suitable for different tiers of devices. To address security and privacy concerns for data collected through wearable devices, service providers partnering with wearable entities must adhere to HIPAA and sign business associate contracts (102).

As mHealth data interoperability becomes increasingly important for providers, developers, and patients, attention to data output standardization has become a pressing concern. Although organizations such as the IEEE (Institute of Electrical and Electronics Engineers) and Open mHealth developed schema-based standards in the early 2000s, adoption has been slow (103, 104); experts agree that quality assurance approaches for data output have not yet been universally adopted by the community (105). Reasons for the absence of widespread quality assurance guidelines may include a lack of digital health literacy, challenges of wearable accuracy, difficulty in data interpretation, and difficulties of data integration with current EMR systems (105). The Fast Healthcare Interoperability Resource (FHIR) is a data standard developed by Health Level Seven International to address the difficulties of data standardization with EMRs (106). FHIR consists of protocols for joining disparate systems together with the goal of seamless, on-demand information exchange and interoperability for the healthcare system. Although FHIR is a relatively new standard, it has enjoyed substantial early uptake, and as the complications of transparency and data sharing issues are currently being standardized and addressed, the benefits of having health information quickly and easily accessible to users and healthcare providers seem worth the costs of establishing new methods to overcome some of these challenges. Projects are also underway to support Open mHealth schemas within an FHIR environment (107, 108). Lastly, some of the challenges involved in patient-generated health related to digital health literacy, wearable accuracy, difficulty in data interpretation, and lack of PGHD integration with EMR systems must be considered in the development of guidelines for the collection and use of PGHD (105).

CONCLUSION/PERSPECTIVE

The use of wearable monitors has been limited to the collection of data on a limited number of metrics, largely by the scientific community for research purposes. As technology has improved and the consumer market has been inundated with a multitude of monitors, a shift has occurred in which individuals always have access to a large amount of health and health behavior data. As with other precision medicine tools (e.g., genetic testing), the amount of data available to consumers is greater than users' ability to interpret that data. Efforts such as the device validation datahub (**https://precision.stanford.edu**) that are designed to standardize the validation of wearable monitors are starting to create an environment in which clinicians and researchers may apply these devices to mHealth platforms to more precisely guide individuals in their health and fitness goals. In the future, wearable monitors of cardiovascular health will likely play a large role in the prevention of CVD and mortality.

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LITERATURE CITED

1. Benjamin EJ, Muntner P, Bittencourt MS. 2019. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation* 139(10):e56–528
2. Loprinzi PD. 2018. Estimated cardiorespiratory fitness assessment as a patient vital sign. *Mayo Clin. Proc.* 93(7):821–23
3. Ross R, Blair SN, Arena R, Church TS, Després J-P, et al. 2016. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. *Circulation* 134(24):e653–99
4. Ong MEH, Perkins GD, Cariou A. 2018. Out-of-hospital cardiac arrest: prehospital management. *Lancet* 391(10124):980–88
5. Larsen MP, Eisenberg MS, Cummins RO, Hallstrom AP. 1993. Predicting survival from out-of-hospital cardiac arrest: a graphic model. *Ann. Emerg. Med.* 22(11):1652–58
6. Stokes NA, Scapigliati A, Trammell AR, Parish DC. 2012. The effect of the AED and AED programs on survival of individuals, groups and populations. *Prehosp. Disaster Med.* 27(5):419–24
7. Hickey AM, Freedson PS. 2016. Utility of consumer physical activity trackers as an intervention tool in cardiovascular disease prevention and treatment. *Prog. Cardiovasc. Dis.* 58(6):613–19
8. Free C, Phillips G, Watson L, Galli L, Felix L, et al. 2013. The effectiveness of mobile-health technologies to improve health care service delivery processes: a systematic review and meta-analysis. *PLOS Med.* 10(1):e1001363
9. Pfaeffli Dale L, Dobson R, Whittaker R, Maddison R. 2016. The effectiveness of mobile-health behaviour change interventions for cardiovascular disease self-management: a systematic review. *Eur. J. Prev. Cardiol.* 23(8):801–17
10. Supervía M, Medina-Inojosa JR, Yeung C, Lopez-Jimenez F, Squires RW, et al. 2017. Cardiac rehabilitation for women: a systematic review of barriers and solutions. *Mayo Clin. Proc.* 92(4):565–77
11. Sun EY, Jadotte YT, Halperin W. 2017. Disparities in cardiac rehabilitation participation in the United States: a systematic review and meta-analysis. *J. Cardiopulm. Rehabil. Prev.* 37(1):2–10
12. Castellanos LR, Viramontes O, Bains NK, Zepeda IA. 2018. Disparities in cardiac rehabilitation among individuals from racial and ethnic groups and rural communities—a systematic review. *J. Racial Ethn. Health Disparities* 6(1):1–11
13. Burke LE, Ma J, Azar KMJ, Bennett GG, Peterson ED, et al. 2015. Current science on consumer use of mobile health for cardiovascular disease prevention. *Circulation* 132(12):1157–213
14. Frederix I, Caiani EG, Dendale P, Anker S, Bax J, et al. 2019. ESC e-cardiology working group position paper: overcoming challenges in digital health implementation in cardiovascular medicine. *Eur. J. Prev. Cardiol.* 26(11):1166–77
15. Parmar P, Krishnamurthi R, Ikram MA, Hofman A, Mirza SS, et al. 2015. The Stroke Riskometer(TM) App: validation of a data collection tool and stroke risk predictor. *Int. J. Stroke* 10(2):231–44
16. Masterson Creber RM, Maurer MS, Reading M, Hiraldo G, Hickey KT, Iribarren S. 2016. Review and analysis of existing mobile phone apps to support heart failure symptom monitoring and self-care management using the mobile application rating scale (MARS). *JMIR mHealth uHealth* 4(2):e74
17. Lloyd-Jones DM, Huffman MD, Karmali KN, Sanghavi DM, Wright JS, et al. 2017. Estimating longitudinal risks and benefits from cardiovascular preventive therapies among Medicare patients: The Million Hearts longitudinal ASCVD risk assessment tool: a special report from the American Heart Association and American College of Cardiology. *Circulation* 135(13):e793–813

18. Zisko N, Skjerve KN, Tari AR, Sandbakk SB, Wisløff U, et al. 2017. Personal Activity Intelligence (PAI), sedentary behavior and cardiovascular risk factor clustering—the HUNT study. *Prog. Cardiovasc. Dis.* 60(1):89–95
19. Bassett DR Jr., Toth LP, LaMunion SR, Crouter SE. 2017. Step counting: a review of measurement considerations and health-related applications. *Sports Med*. 47(7):1303–15
20. Yang C-C, Hsu Y-L. 2010. A review of accelerometry-based wearable motion detectors for physical activity monitoring. *Sensors* 10(8):7772–88
21. Burke E. 1998. *Precision Heart Rate Training*. Champaign, IL: Human Kinetics
22. Howley ET. 1998. Precision heart rate training. *Med. Sci. Sports Exerc.* 30(12):1751–52
23. Chen KY, Bassett DR Jr. 2005. The technology of accelerometry-based activity monitors: current and future. *Med. Sci. Sports Exerc.* 37(11):S490–500
24. Plasqui G, Westerterp KR. 2007. Physical activity assessment with accelerometers: an evaluation against doubly labeled water. *Obesity* 15(10):2371–79
25. Morris JRW. 1973. Accelerometry—a technique for the measurement of human body movements. *J. Biomech.* 6(6):792–32
26. Freedson P, Bowles HR, Troiano R, Haskell W. 2012. Assessment of physical activity using wearable monitors. *Med. Sci. Sports Exerc.* 44:S5–12
27. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NAM 3rd, Freedman RA, et al. 2008. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities. *J. Am. Coll. Cardiol.* 51(21):e350–408
28. Health Quality Ontario. 2018. Remote monitoring of implantable cardioverter-defibrillators, cardiac resynchronization therapy and permanent pacemakers: a health technology assessment. *Ont. Health Technol. Assess. Ser.* 18(7):1–199
29. Pantelopoulos A, Bourbakis NG. 2010. A survey on wearable sensor-based systems for health monitoring and prognosis. *IEEE Trans. Syst. Man Cybern. C* 40(1):1–12
30. Bansal A, Joshi R. 2018. Portable out-of-hospital electrocardiography: a review of current technologies. *J. Arrhythm.* 34(2):129–38
31. Challoner AV, Ramsay CA. 1974. A photoelectric plethysmograph for the measurement of cutaneous blood flow. *Phys. Med. Biol.* 19(3):317–28
32. Elgendi M. 2012. On the analysis of fingertip photoplethysmogram signals. *Curr. Cardiol. Rev.* 8(1):14–25
33. Wang R, Blackburn G, Desai M, Phelan D, Gillinov L, et al. 2017. Accuracy of wrist-worn heart rate monitors. *JAMA Cardiol.* 2(1):104–6
34. Majumder S, Mondal T, Deen MJ. 2017. Wearable sensors for remote health monitoring. *Sensors* 17(1):130
35. Shcherbina A, Mattsson CM, Waggott D, Salisbury H, Christle JW, et al. 2017. Accuracy in wrist-worn, sensor-based measurements of heart rate and energy expenditure in a diverse cohort. *J. Pers. Med.* 7(2):3
36. Speier W, Dzubur E, Zide M, Shufelt C, Joung S, et al. 2018. Evaluating utility and compliance in a patient-based eHealth study using continuous-time heart rate and activity trackers. *J. Am. Med. Inform. Assoc.* 25(10):1386–91
37. Lamkin P. 2017. Wearable tech market to double by 2021. *Forbes*, June 22. **https://www.forbes.com/sites/paullamkin/2017/06/22/wearable-tech-market-to-double-by-2021/#2369480fd8f3**
38. Pevnick JM, Birkeland K, Zimmer R, Elad Y, Kedan I. 2018. Wearable technology for cardiology: an update and framework for the future. *Trends Cardiovasc. Med.* 28(2):144–50
39. World Health Organ. 2011. *mHealth: New Horizons for Health Through Mobile Technologies*. Geneva: World Health Organ.
40. Ackerman MJ. 2015. M-Health: evolution or revolution? *J. Med. Pract. Manag.* 30(4):292–93
41. Kurtzman GW, Day SC, Small DS, Lynch M, Zhu J, et al. 2018. Social incentives and gamification to promote weight loss: the LOSE IT randomized, controlled trial. *J. Gen. Intern. Med.* 33(10):1669–75
42. Kumar RB, Goren ND, Stark DE, Wall DP, Longhurst CA. 2016. Automated integration of continuous glucose monitor data in the electronic health record using consumer technology. *J. Am. Med. Inform. Assoc.* 23(3):532–37

43. Milani RV, Lavie CJ, Bober RM, Milani AR, Ventura HO. 2017. Improving hypertension control and patient engagement using digital tools. *Am. J. Med.* 130(1):14–20
44. Milani RV, Bober RM, Lavie CJ. 2016. The role of technology in chronic disease care. *Prog. Cardiovasc. Dis.* 58(6):579–83
45. Tai-Seale M, Downing NL, Jones VG, Milani RV, Zhao B, et al. 2019. Technology-enabled consumer engagement: promising practices at four health care delivery organizations. *Health Aff.* 38(3):383–90
46. Wilbanks J. 2018. Design issues in e-consent. *J. Law Med. Ethics* 46(1):110–18
47. Zens M, Grotejohann B, Tassoni A, Duttenhoefer F, Südkamp NP, Niemeyer P. 2017. Development of a modular research platform to create medical observational studies for mobile devices. *JMIR Res. Protoc.* 6(5):e99
48. Ades PA, Keteyian SJ, Wright JS, Hamm LF, Lui K, et al. 2017. Increasing cardiac rehabilitation participation from 20% to 70%: a road map from the Million Hearts Cardiac Rehabilitation Collaborative. *Mayo Clin. Proc.* 92(2):234–42
49. Anderson L, Thompson DR, Oldridge N, Zwisler A-D, Rees K, et al. 2016. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst. Rev.* 2016(1):CD001800
50. Christle JW, Schlumberger A, Haller B, Gloeckl R, Halle M, Pressler A. 2017. Individualized versus group exercise in improving quality of life and physical activity in patients with cardiac disease and low exercise capacity: results from the DOPPELHERZ trial. *Disabil. Rehabil.* 39(25):2566–71
51. Christle JW, Schlumberger A, Zelger O, Haller B, Beckers P, et al. 2018. Effect of individualized combined exercise versus group-based maintenance exercise in patients with heart disease and reduced exercise capacity: the DOPPELHERZ trial. *J. Cardiopulm. Rehabil. Prev.* 38(1):31–37
52. Sun EY, Jadotte YT, Halperin W. 2017. Disparities in cardiac rehabilitation participation in the United States: a systematic review and meta-analysis. *J. Cardiopulm. Rehabil. Prev.* 37(1):2–10
53. Rawstorn JC, Gant N, Direito A, Beckmann C, Maddison R. 2016. Telehealth exercise-based cardiac rehabilitation: a systematic review and meta-analysis. *Heart* 102(15):1183–92
54. Lounsbury P, Elokda AS, Gylten D, Arena R, Clarke W, Gordon EEI. 2015. Text-messaging program improves outcomes in outpatient cardiovascular rehabilitation. *Int. J. Cardiol. Heart Vasc.* 7:170–75
55. Dansky KH, Vasey J, Bowles K. 2008. Impact of telehealth on clinical outcomes in patients with heart failure. *Clin. Nurs. Res.* 17(3):182–99
56. Green BB, Cook AJ, Ralston JD, Fishman PA, Catz SL, et al. 2008. Effectiveness of home blood pressure monitoring, Web communication, and pharmacist care on hypertension control: a randomized controlled trial. *JAMA* 299(24):2857–67
57. Widmer RJ, Allison TG, Lerman LO, Lerman A. 2015. Digital health intervention as an adjunct to cardiac rehabilitation reduces cardiovascular risk factors and rehospitalizations. *J. Cardiovasc. Transl. Res.* 8(5):283–92
58. Ong MK, Romano PS, Edgington S, Aronow HU, Auerbach AD, et al. 2016. Effectiveness of remote patient monitoring after discharge of hospitalized patients with heart failure: the better effectiveness after transition–heart failure (BEAT-HF) randomized clinical trial. *JAMA Intern. Med.* 176(3):310–18
59. Pedone C, Rossi FF, Cecere A, Costanzo L, Antonelli Incalzi R. 2015. Efficacy of a physician-led multiparametric telemonitoring system in very old adults with heart failure. *J. Am. Geriatr. Soc.* 63(6):1175–80
60. Steventon A, Bardsley M, Billings J, Dixon J, Doll H, et al. 2013. Effect of telecare on use of health and social care services: findings from the Whole Systems Demonstrator cluster randomised trial. *Age Ageing* 42(4):501–8
61. Gornall J. 2012. Does telemedicine deserve the green light? *BMJ* 345:e4622
62. Cakmak AS, Reinertsen E, Taylor HA, Shah AJ, Clifford GD. 2018. Personalized heart failure severity estimates using passive smartphone data. In *Proceedings of the 2018 IEEE International Conference on Big Data*, ed. N Abe, H Liu, C Pu, X Hu, N Ahmed et al., pp. 1569–74. New York: IEEE
63. Bennett MK, Shao M, Gorodeski EZ. 2017. Home monitoring of heart failure patients at risk for hospital readmission using a novel under-the-mattress piezoelectric sensor: a preliminary single centre experience. *J. Telemed. Telecare* 23(1):60–67

64. Tison GH, Sanchez JM, Ballinger B, Singh A, Olgin JE, et al. 2018. Passive detection of atrial fibrillation using a commercially available smartwatch. *JAMA Cardiol.* 3(5):409–16
65. Barrett PM, Komatireddy R, Haaser S, Topol S, Sheard J, et al. 2014. Comparison of 24-hour Holter monitoring with 14-day novel adhesive patch electrocardiographic monitoring. *Am. J. Med.* 127(1):95.e11–17
66. Vandenberk T, Pelckmans C, Van Schelvergem G, Van Der Auwera J, Thijs I, et al. 2017. Beat-to-beat validation of PPG as a tool to detect regular and irregular heartbeats. *Eur. Heart J.* 38:438
67. Vandenberk T, Stans J, Mortelmans C, Van Haelst R, Van Schelvergem G, et al. 2017. Clinical validation of heart rate apps: mixed-methods evaluation study. *JMIR mHealth uHealth* 5(8):e129
68. Rahman T, Amirfar VA. 2016. AliveCor Mobile ECG: a smartphone with heart. *Pharm. Today* 22(3):56
69. Lau JK, Lowres N, Neubeck L, Brieger DB, Sy RW, et al. 2013. iPhone ECG application for community screening to detect silent atrial fibrillation: a novel technology to prevent stroke. *Int. J. Cardiol.* 165(1):193–94
70. Hickey KT, Hauser NR, Valente LE, Riga TC, Frulla AP, et al. 2016. A single-center randomized, controlled trial investigating the efficacy of a mHealth ECG technology intervention to improve the detection of atrial fibrillation: the iHEART study protocol. *BMC Cardiovasc. Disord.* 16:152
71. Chan P-H, Wong C-K, Poh YC, Pun L, Leung WW-C, et al. 2016. Diagnostic performance of a smartphone-based photoplethysmographic application for atrial fibrillation screening in a primary care setting. *J. Am. Heart Assoc.* 5(7):e003428
72. White RD, Flaker G. 2017. Smartphone-based arrhythmia detection: Should we encourage patients to use the ECG in their pocket? *J. Atr. Fibrillation* 9(6):1605
73. Koole MAC, Kauw D, Winter MM, Dohmen DAJ, Tulevski II, et al. 2019. First real-world experience with mobile health telemonitoring in adult patients with congenital heart disease. *Neth. Heart J.* 27(1):30–37
74. Koshy AN, Sajeev JK, Nerlekar N, Brown AJ, Rajakariar K, et al. 2018. Smart watches for heart rate assessment in atrial arrhythmias. *Int. J. Cardiol.* 266:124–27
75. Rozen G, Vaid J, Hosseini SM, Kaadan MI, Rafael A, et al. 2018. Diagnostic accuracy of a novel mobile phone application for the detection and monitoring of atrial fibrillation. *Am. J. Cardiol.* 121(10):1187–91
76. Perez MV, Mahaffey KW, Hedlin H, Rumsfeld JS, Garcia A, et al. 2019. Large-scale assessment of a smartwatch to identify atrial fibrillation. *N. Engl. J. Med.* 381(20):1909–17
77. Doshi AM, Ebert RM, Grinnell JD, Saxon LA. 2019. Consumer-facing diagnostic sensors in a patient with an implantable cardioverter-defibrillator. *J. Innov. Cardiac Rhythm Manag.* 10(9):3822–25
78. Overbeek DL, Hogikyan EM, Davis M, McGillicuddy DC. 2019. A unique case of bradycardia recognized by wearable technology as first presentation of complete heart block. *Am. J. Emerg. Med.* 37(10):1989.e5–7
79. Pektok E, Demirozu ZT, Arat N, Yildiz O, Oklu E, et al. 2013. Remote monitoring of left ventricular assist device parameters after HeartAssist-5 implantation. *Artif. Organs* 37(9):820–25
80. Duquenoy P, Mekawie NM, Springett M. 2013. Patients, trust and ethics in information privacy in eHealth. In *eHealth: Legal, Ethical and Governance Challenges*, ed. C George, D Whitehouse, P Duquenoy, pp. 275–98. Berlin: Springer
81. Fisk MJ, Rudel D. 2013. Telehealth and service delivery in the home: care, support and the importance of user autonomy. In *eHealth: Legal, Ethical and Governance Challenges*, ed. C George, D Whitehouse, P Duquenoy, pp. 211–25. Berlin: Springer
82. Ionescu-Dima C. 2013. Legal challenges regarding telemedicine services in the European Union. In *eHealth: Legal, Ethical and Governance Challenges*, ed. C George, D Whitehouse, P Duquenoy, pp. 107–34. Berlin: Springer
83. Reiss N, Schmidt T, Boeckelmann M, Schulte-Eistrup S, Hoffmann J-D, et al. 2018. Telemonitoring of left-ventricular assist device patients—current status and future challenges. *J. Thorac. Dis.* 10(Suppl. 15):S1794–801
84. Hohmann S, Veltmann C, Duncker D, König T, Berliner D, et al. 2019. Initial experience with telemonitoring in left ventricular assist device patients. *J. Thorac. Dis.* 11(Suppl. 6):S853–63

85. Rali AS, Vuddanda V, Masoomi R, Shah Z, Gupta B, et al. 2017. Trends in LVADs in the geriatric population: demographics for 2003–2014. *J. Cardiac Fail.* 23(8):s17
86. McConnell MV, Shcherbina A, Pavlovic A, Homburger JR, Goldfeder RL, et al. 2017. Feasibility of obtaining measures of lifestyle from a smartphone app: The MyHeart Counts cardiovascular health study. *JAMA Cardiol.* 2(1):67–76
87. Hershman SG, Bot BM, Shcherbina A, Doerr M, Moayedi Y, et al. 2019. Physical activity, sleep and cardiovascular health data for 50,000 individuals from the MyHeart Counts Study. *Sci. Data* 6(1):24
88. Shcherbina A, Hershman SG, Lazzeroni L, King AC, O'Sullivan JW, et al. 2019. The effect of digital physical activity interventions on daily step count: a randomised controlled crossover substudy of the MyHeart Counts Cardiovascular Health Study. *Lancet Digit. Health* 1(7):e344–52
89. Califf RM. 2018. Biomarker definitions and their applications. *Exp. Biol. Med.* 243(3):213–21
90. Khoury MJ, Bowen MS, Clyne M, Dotson WD, Gwinn ML, et al. 2018. From public health genomics to precision public health: a 20-year journey. *Genet. Med.* 20(6):574–82
91. Cent. Medicare Medicaid Serv. 2018. Medicare program; revisions to payment policies under the physician fee schedule and other revisions to part B for CY 2019; Medicare Shared Savings Program requirements; Quality Payment Program; Medicaid Promoting Interoperability Program; Quality Payment Program—extreme and uncontrollable circumstance policy for the 2019 MIPS payment year; provisions from the Medicare Shared Savings Program—Accountable Care Organizations—Pathways to Success; and expanding the use of telehealth services for the treatment of opioid use disorder under the Substance Use-Disorder Prevention that Promotes Opioid Recovery And Treatment (SUPPORT) for Patients and Communities Act. *Fed. Reg.* 83:59452–60303
92. Lim WK, Davila S, Teo JX, Yang C, Pua CJ, et al. 2018. Beyond fitness tracking: the use of consumer-grade wearable data from normal volunteers in cardiovascular and lipidomics research. *PLOS Biol.* 16(2):e2004285
93. Hannun YA, Obeid LM. 2018. Sphingolipids and their metabolism in physiology and disease. *Nat. Rev. Mol. Cell Biol.* 19(3):175–91
94. Kim S, Iravantchi Y, Gajos K. 2019. SwellFit: developing a wearable sensor for monitoring peripheral edema. In *Proceedings of the 52nd Hawaii International Conference on System Sciences*, pp. 3868–76. Manoa, HI: ScholarSpace
95. Conn NJ, Schwarz KQ, Borkholder DA. 2019. In-home cardiovascular monitoring system for heart failure: comparative study. *JMIR mHealth uHealth* 7(1):e12419
96. Modena BD, Bellahsen O, Nikzad N, Chieh A, Parikh N, et al. 2018. Advanced and accurate mobile health tracking devices record new cardiac vital signs. *Hypertension* 72(2):503–10
97. Muse ED, Barrett PM, Steinhubl SR, Topol EJ. 2017. Towards a smart medical home. *Lancet* 389(10067):358
98. Sepah SC, Jiang L, Peters AL. 2015. Long-term outcomes of a Web-based diabetes prevention program: 2-year results of a single-arm longitudinal study. *J. Med. Internet Res.* 17(4):e92
99. Su W, Chen F, Dall TM, Iacobucci W, Perreault L. 2016. Return on investment for digital behavioral counseling in patients with prediabetes and cardiovascular disease. *Prev. Chronic Dis.* 13:150357
100. Eur. Union. 2016. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation). *Off. J. Eur. Union* 119:1–88. **https://eur-lex.europa.eu/eli/reg/2016/679/oj**
101. Cent. Devices Radiol. Health. 2019. *General wellness: policy for low risk devices: guidance for industry and Food and Drug Administration staff*. Guidance Doc. FDA-2014-N-1039, US Food Drug Admin., Rockville, MD. **http://www.fda.gov/regulatory-information/search-fda-guidance-documents/general-wellness-policy-low-risk-devices**
102. Office Civ. Rights. 2013. *Summary of the HIPAA privacy rule*. Media Resour., Off. Civ. Rights, Washington, DC. **https://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/index.html**

103. Estrin D, Sim I. 2010. Health care delivery. Open mHealth architecture: an engine for health care innovation. *Science* 330(6005):759–60
104. IEEE 11073 Stand. Comm. 2009. *IEEE/ISO international standard—health informatics—personal health device communication—part 10441: device specialization—cardiovascular fitness and activity monitor*. Device Commun. Stand., IEEE Stand. Assoc. **https://standards.ieee.org/standard/11073-10441-2008.html**
105. Abdolkhani R, Gray K, Borda A, DeSouza R. 2019. Patient-generated health data management and quality challenges in remote patient monitoring. *JAMIA Open* 2(4):471–78
106. HL7 (Health Level Seven Int.). 2011. *Overview: FHIR v4.0.1*. Media Resour., HL7, Ann Arbor, MI. **https://www.hl7.org/fhir/overview.html**
107. Eapen BR, Archer N, Sartipi K, Yuan Y. 2019. Drishti: a sense-plan-act extension to open mHealth framework using FHIR. In *Proceedings of the 2019 IEEE/ACM 1st International Workshop on Software Engineering for Healthcare (SEH)*, pp. 49–52. New York: IEEE
108. 2019. OMH-on-FHIR. Github. **https://github.com/gt-health/OMH-on-FHIR**
109. Gambhir SS, Ge TJ, Vermesh O, Spitler R. 2018. Toward achieving precision health. *Sci. Transl. Med.* 10(430):eaao3612