Integration of novel monitoring devices with machine learning technology for scalable cardiovascular management

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Abstract | Ambulatory monitoring is increasingly important for cardiovascular care but is often limited by the unpredictability of cardiovascular events, the intermittent nature of ambulatory monitors and the variable clinical significance of recorded data in patients. Technological advances in computing have led to the introduction of novel physiological biosignals that can increase the frequency at which abnormalities in cardiovascular parameters can be detected, making expert-level, automated diagnosis a reality. However, use of these biosignals for diagnosis also raises numerous concerns related to accuracy and actionability within clinical guidelines, in addition to medico-legal and ethical issues. Analytical methods such as machine learning can potentially increase the accuracy and improve the actionability of device-based diagnoses. Coupled with interoperability of data to widen access to all stakeholders, seamless connectivity (an internet of things) and maintenance of anonymity, this approach could ultimately facilitate near-real-time diagnosis and therapy. These tools are increasingly recognized by regulatory agencies and professional medical societies, but several technical and ethical issues remain. In this Review, we describe the current state of cardiovascular monitoring along the continuum from biosignal acquisition to the identification of novel biosensors and the development of analytical techniques and ultimately to regulatory and ethical issues. Furthermore, we outline new paradigms for cardiovascular monitoring.

Patients with cardiovascular conditions can have variable clinical presentations ranging from no symptoms to haemodynamic collapse, from hypertensive urgency to hypotension and from silent coronary ischaemia to acute coronary syndrome, as well as decompensated heart failure (HF), stroke or sudden death. This diversity in clinical presentation of cardiovascular disorders poses a major challenge for disease monitoring. Although clinicians use a variety of implanted, ambulatory and consumer wearable technologies for disease monitoring, the devices that are best suited to individual patients are difficult to establish. Indeed, optimal monitoring strategies have yet to be developed for some applications.

HF can worsen progressively over days or weeks, but current telemedicine systems might not be sufficient to detect acute exacerbations in HF or to prevent rehospitalization[1,2]. Conversely, arrhythmias can often occur suddenly or intermittently and might require immediate intervention[3,4]. Ambulatory rhythm-monitoring devices that allow only sporadic interpretation of data might be appropriate for benign events but not for life-threatening arrhythmias. This misalignment between clinical need and current monitoring technologies is also illustrated by the lack of robust strategies for the detection of impending coronary syndromes, hypertensive emergencies, hypotensive events or stroke in high-risk patients with atrial fibrillation (AF).

Advances in cardiovascular monitoring technologies, such as the use of ubiquitous mobile devices and the development of novel portable sensors with seamless wireless connectivity and machine learning algorithms that can provide specialist-level diagnosis in near real time, have the potential for a more personalized care. Devices have been developed to assess haemodynamics, which can detect potential signs of worsening HF[2]. Furthermore, continuous electrocardiogram (ECG) recordings have been used to redefine phenotypes for AF[4] and ventricular arrhythmias[3], and can predict success of antiarrhythmic therapy[5]. Wearable activity trackers and smartwatches can measure physiological indices such as heart rate, breathing patterns and cardiometabolic activity[6], and can even detect AF[7]. Furthermore, smartphone applications have been successful in shortening the time to first response for sudden cardiac

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Key points

- Advances in the use of cardiovascular monitoring technologies, such as the development of novel portable sensors and machine learning algorithms that can provide near-real-time diagnosis, have the potential to provide personalized care.
- Wearable sensor technologies can detect numerous biosignals, such as cardiac output, blood-pressure levels and heart rhythm, and can integrate multiple modalities.
- The use of novel biosignals for diagnosis raises concerns regarding accuracy and actionability within clinical guidelines, in addition to medical, legal and ethical issues.
- Machine learning-based interpretation of biosensor data can facilitate rapid evaluation of the haemodynamic consequences of heart failure or arrhythmias, but is limited by the presence of noise and training data that might not be representative of the real-world clinical setting.
- The use of data derived from cardiovascular monitoring devices is associated with numerous challenges, such as data security, accessibility and ownership, in addition to other ethical and regulatory concerns.

arrest[8]. This confluence of novel technologies has also attracted much public interest and the promise to expand applications for cardiovascular monitoring.

In this Review, we describe the latest advances in cardiovascular monitoring technology, focusing first on biosignal acquisition and analytical techniques that enable accurate diagnosis, triage and management (FIG. 1). We discuss monitoring in the context of likely future directions in cardiovascular care and identify numerous technical and clinical obstacles, issues regarding data security and privacy, and ethical dilemmas and regulatory challenges that must be overcome before integrated and scalable cardiovascular monitoring tools can be developed.

Biosignal acquisition

Biosignals, physiological signals that can be continuously measured and monitored to provide information on electrical, chemical and mechanical activity, are the foundations of assessment of health and disease, and have been used to develop personalized physiological 'portraits' of individuals. Numerous current and emerging wearable technologies can measure multiple physiological biosignals such as pulse, cardiac output, blood-pressure levels, heart rhythm, respiratory rate, electrolyte levels, sympathetic nerve activity, galvanic skin resistance and thoracic and lower-extremity oedema (FIG. 2). Some devices can acquire multiple biosignals simultaneously, which can provide inputs to powerful integrated monitors and diagnostic systems. In developing scalable monitoring technology, the short-term goal is to implement guideline-driven care, whereas a longer-term goal is to expand the scope of care by tracking physiological variables continuously in each individual.

TABLE 1 summarizes the use of wearable sensor technologies to detect biosignals. Some sensor technologies can now integrate multiple modalities, such as chest patches that monitor heart rate, heart rhythm, respiration rate and skin temperature[7,9]. Sensors are being developed to measure myocardial contractility and cardiac output (ballistocardiography), cardiac acoustic data (phonocardiography) and other indices[10]. We describe various biosensors in the following sections, with reference to their target biosignals and potential clinical applications.

Implanted intracardiac monitors

To date, more than three million people living in the USA have cardiac implantable electronic devices (CIEDs) such as pacemakers, defibrillators or left ventricular assist devices[11]. Many more patients have other non-CIEDs such as cochlear implants and nerve stimulators. CIEDs are the gold standard for cardiac rhythm detection, providing sensitive and specific measurements with little noise continuously over long time frames of several years. CIEDs are also highly effective prototypes for real-time automatic diagnosis and therapy. Indications for CIED use include pacing for bradyarrhythmias, and tachypacing and defibrillation for tachyarrhythmias. Additionally, most CIEDs also record intracardiac electrograms as a surrogate for ECGs. CIEDs that are prescribed for one indication might provide monitoring that confers clinical benefits for a separate indication, such as the monitoring of atrial arrhythmias by atrial leads in pacemakers or defibrillators, or the monitoring of atrial arrhythmias by far-field atrial electrograms from ventricular leads in some pacemakers or implantable cardioverter–defibrillators (ICDs)[12].

CIEDs are well suited to monitor symptoms of HF. In patients with an ICD or a pacemaker, CIEDs can provide indices of heart rate variability and pulmonary impedance, which can track HF and prove an alert for possible decompensation[13]. Diminished heart rate variability (<100 ms) has been shown to indicate increased sympathetic and decreased vagal modulation, and is associated with increased risk of death, worsening HF and malignant ventricular arrhythmias[14]. A decline in electrical impedance of the thorax is indicative of pulmonary congestion[15]. Another promising biosignal for the detection of HF is pulmonary artery pressure. COMPASS-HF[16] was the first randomized trial to investigate the efficacy of intracardiac pressure monitoring for HF management with the use of a right ventricular sensor (Chronicle, Medtronic) that measures estimated pulmonary artery diastolic pressure as a surrogate for pulmonary artery pressure. Notably, continuous haemodynamic monitoring did not significantly reduce the incidence of HF-related events compared with optimal medical management. The subsequent CHAMPION

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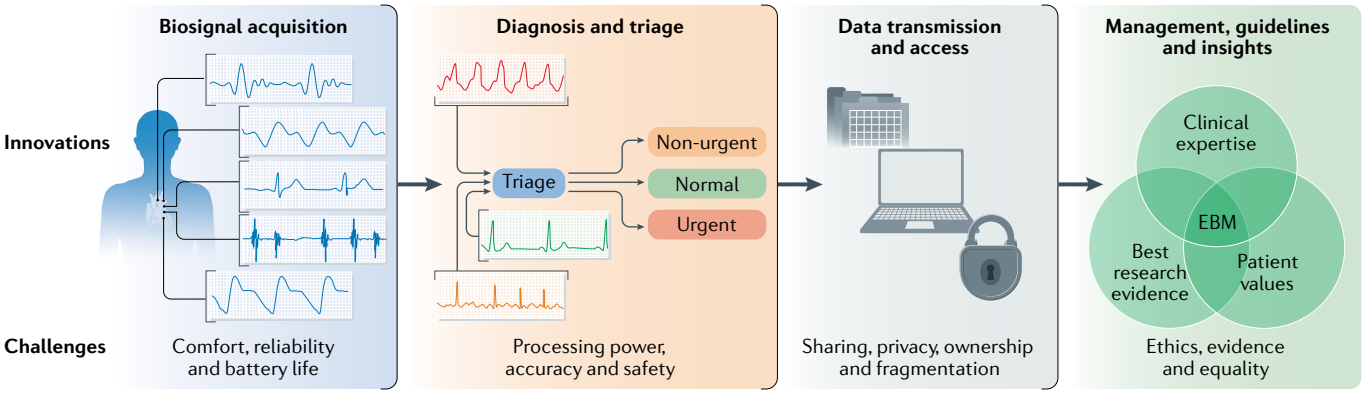

Fig. 1 | **Emerging paradigms for ambulatory monitoring.** Numerous innovations in biosignal acquisition, diagnosis and medical triage, and data access enable the curation of data as a dynamic resource that can ultimately be used to alter management guidelines and provide novel pathophysiological insights into cardiovascular diseases. However, the acquisition, processing and use of these innovative technologies is associated with various challenges. EBM, evidence-based medicine.

study[17] showed that monitoring pulmonary artery pressure using the CardioMEMS system (Abbott) significantly lowered the rate of repeated HF hospitalization and was associated with reduced costs compared with standard care. A 2019 meta-analysis involving mostly patients with HF with reduced ejection fraction found that pressure monitoring, but not impedance monitoring, was associated with a lower rate of hospital admission for HF[18]. Other forms of HF monitors in development integrate pulmonary artery pressure monitoring with vital sign monitoring (Cordella Heart Failure System, Endotronix), left atrial pressure monitoring and various wearable devices[19].

Additional CIED-based biosensors for cardiovascular monitoring are likely to emerge in the next 2–3 years. An implanted device that provides neurostimulation of the phrenic nerve has been shown to be effective in reducing episodes of central sleep apnoea[20]. Such novel CIEDs could, in principle, detect physiological markers that correlate with symptoms of AF or HF that frequently accompany sleep apnoea. Numerous leadless, extravascular devices currently under investigation can defibrillate[21] or pace the heart[22]. Future innovations might eliminate the need to extract the device for battery replacement by using external recharging systems or designs that can transduce energy from respiratory or cardiac motion[23].

ECG monitoring

The body surface ECG is a widely used biosignal in medically prescribed monitors and consumer devices (FIG. 2). Ambulatory ECG monitors typically consist of three or more chest electrodes connected to an external recorder or a fully contained patch monitor, and can record continuously for 1–14 days. Some devices have fewer leads, such as the Spider Flash (Datacard Group), which consist of two leads and can record for up to 6 min before and 3 min after detecting an event, and the CardioSTAT (Icentia), a single-lead ECG monitor that can provide continuous recordings. Data from such ECG monitors are uploaded to a central server either wirelessly or by direct device 'interrogation', interpreted using semiautomated algorithms and manually confirmed to generate reports and alerts. Some devices can provide near-real-time management options. The mobile cardiac outpatient telemetry (MCOT) system is an ambulatory ECG monitoring system that can transmit signals over a cellular network without activation by the patient and might increase diagnostic yield compared with other systems[24,25].

A major application for ECG sensors is to optimize the detection of AF[26]. AF is, in many ways, an ideal target for biosensors. Numerous ECG sensors focus on detecting rapid and irregularly irregular QRS complexes in AF, but other metrics of rapid and irregular atrial rate and irregular beat-to-beat waveforms might increase diagnostic specificity[27]. AF can also cause beat-to-beat changes in perfusion and haemodynamics that might allow detection from non-electrical biosignals.

Another major indication for ECG monitors is the detection of ST-segment shifts indicative of coronary ischaemia, which requires relatively noise-free ECGs and sophisticated detection algorithms. Machine learning technologies have been incorporated into wearable devices for the detection of ST-segment elevation with an accuracy of up to 97.4% (REF.[28]). In principle, coronary ischaemia monitoring could also use optical, electrochemical, mechanical or microRNA-based biosensors, but these applications have not yet been widely adopted. Limitations of ECG-based ambulatory monitoring include noise (particularly during physical activity), the typically limited monitoring duration of 1–2 weeks (which might be insufficient to detect infrequent events) and delays in generating reports and instigating appropriate actions[29].

Insertable or implantable loop recorders are minimally invasive devices that can provide long-term ECG monitoring for months or years and include the Reveal LINQ system (Medtronic), the Confirm Rx insertable cardiac monitor (Abbott) and the BioMonitor (Biotronik). The devices are inserted subcutaneously over the sternum or under the clavicle to mimic V leads and to optimize ECG recordings. Data are uploaded during device checks on a 3–6-monthly basis. The advantages of implantable loop recorders include the capacity for long-term monitoring and consistent ECG wave morphologies owing to a fixed spatial orientation. Paradoxically, such devices

are suboptimal for the diagnosis of arrhythmias of short durations (tens of seconds to minutes) and for classifying the type of atrial arrhythmia[30]. These limitations might be overcome with improvements in signal processing algorithms[31]. Furthermore, most implantable loop recorders cannot establish the haemodynamic significance of detected arrhythmias, although the Reveal LINQ system does include an accelerometer that measures patient activity. A modified Reveal LINQ device was used to capture ECG data, temperature, heart rate and other parameters in American black bears and detected low activity and extreme bradycardia during hibernation[32]. Lastly, delays in the reporting of urgent events measured by implanted devices might be worsened by longer recording durations between device checks, although some platforms (Reveal LINQ and Confirm Rx) allow home monitoring with programmable alerts.

Finally, numerous wearable ECG devices are available to the public. The Apple Watch (Apple) and KardiaMobile (Alivecor) are approved by the FDA for rhythm monitoring and have clinical-level accuracy for the detection of arrhythmias such as AF[33]. None of these devices provides continuous monitoring, although daily and nightly use for months might ultimately provide near-continuous recordings. However, at present, these devices require activation by the patient to record the ECG, and smartwatch pulse checks (via photoplethysmography (PPG)) occur only intermittently. Therefore, these monitors can miss paroxysmal arrhythmia events that are too short in duration or too catastrophic in nature to be captured by the patient and cannot measure arrhythmia burden. As wearable devices become increasingly flexible, stretchable and weightless, they can be comfortably worn continuously to provide uninterrupted ECG data[34].

At present, unclassifiable tracings are common among all ECG monitoring devices, which is likely to improve with technological advances[35]. Some systems have increased signal fidelity, such as the KardiaMobile six-lead device (Alivecor) or the CAM device (BardyDx), which might reduce noise and improve P-wave discernment[27]. Patients are increasingly opting for FDA-approved consumer devices, which increases the urgency to extend guidelines to adopt such technologies when appropriate[36].

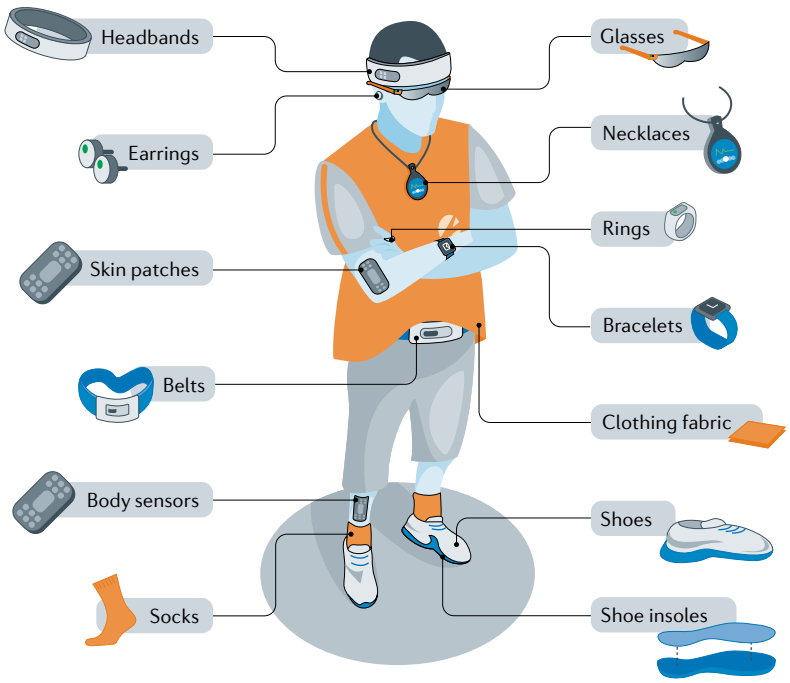

Fig. 2 | **Current and emerging wearable technologies.** Examples of emerging wearable technologies include mobile phones, body sensors (TempTraq, Blue Spark Technologies, USA), glasses (OrCam MyEye, OrCam Technologies, Israel), necklaces (toSense, USA), earrings (Joule, Ear-O-Smart, BioSensive Technologies, USA), headbands (SmartSleep, Philips, USA, and EPOC, Emotiv, USA), rings (Motiv Ring, Motiv, USA), bracelets (Bangle Activity Tracker, Kate Spade New York, USA), skin patches (BioStampRC, MC10, USA, VitalPatch, VitalConnect, USA, and BodyGuardian Heart, Preventice Solutions, USA), clothing fabric (Nanowear, USA, Hexoskin Smart Shirt, Hexoskin, Canada, and SmartSleep Snoring Relief Band, Philips, USA), belts (Smart Belt Pro, WELT Corp., South Korea, and LumiDiet, Double H, South Korea), socks (Sensoria Socks 2.0, Sensoria, USA, and Siren Diabetic Socks, Siren, USA), shoes (Nike Adapt, Nike, USA) and shoe insoles (Energysole, MEGAComfort, USA).

Photoplethysmography

PPG is an optical technique used to detect fluctuations in reflected light that can provide data on the cycle-by-cycle changes in cardiac haemodynamics[37]. PPG uses a light source, such as a light-emitting diode, to illuminate the face, fingertips or other accessible parts of the body. Early fitness trackers used this technology to estimate heart rate, but PPG-measured heart rate is associated with a low positive predictive value[38], particularly if patients are ambulatory[39] or exercising[40]. The WATCH-AF trial[41] was a prospective, case–control study that compared the diagnostic accuracy of a smartwatch-based algorithm using PPG signals with ECG data measured by cardiologists. The PPG algorithm had very high specificity and diagnostic accuracy, but was limited by a high dropout rate owing to insufficient signal quality. Although few comparison studies have been performed, PPG-based analysis of heart rate and rhythm might be less accurate than ECG-based assessment[42].

An emerging area for PPG-based sensors is for the monitoring of blood-pressure levels. PPG-based blood-pressure assessment requires the mapping of pulsatile peripheral waveforms to aortic pressure and uses algorithms that incorporate machine learning technologies[43,44]. However, the sensitivity and specificity of such a sensor in measuring blood-pressure levels in the general population have not yet been defined, and measurement variability might affect their accuracy[45]. PPG data can also be measured without body surface contact[46]. Video cameras can detect subtle fluctuations in facial perfusion with normal heartbeats to identify arrhythmias, including AF[47]. Once technical, workflow and regulatory challenges are overcome, this contactless approach could be used for health screening in a physician's office, in a nursing home or in public spaces. However, this approach also highlights societal and ethical issues related to patient privacy and confidentiality, and the physician's responsibility to inform and treat patients[48]. The infrastructure needed to inform a passer-by of an abnormality detected by contactless sensing technology is not yet available, and whether this protocol is appropriate given that consent for testing was

Table 1 | **Emerging sensor technologies for wearable cardiovascular devices**

Disease or indication	Biological measurement	Sensor type	Wearable device
Cardiac haemodynamics	Heart rate and blood pressure	Wireless sensors	Wireless sensors
	Blood pressure	Potential difference	Skin patch
		Pressure sensor	Wristband
		Optical sensor	Smartglasses
	Myocardial contractility	Ballisticardiography	Patch, wristbands, watches
	Cardiac output	Ballisticardiography	Chest patch, ear buds
Heart failure	Heart rate, rhythm analyses, respiration rate, skin temperature	ECG and accelerometer	Chest patch
	Exercise tolerance, 6-min walking distance	Seismocardiography	Chest patch
	Peripheral oedema	Two magnetic sensors and an electromagnet	Fabric socks
	Pulmonary rales	Acoustocardiography	Chest sensor
Cardiac arrhythmia	Heart rate and rhythm analyses	ECG	Sensor patch
		Electrical pulse	Pulse glasses
		Pulse oximeter	Fingertip pulse oximeter and earrings
		3D accelerometer	Shirt
		Gyroscope, accelerometer, camera	Smartglasses
		PPG sensor	Earpiece
		Special fibres	Chest strap
Acute coronary syndrome	Myocardial ischaemia	ECG and microcontroller board	Smartphone-based system
	Subclinical myocardial ischaemia	ECG	ECG patch
	Cardiac tissue hypoxia	Microfluidic chip	Watches, skin patch
	Blood chemistry (such as lactate levels)	Galvanic skin resistance and sweat sensors	Skin patch
Metabolic monitoring	Activity levels	Surface electromyography sensor	Smartsocks
	Electrolytes	Sweat sensor	Smartglasses
	Glucose and lactic acid	Sweat sensor	Skin patch
	Tissue chemistry (for example, lactate, glucose and pH levels)	Sweat sensor	Skin patch

ECG, electrocardiogram; PPG, photoplethysmogram.

not obtained and which stakeholders would be responsible for informing the individual and then ensuring adequate therapy and follow-up are unclear.

Nevertheless, major advances in PPG sensor technology could facilitate the acquisition of haemodynamic data and assessment of their clinical significance in multiple domains, including HF, coronary ischaemia and arrhythmia monitoring. Importantly, these devices could also be used to augment traditional home sphygmomanometer devices for haemodynamic monitoring.

Innovative biosensors for HF detection

Numerous biosensors are being developed that can monitor HF progression. Intrathoracic impedance can be used to detect pulmonary congestion in patients with HF. Daily self-measurement of lung impedance using non-invasive devices has been described. In patients with HF, use of the Edema Guard Monitor (CardioSet Medical) combined with a symptom diary was associated with increases in self-behaviour score for 30 days after hospital discharge[49]. In an analysis of more than 500,000 individuals in the UK Biobank, a machine learning model revealed that leg bioimpedance was inversely associated with HF incidence[50]. Numerous innovative and non-invasive tools can be used to detect leg impedance, such as sock-based sensors[51]. Furthermore, microphone-based devices have been used to transform cardiac acoustic vibrations to biomedical signals in quantitative versions of the phonocardiogram[52]. Such devices can track respiratory rate, heart and lung sounds, and body motion or position, and might be superior to physical examination for predicting worsening HF[53].

Biosensors for other cardiovascular indications are in development. An external device has been described

that can monitor impending thrombosis in intra-arterial mechanical pumps with the use of an accelerometer for real-time analysis of pump vibrations to detect thrombosis and possibly prevent thromboembolic events[54]. Ballistocardiography, a non-invasive measure of body motion generated by the ejection of blood in each cardiac cycle[10], has been incorporated into devices such as weighing scales to measure heart rate[55], whereas a digital artificial intelligence (AI)-powered stethoscope that integrates both ECG and phonocardiogram data was approved in 2020 by the FDA to assess patients for the presence of AF and heart murmurs[56]. The most promising systems might combine multimodality biosignals rather than using a single biosignal.

Challenges of novel monitoring platforms

Several challenges must be overcome before novel monitoring strategies can be adopted for clinical use in the ambulatory setting, which introduces noise from motion, electromagnetic interference and various patient activities, which are more controlled in the clinic. Biosensor design must match hardware specifications to biosignal characteristics for each clinical indication. Furthermore, device design must take into account the trade-off between duration and quantity of collected data, required battery power and device size, and durability in real-world use. Importantly, devices tested under one set of clinical conditions are not applicable for use for other clinical conditions, a particularly relevant point to remember given the growth of poorly regulated consumer medical devices.

Subtle changes in biosignals might also confound analysis, such that testing and validation might need to be repeated de novo for each device being investigated. Of note, many widely used consumer devices have only modest accuracy even for the 'simple' biosignals of heart rate or energy expenditure[40]. Whether accuracy is reduced owing to differences in study cohorts between initial device validation and real-world users[57], biological differences in biosignals owing to varying activity levels or other factors is unknown[39,58,59]. Biosignals that are calibrated in healthy volunteers might differ in accuracy when detecting disease. For example, tachycardia or irregularly irregular AF might introduce noise or variabilities in QRS morphology compared with sinus rhythm and can influence ECG algorithms[59]. Similarly, variability in pulse waveforms might influence PPG algorithms. Accordingly, algorithms developed with machine learning technology are best applied when the training and test populations are analogous. When these populations differ, learned features might become inaccurate, compounded in machine learning by limited methods to interpret its decisions (justifying why machine learning has sometimes been described as a 'black box')[60]. Testing and validation for each specific clinical application are, therefore, critical in device development.

Machine learning for biosignal analysis

The large quantity of data generated by ambulatory monitoring devices necessitates accurate and automated diagnosis and an infrastructure to enable quick clinical actions. The time-honoured method of human review and annotation of clinical data is also time-consuming, expensive and not scalable. Novel, scalable approaches to data interpretation and actionability might allow the potential of novel ambulatory monitoring to be realized. By reducing the time needed for data interpretation, ambulatory monitoring can detect acute events, such as worsening HF, incipient coronary syndrome or impending sudden cardiac arrest, and provide timely feedback for less urgent events.

Traditional analytical models for ambulatory monitoring rely on a limited number of biosignals and apply intuitive rules, such as those related to rate or regularity of heart rhythm, to flag a normal or abnormal result (FIG. 3a). Such forms of AI systems are known as 'expert systems'[60]. Although these traditional models might introduce inaccuracy in data interpretation, slight inaccuracies might be acceptable in traditional health-care paradigms in which data flagged by the device are verified by clinicians. However, this approach might not be safe for wearable consumer devices with little or no clinician input.

Machine learning is a rapidly developing branch of AI that has shown early promise for use in cardiovascular medicine[61] through the extraction of clinically relevant patterns from complex data, such as detecting myocardial ischaemia from cardiac CT images[62] and interpreting arrhythmias from wearable ECG monitors[33]. Machine learning can also facilitate novel strategies for communication between patients and the health-care team (FIG. 3b). Machine learning-based classification of biosensor data from multiple sensors can automatically evaluate the haemodynamic consequences of HF, arrhythmias or coronary syndromes, and can enable rapid triage without the need to develop, test and separately implement complex rules. Conversely, machine learning algorithms are not perfect and are limited by the presence of noise and training data that might not adequately represent the real-world clinical setting. In a study to detect AF, a third of ECGs could not be interpreted by a consumer device but could be classified by experts[35]. Furthermore, in a proof-of-concept study involving the use of smartwatch-based PPG sensor data analysed by a deep neural network, AF was diagnosed accurately in recumbent patients (*C* statistic 0.97) but not in ambulatory patients (*C* statistic 0.72)[39].

Integration of multiple data streams

Advanced monitoring systems that integrate data from multiple streams can better mimic the diagnostic performance of a clinician than current devices that monitor a single data stream. A system that identifies an impending event is likely to be more accurate if an event detected from the ECG is combined with evaluation of potential haemodynamic compromise (such as from a PPG signal) than use of either signal alone. The integration of multiple physiological data streams is a complex task for which simple rules might not readily exist. Machine learning might provide such decision-making potential because of its proven capacity to classify complex data.

FIGURE 3b illustrates a typical machine learning architecture comprising an artificial neural network with multiple inputs. This type of architecture can capture

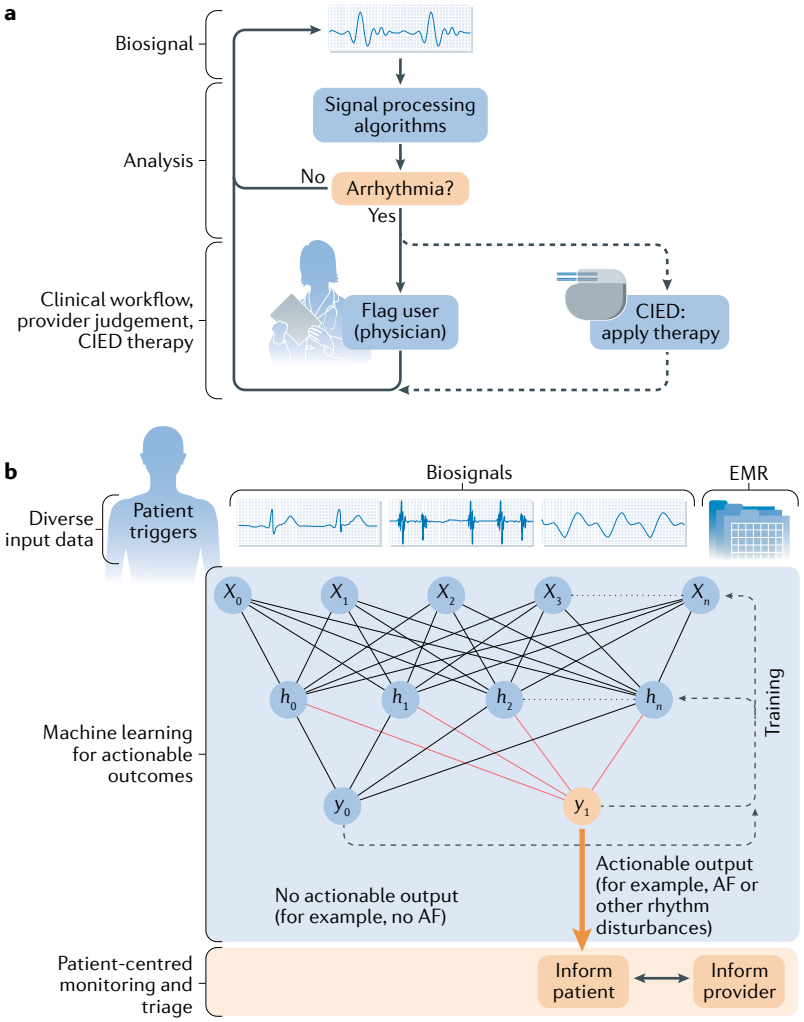

Fig. 3 | **Traditional analytical models for ambulatory monitoring versus future models incorporating machine learning technology. a** | Traditional systems for the analysis of ambulatory monitoring data rely on a limited number of biosignals and apply signal processing algorithms related to the rate or regularity of heart rhythm to flag a normal or abnormal result. The provider is then alerted to the result for management purposes. In a parallel pathway involving cardiac implanted electronic devices (CIEDs; dashed line), data analysed by the CIED can be used to deliver therapy by altering pacing or delivering implantable cardioverter–defibrillator therapy. **b** | A potential future model for monitoring might incorporate multiple inputs including biosignals (such as electrograms, haemodynamics and activity levels), patient input and clinical data, which are analysed by a machine learning algorithm. Deep neural networks, a type of machine learning technology, facilitate the classification of multiple diverse inputs even if traditional rules would be difficult to devise. In this scenario, deep neural networks receive inputs (denoted X_0, X_1, X_2, X_3 and X_n) and use hidden nodes (denoted h_0, h_1, h_2 and h_n) to classify them into actionable outputs (denoted y_0 and y_1). This model can be tailored to the patient and the type of sensor available. Given that many ambulatory devices are likely to be patient-driven, data will be directly sent to the patient. Additional infrastructure is needed to inform health-care providers of actionable diagnoses[138]. AF, atrial fibrillation; EMR, electronic medical record.

multimodal biosignals such as ECG, pulse oximetry and electronic medical record (EMR) data (denoted X_n in FIG. 3b) and classify them by adjudicated outcome (denoted y_0 or y_1), which might represent response or non-response to therapy, or the presence or absence of a haemodynamically significant event. Layers in the model (denoted h_0–h_n) distil input biosignals into archetypes of data that are relevant to the outcomes, constructed iteratively in the hidden 'deeper' layers during algorithm training. These hidden layers are integrated at lower levels to reduce the extent (or dimensionality) of data and identify patterns that best match with the critical event[60,61]. Although decisions made by such machine learning models are not always readily interpretable, studies have shown that these models make mistakes similar to those made by humans[33] and can learn 'expert' decision-making processes even if not trained in these processes, raising confidence that machine learning decisions are medically intuitive[63].

Machine learning algorithms for diagnosis

Several machine learning-based monitoring systems have been assessed for their efficacy in guiding clinical management. The LINK-HF multicentre study[2] investigated the accuracy of a smartphone-based and cloud-based machine learning algorithm that analysed data from a wearable patch for predicting the risk of rehospitalization (via measurement of physiological parameters such as ECG, heart rate, respiratory rate, body temperature, activity level and body position) in 100 patients with HF. This system predicted the risk of imminent HF hospitalization with up to 88% sensitivity and 85% specificity, which is similar to that of implanted devices. A follow-up study to determine whether this approach can prospectively prevent rehospitalizations for HF is ongoing. The 2012 MUSIC study[64] was a multicentre, non-randomized trial to validate a multiparameter algorithm in an external multisensor monitoring system to predict impending acute HF decompensation in 543 patients with HF with reduced ejection fraction. Algorithm performance met the prespecified end point with 63% sensitivity and 92% specificity for the detection of HF events.

Numerous monitoring devices that use machine learning technology have been developed to detect ventricular arrhythmias and impending sudden cardiac arrest. The design of the 100Plus Emergency watch (formerly the iBeat Heart Watch) involves a closed-loop system that uses machine learning algorithms to monitor signals detected from a dedicated watch, which then automatically contacts emergency services if the wearer does not respond to a notification within 10 s (REF.[65]). Machine learning technology ('deep learning')[60] has also been shown to improve the performance of shock advice algorithms in an automated external defibrillator[66] to predict the onset of ventricular arrhythmias with the use of an artificial neural network[67] and to predict the onset of sudden cardiac arrest within 72 h by incorporating heart rate variability parameters with vital sign data[68]. A system that can warn patients of an impending life-threatening cardiac event, even if only by several minutes, will greatly increase the availability and efficacy of a bystander or emergency medical response[67].

Pathophysiological insights

The application of machine learning to continuous biosensor data is beginning to provide insights into the pathophysiological mechanisms underlying numerous cardiovascular conditions, such as the identification of novel disease phenotypes that might respond

differentially to therapy. Novel immune phenotypes for pulmonary arterial hypertension were identified by unsupervised machine learning analysis of a proteomic panel including 48 cytokines and chemokines from whole-blood samples[69]. The investigators identified four clusters independent of WHO-defined pulmonary arterial hypertension subtypes, which showed distinct immune profiles and predicted a 5-year transplant-free survival of 47.6% in the highest-risk cluster and 82.4% in the lowest-risk cluster. A machine learning-based cluster analysis of echocardiogram data from patients in the TOPCAT trial revealed three novel phenotypes of HF and preserved ejection fraction with distinct clinical characteristics and long-term outcomes[70]. In a study involving 44,886 patients with HF with reduced ejection fraction from the Swedish HF Registry, the use of machine learning to analyse demographic, clinical and laboratory data resulted in a random forest-based model that predicted 1-year survival with a *C* statistic of 0.83 (REF.[71]). Cluster analysis led to the identification of four distinct phenotypes of HF with reduced ejection fraction that differed in terms of outcomes and response to therapeutics, highlighting the role of such novel analytical strategies in increasing the effectiveness of current therapies.

Machine learning data have also provided mechanistic insights into the pathophysiology of AF. Patients with persistent or paroxysmal AF show rates of response to antiarrhythmic medications of 40–60% and to cardiac ablation of 50–70%[72]. Data from continuous ECGs show that current clinical classifications poorly reflect the true temporal persistence of AF[4]. Additional studies could identify AF patterns or other physiological phenotypes in patients with 'less advanced' persistent AF in whom pulmonary vein isolation alone might be effective, or conversely those with 'more advanced' paroxysmal AF in whom pulmonary vein isolation might be less effective. Patients could thus be stratified for treatment according to newly recognized patterns of AF (that is, staccato versus legato)[73] or by incorporating haemodynamic or clinical data. A 2019 proof-of-concept study showed that machine learning trained on daily AF burden from continuous CIED tracings revealed signatures with incremental prognostic value for the risk of stroke beyond the CHA_2DS_2–VASc score[74]. Patients with HF and arrhythmias could thus show differing prognosis depending on arrhythmia burden[75]. Therefore, although in the near future digital health platforms are unlikely to provide 'precision medicine' at the granular level of individualizing therapy according to genotype, such platforms might still provide the opportunity for personalized care on the basis of deep patient phenotyping to provide novel disease insights.

Regulatory framework and data ownership

The FDA published a discussion paper in April 2019 describing the development, testing and regulatory oversight for machine learning approaches between the stages of premarketing and postmarketing performance[76]. In general, a desirable system should accurately identify and separate data indicative of urgent or non-urgent clinical states. In the absence of such a system, all biosensor data that meet prescribed cut-off points, such as extreme bradycardia or tachycardia, are flagged and the health-care provider is alerted. This FDA guidance allows device manufacturers to invest in the development of models with a lower-risk pathway to implementation and is intended to increase clinician–patient interactions and promote wellness. However, a drawback of applying traditional regulatory processes to rapidly evolving devices is that machine learning algorithms are typically 'frozen', with no further changes permitted, when a 'software as a medical device' (SaMD) application is submitted (defined as software that is intended to be used for medical purposes that performs these tasks without being part of a hardware medical device)[76]. This process limits the opportunity to approve self-learning algorithms, which would ultimately differ from the submitted version, and this limitation is amplified by the inevitable time between receiving trial data and approving the data for use in patients. One potential solution could be to submit several versions of a device for approval, including a base case for the most validated primary labelling indication, plus alternatives with preliminary data for secondary labelling indications. Another approach is to approve a 'snapshot' of the SaMD self-learning algorithms associated with a registry, which is similar to postmarketing studies for devices and drugs that require repeated evaluation at predetermined intervals.

Databases for monitoring systems

Development and training of algorithms requires gold-standard data (often termed a 'ground truth'), yet such data can be difficult to obtain in patients, which complicates the regulatory and clinical pathway. Biosignals are typically complex, non-linear, high-dimensional (comprising many variables) and dynamic. High-quality labelled datasets are scarce both for novel biosignals such as ballistocardiograms and for well-established biosignals such as thoracic impedance, energy expenditure or ECGs measured from atypical locations. Although new datasets can be created for such signals, the accuracy of the sets must be validated de novo. Bias is introduced whenever humans interact with data, which should be considered when scalable systems are being designed. One ideal solution would be the development of curated databases with specific biosignal data streams that are labelled by adjudicated outcomes and tailored to each use[77]. Although standardized databases such as Physionet have been useful for testing algorithms for research[78], these databases are small and might not include data from novel biosensors. The plethora of commercially available health monitoring devices has facilitated the generation of large proprietary datasets, yet these databases are not always transparent or available for validation[33]. Therefore, the regulatory pathway might require several clinical tests with prototypes in each class of device or algorithm, and multiple well-curated datasets. Device manufacturers should demonstrate that emerging devices can be operated by untrained users to acquire recordings that will perform well with their systems, including analysis of human factors that can bias the results and analyses specific to their algorithms. Therefore, although standardization of novel biosensors across manufacturers is

ultimately desirable, this goal might need to be deferred until technologies become more mature.

Patient-centred data access

Regulatory agencies in the USA, including the FDA, and patient advocacy groups have unanimously taken the position that patients must be empowered in their relationship with health-care providers and have access to their data[79]. Meaningful use criteria for EMRs require data sharing through patient access portals, yet such data might be difficult for patients to interpret (TABLE 2). Historically, medical device data have been kept in databases owned and maintained by industry and accessible by health-care providers, yet with more limited accessibility for patients. Consumer devices have shifted this landscape, empowering individuals to access their data from device companies, who then directly provide automated reports without having to notify a caregiver (FIG. 1).

This model introduced several potential challenges. Whether meaningful use criteria for EMRs apply to consumer device-based data is unclear. Moreover, whether a health-care organization can have timely and unfettered access to data 'ordered' then paid for by a consumer and then stored in devices that are also paid for by the consumer is unclear (TABLE 3).

One important additional point is that these devices have already been developed with use of data that arguably belong to the consumer. In 2016, the Alphabet-owned AI company DeepMind Technologies partnered with health-care authorities in the UK to access health data without the need for patients' permission[80]. This model introduces potential risks of a 'services for data' social media business model in which personal data are commoditized for sale to or by third-party companies. Alternatively, if medical devices and data are owned and paid for by consumers, an opportunity exists for market forces or legislation to return control to data owners. Device manufacturers or third parties could conceivably compete in providing patient-friendly data visualization tools, to which medical providers could also pay for access. This scenario has its own challenges and is likely to be a point of contention in coming years.

Data security

A complicated responsibility exists for data that are shared between users (patients, health-care providers and algorithm developers), data owners (health-care organizations, individuals and industry) and industry. Health-care organizations are liable for unauthorized access to EMRs, yet numerous privacy concerns exist for non-health-related mobile data. Consumer devices are also likely to encounter cybersecurity risks, which must be addressed proactively.

Data breaches, both unintentional and malicious in nature, have been reported by many companies that are now entering the health-care market, as well as diagnostic companies[81] and CIED manufacturers[82]. The technical shift to consumer-driven technology might provide a catalyst to standardize biosensor and data formats, and in turn increase security. Blockchain technology, which has been successfully used in financial markets and other industries, might have a role in patient-centred monitoring by tagging data ownership, providing traceability and enabling incentive programmes for sharing data[83].

Geopolitical regulations are also in development. The General Data Protection Regulation was enacted in

Table 2 | **Current challenges in cardiovascular monitoring**

Topic	Challenges for health-care providers	Challenges for technology providers	Challenges for patients
Biosensors	Limited sensors in mainstream practice	Need to determine which biosignals are the most promising	Enthusiastic about new technology but unsure which devices will ultimately prove to be useful
Data interpretation	Scepticism regarding automated diagnoses and a limited understanding of novel analytical algorithms. Data from large trials are needed	Limited knowledge of disease pathophysiology, available treatments and how to integrate data into treatment pathways	Often confused by medical jargon and rely on health-care providers to clarify results. At present, limited guidance is available on how to deal with results
Data privacy	Less familiar with emerging patient-centric models than traditional provider-centric health-care models, and poor access to data from consumer devices	Poor access to curated patient-health databases and limited data interoperability between health-care silos	Poor control over protected health information in older provider-centric models, as well as limited tools to manage protected health information in new patient-centric health models. More guidance and options for data sharing and storage are needed
Clinical practice	Need to consider the value of cardiovascular monitoring, as well as complex medical and ethical issues associated with monitoring interventions	Clinical significance of findings is unknown, as well as a lack of new treatment pathways devised	Diagnoses might cause anxiety or depression, or might lead to unnecessary treatment. Additional guidance is needed to clarify findings from monitoring data, and treatment options need to be thoroughly explained
Literature	Limited familiarity with engineering and computer science data	Limited familiarity with medical journals and latest clinical trial data	Over-reliance on media and internet sources of variable quality for latest medical news. Credible, patient-friendly information outlets and tools are needed

Table 3 | **Selected clinical studies in cardiovascular monitoring with wearable technologies**

Study (year)	Type of study	Device	*n*	Age (years)	Follow-up duration	Aim of study	Major findings	Ref.
LINK-HF multicentre study (2020)	Phase II, multicentre, prospective study	Multisensor chest patch (HealthPatch, Vital Connect, USA)	100	68 ± 10	3 months	Use of machine learning algorithm to predict HF rehospitalization	Predictive accuracy of HealthPatch for impending HF rehospitalization was similar to that of implanted devices	2
Vetrovsky et al. (ongoing)	Randomized, controlled trial	ActiGraph watch (ActiGraph, USA)	200	NR	6 and 12 months	Primary outcome is change in 6-min walking distance at 6 months in patients with HFrEF or HFpEF	Ongoing	114
NEAT-HFpEF trial (2015)	Randomized, crossover trial	Belt with two kinetic activity monitors containing accelerometers (Kionix, USA)	110	69 ± 9	6 weeks	Efficacy of isosorbide mononitrate in improving activity levels or exercise capacity	Patients with HFpEF who received isosorbide mononitrate were less active and did not have better exercise capacity than placebo-treated patients	115
Apple Heart study (2019)	Multicentre, prospective, single-group study in 50 US states	Apple smartphone-based application (Apple, USA) and ECG patch (ePatch, BioTelemetry Inc., USA)	419 and 297	41 ± 13	8 months	AF detection	Approximately 0.52% of participants received irregular pulse notifications	7
DETECT AF PRO study (2018)	Two-centre, prospective study	Smartphone-based application and iECG (AliveCor, USA)	592	78 ± 13	1 year	AF detection	On the basis of 5 min of PPG heart rhythm analysis, the algorithm detected AF with sensitivity of 91.5% and specificity of 99.6%	116
MATLAB Mobile platform study (2018)	Retrospective study	MATLAB Mobile platform (The MathWorks, USA)	48	NR	NR	Validation of the efficacy of an ECG R peak-detector algorithm in diagnosing AF on a mobile device	Algorithm detected the ECG R peak with a sensitivity of 99.7% and positive predictive rate of 99.4%	117
MODE-AF study (2018)	Case–control study	Mechano-cardiography recording using Sony Xperia smartphone	150	75 ± 1	NR	AF detection	Smartphone-based mechanocardiography accurately discriminated AF from sinus rhythm without additional hardware	118
mSToPS trial (2018)	Randomized and observational cohort studies	Self-applied wearable ECG patch (Zio^{XT}, iRhythm, USA)	2,659	72 ± 7	1 year	AF detection	In individuals at high risk of AF, immediate monitoring with the wearable ECG patch led to a higher rate of AF diagnosis after 4 months than with delayed monitoring	119
SAFETY study (2018)	Multicentre, case–control study	AF detection devices (AliveCor, USA, and WatchBP, Microlife, Switzerland) and consumer ECG sensing devices (Polar-H7, Polar, Finland, and Bodyguard 2, Firstbeat, Finland)	418	73.9 ± 6.1	NR	AF detection	Overall accuracy for detecting AF of 96.7% for AliveCor, 94.0% for WatchBP, 97.9% for Polar-H7 and 98.1% for Bodyguard 2	120
iHEART trial (2017)	Single-centre, randomized trial	KardiaMobile ECG monitor (AliveCor, USA)	262	61 ± 12	6 months	AF and atrial flutter detection	AliveCor home monitoring device is beneficial for prompt detection of AF or atrial flutter recurrence after cardiac ablation or cardioversion	121

Table 3 (cont.) | **Selected clinical studies in cardiovascular monitoring with wearable technologies**

Study (year)	Type of study	Device	*n*	Age (years)	Follow-up duration	Aim of study	Major findings	Ref.
mAF App trial (2017)	Prospective, randomized trial	mAF mobile application	113	67 ± 11	1 year	Validation of the use of the mAF application in improving patient-related parameters in patients with AF	The mAF application improved disease knowledge, quality of life, treatment adherence and anticoagulation satisfaction in patients with AF	122
Ghanbari et al. (2017)	Pilot study	miAfib mobile application	10	>21	4 weeks	Validation of the use of the miAfib application to assess daily symptoms in patients with AF	Patients regularly used the application to report daily symptoms and found the application easy to use	123
MOBILE-AF trial (ongoing)	Multicentre, randomized trial	KardiaMobile ECG monitor (AliveCor, USA)	200	NR	1 year	Detection of AF in patients after cryptogenic stroke or transient ischaemic attack	Ongoing	124
REHEARSE-AF trial (2017)	Randomized, controlled trial	iECG (AliveCor, USA)	1,001	73 ± 5	1 year	AF detection	Regular twice-weekly iECG screening results in an almost fourfold increase in AF diagnosis compared with routine care	125
SMART-India study (2018)	Population-based study	iECG (AliveCor, USA)	2,100	>50	5 days	AF screening among individuals in rural India by village health workers	Prevalence of AF (1.6%) is at least threefold higher than previously reported in India and is similar to rates found in North American and European studies	126
Chan et al. (2017)	Prospective study	AF detection devices (AliveCor, USA, and WatchBP, Microlife, Switzerland)	2,052	68 ± 11	5 months	Comparison of diagnostic performance of two AF detection devices	The sensitivity for detecting AF was 66.7% for the AliveCor device and 83.3% for the Microlife device, but both devices had high specificity (>98%)	127
WEARIT-IN trial (2016)	Prospective, observational study	Fitbit Charge HR wireless activity wristband (Fitbit, USA)	50	64	24 h	Evaluation of the accuracy of heart rate monitoring using a personal fitness tracker among hospital inpatients	Personal fitness tracker-derived heart rates were slightly lower than those derived from continuous ECG monitoring in a real-world setting	128
SEARCH-AF (2014)	Cross-sectional study	iECG (AliveCor, USA)	1,000	76 ± 7	NR	Determination of efficacy and cost-effectiveness of a pharmacy-based community screening programme for AF detection using an iPhone ECG device	The automated iECG algorithm showed 98.5% sensitivity and 91.4% specificity for AF detection and was both feasible and cost-effective	129
de Asmundis et al. (2014)	Prospective study	HeartScan portable ECG monitor (Omron Healthcare Co., Japan)	625	37 ± 11	20 months	Comparison of the diagnostic value of Holter ECG monitoring with a patient-activated event recorder in detecting arrhythmias among patients with palpitations or dizziness	Symptom-related arrhythmia was detected in more individuals using the HeartScan devices than the Holter monitor (558 versus 11 individuals)	130

Table 3 (cont.) | **Selected clinical studies in cardiovascular monitoring with wearable technologies**

Study (year)	Type of study	Device	*n*	Age (years)	Follow-up duration	Aim of study	Major findings	Ref.
Kearley et al. (2014)	Prospective study	HeartScan portable ECG monitor (Omron Healthcare Co., Japan) and WatchBP (Microlife, Switzerland)	1,000	79.7 (75.1–99.8)	17 months	Assessment of performance of a blood-pressure monitor and two single-lead ECG devices for the detection of AF	The WatchBP device was more specific for identifying AF, and thus a better triage test than the single-lead ECG monitors (89.7% versus 78.3%)	131
Weisel et al. (2014)	Observational study	Blood pressure monitor (Omron Healthcare Co., Japan) and WatchBP (Microlife, Switzerland)	199	74 (50–100)	NR	Comparison of two blood-pressure monitors in detecting AF among general cardiology patients	The specificity of both devices was acceptable, but only the WatchBP had a sensitivity that was high enough to be used for AF screening in clinical practice	132
Lau et al. (2013)	Cross-sectional study	iECG (AliveCor, USA)	109	≥65	NR	AF detection	Overall accuracy of 97% in both the learning set and the validation set	133
Kaleschke et al. (2019)	Single-blind, prospective study	HeartScan portable ECG monitor (Omron Healthcare Co., Japan)	508	61 ± 15	8 months	Evaluation of the diagnostic accuracy of a leadless, patient-operated ECG device versus a standard 12-lead ECG	Patient-operated ECG device detected arrhythmias with higher accuracy than standard ECG	134
Doliwa et al. (2009)	Prospective study	Zenicor-ECG (Zenicor Medical Systems, Sweden)	606	64 (43–87)	1 month	Evaluation of the sensitivity and specificity of a thumb ECG device in diagnosing AF	The thumb ECG device correctly diagnosed AF in 96% of cases and sinus rhythm in 92% of cases	135
Wiesel et al. (2009)	Observational study	WatchBP (Microlife, Switzerland)	405	32.3	NR	Assessment of the sensitivity and specificity of an automatic oscillometric sphygmomanometer designed to detect AF	The device diagnosed AF with high sensitivity (95%) and specificity (86%)	136
TARGET-HFDM trial (ongoing)	Randomized, controlled trial	Withings Go smartwatch (Nokia Health, Finland)	200	NR	6 months	Mobile health intervention to improve health behaviours	Ongoing	137

AF, atrial fibrillation; ECG, electrocardiogram; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; NR, not reported; PPG, photoplethysmography.

the EU in 2016 with the primary goal of giving individuals control over their personal data, and aims to unify the regulations within the region and provide safeguards to protect data, requiring all stakeholders to disclose data collection practices and breaches that occur. This regulation has become a model for privacy laws elsewhere and is similar in structure to the California Consumer Privacy Act. However, it is unclear how general consumer regulations will apply to or potentially influence the US Health Insurance Portability and Accountability Act, which could also be modified given that it covers only a fraction of an individual's health-related data[84].

Real-time cardiovascular care delivery

Devices that integrate high-fidelity biosignal detection with broadband wireless connectivity and cloud processing could, in principle, facilitate real-time care. A similar landscape is rapidly developing in the automotive industry with regard to the design of autonomous driving vehicles that apply multimodal, ultrafast fusion algorithms to multiple data streams that can provide an immediate response. To apply this technology to wearable devices, collected data must interact within a rapidly changing clinical context, which has already occurred for ICD therapy for tachyarrhythmia or pacing technology for bradycardia[85]. However, this technology is less developed for other domains such as AF management and HF or blood-pressure monitoring and devices that require multimodal data. Several clinical studies of mobile and wearable device platforms are summarized in TABLE 3.

One early model is the currently available MCOT system for arrhythmia monitoring. The MCOT system includes ECG sensors and a device that automatically transmits data to a central analysis hub for annotation

and alerts the health-care provider[25]. The cycle time for this process ranges from minutes to hours. This approach can increase the diagnostic yield over that of other ambulatory ECG systems[25] and has been used during the coronavirus disease 2019 (COVID-19) pandemic to monitor the QT interval in patients receiving hydroxychloroquine or azithromycin while simultaneously minimizing clinician exposure and preserving personal protective equipment resources[86]. During the COVID-19 pandemic, the Heart Rhythm Society (HRS) recommended the use of digital wearable devices to obtain vital signs and ECG tracings, as well as the use of MCOT after hospital discharge[87]. Furthermore, the HRS recommended the replacement of in-person clinic visits and CIED checks with telehealth consultations whenever feasible. These approaches are not yet recommended as an 'emergency response' system for scenarios such as impending sudden cardiac arrest.

New real-time systems might lay the foundation for real-time data transmission and response that are coordinated with emergency medical services and bystanders[88]. Early proof-of-concept systems have shown success in rapidly alerting bystanders and emergency medical providers to expedite first response[89]. In Europe, community volunteers can rapidly deliver automated external defibrillator to people experiencing sudden cardiac arrest[90]. Possible future directions include the development of a wireless internet of things (in which multiple devices are connected in their own dedicated network) for real-time cardiovascular care delivery. An important consideration is that medical care systems are not required to be fully automatic, unlike self-driving cars. Optimal medical systems might require only conditional autonomy, in that input from medical professionals and patients should be considered, rather than complete autonomy[61]. Although this need for conditional autonomy reduces some technical challenges, conditional autonomy also introduces limitations such as the need for integration with contemporaneous medical systems and to allow practitioner oversight while retaining speed of response and accuracy.

Cardiovascular monitoring guidelines

A growing number of publications support the use of monitoring devices in cardiovascular diagnostics and decision-making, including those that integrate machine learning technology. This rapid expansion of the evidence base has coincided with increased FDA guidance supporting the use of wearable devices for health care. TABLE 3 summarizes clinical studies of mobile and wearable device platforms.

Current monitoring strategies

Detection of subclinical AF in patients with cryptogenic stroke. The 2019 AHA/ACC/HRS guidelines for the management of AF recommend ambulatory monitoring to screen patients for AF and, if this is inconclusive, a cardiac monitor should be implanted[91]. The CRYSTAL-AF trial[92] showed that ECG monitoring with an insertable cardiac monitor was superior to conventional follow-up for detecting AF in patients after cryptogenic stroke. The EMBRACE trial[93] extended these observations by showing that a high burden of premature atrial beats predicted AF in patients with cryptogenic stroke. The long recording duration of wearable ECG devices makes them desirable for detecting subclinical AF, although whether such information can influence therapeutic decisions to prevent stroke is yet to be shown. Future studies should thus compare the accuracy and cost-effectiveness of wearable devices with those of traditional monitors in patients at risk of stroke and after stroke.

Screening for sudden cardiac arrest. Individuals at risk of sudden cardiac death have a diverse spectrum of phenotypes. The 2017 AHA/ACC/HRS guidelines provided a class I indication for ambulatory monitoring in patients with palpitations, presyncope or syncope to undergo monitoring to detect potential ventricular arrhythmias[85]. A class IIA recommendation was indicated for patients with suspected long QT syndrome and to determine whether symptoms, including palpitations, presyncope or syncope, are caused by ventricular arrhythmias. Ambulatory ECG monitoring was also recommended for patients starting certain antiarrhythmic medications (including disopyramide, dofetilide, ibutilide, procainamide or sotalol) with or without risk factors for torsades de pointes[85]. The 2014 ESC guidelines on the diagnosis and management of hypertrophic cardiomyopathy recommended ambulatory ECG monitoring every 6–12 months in patients with hypertrophic cardiomyopathy with left atrial dilation of ≥45 mm or after septal reduction therapies[94]. The diversity of patient phenotypes in this group introduces challenges and might require non-uniform monitoring intensity between patient populations. The current lack of infrastructure to facilitate actions in response to data from wearable devices might limit their use in detecting life-threatening arrhythmias. However, professional society guidelines have provided recommendations on the use of wearable cardioverter–defibrillators to prevent sudden cardiac death[95] and have called for increased transparency in monitoring data from CIEDs and consumer arrhythmia-monitoring devices[96].

Arrhythmia screening in patients with syncope. The 2018 ESC guidelines for the diagnosis and management of syncope recommend ambulatory ECG monitoring in patients with recurrent and unexplained syncope[97]. Depending on the frequency of events and the clinical context, patients can be monitored with the use of implanted devices or external devices that send alerts to health-care providers. Devices that encompass multiple sensor streams, such as activity, pulse oximetry and haemodynamics, to track the temporal relationship between episodes of hypotension, posture and cardiac rhythm might provide pathophysiological insights in different populations and are currently under investigation[6].

Monitoring for patients with non-arrhythmic conditions. The 2017 AHA guidelines and the 2017 ESC guidelines recommend ambulatory arrhythmia monitoring for various subgroups of patients with acute coronary syndromes, including those with left ventricular ejection fraction <40%, failed reperfusion and high risk of ventricular arrhythmia, and patients requiring β-blocker therapy adequacy assessment[85,98]. Similarly, a 2017 expert

consensus statement from the International Society for Holter and Noninvasive Electrocardiology and the HRS provided a class I recommendation for ambulatory monitoring in patients with arrhythmic and non-arrhythmic conditions, including non-ischaemic cardiomyopathy[99]. Although these recommendations were largely instituted for arrhythmia detection, signals for recurrent ischaemia might also be derived from these data.

Fitness and health-tracking devices. In July 2016, the FDA issued guidance for general wellness devices such as activity trackers, smartwatches and other products intended to improve physical fitness, nutrition or other wellness goals[99]. Subsequently, in September 2019, the FDA issued new draft guidance for clinical support applications that provides diagnostic and treatment recommendations for physicians but not for patients[76].

Emerging monitoring strategies

Screening of the general population for AF. In 2018, the US Preventive Services Task Force concluded that insufficient evidence is available to determine whether the benefits of AF screening outweigh the associated risks[100]. This conclusion was formed on the basis of the potential physical and psychological risks of unnecessary treatment (false positives) in asymptomatic individuals aged ≥65 years. Conversely, the 2016 ESC guidelines recommend screening for AF in individuals older than 65 years in order to consider anticoagulation[101] on the basis of findings from the SAFE[102] and STROKESTOP[103] studies, in which AF screening of asymptomatic individuals aged ≥65 years and ≥75 years, respectively, was shown to be cost-effective. Investigators in the ongoing SCREEN-AF trial[104] will randomly assign individuals aged ≥75 years to 2 weeks of ambulatory ECG monitoring with a home blood-pressure monitor that can automatically detect AF or to the standard of care, to assess the primary end point of AF detection.

The Apple Heart study[7] enroled 419,297 participants in the USA over 8 months to ascertain whether a PPG-enabled device could detect AF in individuals without a known history of the disease. Inclusion criteria included absence of self-reported AF, atrial flutter or oral anticoagulation use in individuals with a compatible Apple smartphone and smartwatch. Overall, 2,161 participants (0.52%) were notified of irregular rhythms with this technology[7]. In a subset of 450 enrollees who wore and returned clinical gold-standard ECG patches containing data that could be analysed, AF (≥30 s) was present in 34% of all participants and in 35% of participants aged ≥65 years. The positive predictive value for simultaneous AF on ambulatory ECG patch monitoring was 84% (95% CI 76–92%). The HUAWEI Heart study[105], conducted by the MAFA II investigators, assessed the use of a wristband or wristwatch with PPG technology to monitor pulse rhythm in 246,541 individuals. Of these individuals, 262 were notified as having suspected AF, including 227 who had AF confirmed by a gold-standard clinical device. Therefore, this wristwatch provided a positive predictive value of 91.6% (95% CI 91.5–91.8%) in the subset of individuals who also had clinical monitoring[105]. The proportion of individuals with positive test results in both studies reflects the expected pretest probability of AF in a wide and relatively healthy population, and can inform on the design of future screening trials and the best target populations for such a strategy.

Personalization of oral anticoagulation therapy. The 2019 AHA/ACC/HRS guidelines for the management of AF emphasize that anticoagulation should not be tailored by the detection of AF episodes, the precise onset of AF or the temporal patterns of AF[91]. Indeed, the IMPACT-AF trial[106] showed that pill-in-the-pocket use of non-vitamin K oral anticoagulants on the basis of detected AF did not reduce bleeding or thromboembolic event rates compared with standard therapy in patients with an indication for oral anticoagulation. Furthermore, the REACT.COM study[107] showed the feasibility of a targeted strategy of implantable cardiac monitor-guided intermittent administration of non-vitamin K oral anticoagulants on the basis of remote monitoring in low-risk AF populations. However, this strategy might be less effective in other patient populations, and the investigators did not assess treatment adherence among participants[108].

In standard clinical practice, oral anticoagulation is indicated as soon as AF is detected in patients with a single CHA_2DS_2–VASc risk factor[91]. Emerging monitoring devices might facilitate the definition of a specific device-detected AF threshold that warrants the initiation of anticoagulation therapy. In the TRENDS study[109], this AF threshold might be an AF duration as short as 5.5 h. By contrast, a substudy of the ASSERT trial suggested a threshold duration of subclinical AF of ≥24 h (REF.[110]). Ongoing clinical trials are testing the use of oral anticoagulants for several proposed thresholds of AF duration. The ARTESiA trial[111] is currently enrolling patients with AF of ≥6 min, and the NOAH trial[112] is enrolling patients with an atrial high rate (≥170 bpm) of duration of ≥6 min. Both trials are enrolling patients with a CIED with an atrial lead and exclude individuals with a single AF episode longer than 24 h. Finally, the LOOP study[113] is using the Reveal LINQ system to detect AF of ≥6 min, confirmed by at least two senior cardiologists. The results of these and other trials will help to define the device-detected AF threshold that warrants the initiation of anticoagulation therapy.

Conclusions

Cardiovascular monitoring is poised for dramatic technological advances through developments in novel biosignal definition and biosensor acquisition, automated diagnosis and expert-level triage, secure data transmission and patient-centric disease management. Numerous challenges remain in ensuring that data are owned and fully accessible by patients, but at the same time allowing relevant stakeholders to access data and enable timely disease management. Once data security and the other ethical and regulatory concerns associated with wearable technologies are addressed, this expanded monitoring paradigm has the potential to revolutionize the cardiovascular care of ambulatory patients.

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C.K. is on the ACC Solution Set Oversight Committee, on the advisory board of *Lancet Digital Health* and on the editorial board of *EHJ Digital Health* and *Journal of the American Heart Association*. K.W.J. has received a salary and equity from Tempus Labs and equity from Oova. M.P.T. has received research grants from AHA, Apple, Bayer, Bristol Myers Squibb, Bristol Myers Squibb–Pfizer Alliance and Janssen and Medtronic and consulting fees from Abbott, Biotronik, Cardiva Medical, Johnson & Johnson and Medtronic, has equity in AliveCor and is an editor for *JAMA Cardiology*. S.M.N. has received consulting fees from Abbott, Beyondlimits.ai and TDK Corporation, and has co-ownership of intellectual property owned by the Regents of the University of California and Stanford University. The other authors declare no competing interests.

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