2021 ISHNE/HRS/EHRA/APHRS Collaborative Statement on mHealth in Arrhythmia Management: Digital Medical Tools for Heart Rhythm Professionals

From the International Society for Holter and Noninvasive Electrocardiology/Heart Rhythm Society/European Heart Rhythm Association/Asia Pacific Heart Rhythm Society

Niraj Varma (ISHNE Chair),1 Iwona Cygankiewicz (ISHNE Vice-Chair),2 Mintu P. Turakhia (HRS Vice-Chair),3 Hein Heidbuchel (EHRA Vice-Chair),4 Yufeng Hu (APHRS Vice-Chair),5 Lin Yee Chen,6 Jean-Philippe Couderc,7 Edmond M. Cronin,8 Jerry D. Estep,1 Lars Grieten,9 Deirdre A. Lane,10 Reena Mehra,1 Alex Page,7 Rod Passman,11 Jonathan P. Piccini,12 Ewa Piotrowicz,13 Ryszard Piotrowicz,13 Pyotr G. Platonov,16 Antonio Luiz Ribeiro,15 Robert E. Rich,1,* Andrea M. Russo,16 David Slotwiner,17 Jonathan S. Steinberg,7 Emma Svennberg18

From the 1Cleveland Clinic, Cleveland, OH, USA, 2Medical University of Lodz, Lodz, Poland, 3Stanford University, Palo Alto, CA, USA, 4Antwerp University and University Hospital, Antwerp, Belgium, 5Taipei Veterans General Hospital, Taipei, Taiwan, 6University of Minnesota, Minneapolis, MN, USA, 7University of Rochester, Rochester, NY, USA, 8Temple University, Philadelphia, PA, USA, 9Hasselt University, Hasselt, Belgium, 10University of Liverpool, Liverpool, UK, 11Northwestern University Feinberg School of Medicine, Chicago, IL, USA, 12Duke University, Durham, NC, USA, 13National Institute of Cardiology, Warsaw, Poland, 14Lund University, Lund, Sweden, 15Faculdade de Medicina, Centro de Telessaúde, Hospital das Clínicas, and Departamento de Clínica Médica, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil, 16Cooper Medical School of Rowan University, Camden, NJ, USA, 17Cardiology Division, NewYork-Presbyterian Queens, and School of Health Policy and Research, Weill Cornell Medicine, New York, NY, USA, and 18Karolinska University Hospital, Stockholm, Sweden.

*Patient Representative

Abstract

This collaborative statement from the International Society for Holter and Noninvasive Electrocardiology/Heart Rhythm Society/European Heart Rhythm Association/Asia Pacific Heart Rhythm Society describes the current status of mobile health (“mHealth”) technologies in arrhythmia management. The range of digital medical tools and heart rhythm disorders that they may be applied to and clinical decisions that may be enabled are discussed. The facilitation of comorbidity and lifestyle management (increasingly recognized to play a role in heart rhythm disorders) and patient self-management are novel aspects of mHealth. The promises of predictive analytics but also operational challenges in embedding mHealth into routine clinical care are explored.
TABLE OF CONTENTS

1. Introduction ........................................ 5
   Document scope and rationale .................. 5
2. mHealth Technologies ............................. 8
   2.1. Ambulatory ECG monitoring ............ 9
   2.2. New mHealth-based modalities for arrhythmia monitoring .... 9
      2.2.1. ECG-based .......................... 10
         2.2.1.1. Handheld devices ............ 10
         2.2.1.2. Wearable patches .......... 12
         2.2.1.3. Biotextiles ................ 12
         2.2.1.4. Smartphone and smartwatch-based devices .......... 12
         2.2.2. Non-ECG-based ................. 14
         2.2.2.1. Photoplethysmography ..... 14
         2.2.2.2. Oscillometry .............. 14
         2.2.2.3. Mechanocardiography ...... 15
         2.2.2.4. Contactless video plethysmography ............. 15
         2.2.2.5. Smart speakers .............. 15
3. mHealth Applications for Arrhythmias ... 17
   3.1. Atrial fibrillation .......................... 17
      3.1.1. Undiagnosed atrial fibrillation identification .......... 17
      3.1.2. Targeted identification in high-risk individuals .......... 20
      3.1.3. Diagnostics in people with established atrial fibrillation .......... 21
      3.1.4. Atrial fibrillation therapy .......... 21
   3.2. Sudden cardiac death ........................ 22
4. Comorbidities ...................................... 26
   4.1. Ischemic heart disease ...................... 26
   4.2. Heart failure .................................. 27
      4.2.1. Mobile technologies for managing heart failure .......... 28
      4.2.2. Hybrid telerehabilitation in patients with heart failure .......... 29
6. Clinical Trials .................................... 39
7. Operational Challenges ......................... 41
   7.1. Healthcare system—eHealth monitoring and hospital ecosystem .......... 41
   7.2. Cybersecurity guidance for mHealth devices .................. 42
      7.2.1. Hacking strategies and methods in mHealth technologies ........ 42
      7.2.2. Recommendations to the manufacturer .................. 42
      7.2.3. Recommendations to clinicians and administrators .......... 43
      7.2.4. Recommendations to patients .......... 43
   7.3. Reimbursement ................................ 43
   7.4. Regulatory landscape for mHealth devices .................. 44
8. Predictive Analytics ............................. 45
9. Future Directions .................................. 47
Concluding Remarks ................................. 49

1. Introduction
Document scope and rationale
Digital health is an umbrella term to describe the use of digital information, data, and communication technologies to collect, share, and analyze health information in order to

KEYWORDS arrhythmias; atrial fibrillation; comorbidities; digital medicine; heart rhythm; mHealth
ABBREVIATIONS AI = artificial intelligence; ACC = American College of Cardiology; ACS = acute coronary syndrome; AED = automated external defibrillator; AF = atrial fibrillation; AHA = American Heart Association; AHRE = atrial high-rate episode; APHRS = Asia Pacific Heart Rhythm Society; BP = blood pressure; CIED = cardiovascular implantable electronic device; CPR = cardiopulmonary resuscitation; EHR = European Heart Rhythm Association; EMR = electronic medical record; ESUS = embolic stroke of unknown source; FDA (U.S.) = Food and Drug Administration; GPS = global positioning system; HCP = healthcare professional; HF = heart failure; HR = heart rate; HRS = Heart Rhythm Society; ICD = implantable cardioverter-defibrillator; ILR = implantable loop recorder; ISHNE = International Society for Holter and Noninvasive Electrocardiology; JITAI = just-in-time adaptive intervention; MCT = mobile cardiac telemetry; OAC = oral anticoagulant; PAC = premature atrial complex; PPG = photoplethysmography; PVC = premature ventricular complexes; SCA = sudden cardiac arrest; TADA = Technology Assisted Dietary Assessment; VT = ventricular tachycardia (Cardiovascular Digital Health Journal 2021;2:4–54)

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited. Editorial review for this article was done by the participating societies and the Cardiovascular Digital Health Journal Editor-in-Chief. Section Editor David Slotwiner had no involvement in peer review for acceptance to this journal. How to cite this article: Varma N, Cygankiewicz I, Turakhia M, et al. 2021 ISHNE/HRS/EHRA/APHRS Collaborative Statement: Digital Medicine and Arrhythmia Management: Digital Medical Tools for Heart Rhythm Professionals. Cardiovascular Digital Health Journal 2021;2:4–54. https://doi.org/10.1016/j.cvdlhj.2020.11.004. Correspondence Niraj Varma, Cleveland Clinic, Cleveland, OH, USA. E-mail address: varman@ccf.org.
improve patient health, education, and healthcare delivery (https://www.fcc.gov/general/five-questions-you-can-ask-your-doctor-about-digital-health#ab) (Turakhia 2016). This concept encompasses telehealth, electronic health records, implantable device monitoring, wearable sensor data, analytics and artificial intelligence (AI), behavioral health, and personalized medicine. Among these, mobile health—or “mHealth” is a component of digital health, defined by the World Health Organization—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” (https://www.who.int/goe/publications/goe_mhealth_web.pdf) (https://apps.who.int/gb/ebwha/pdf_files/WHA71/A71_20-en.pdf?ua=1). Utilization of these devices has proliferated among health-conscious consumers in recent years and is likely to continue rapid expansion and integration into more formalized medical settings. mHealth flows intuitively to health professionals in the field of arrhythmia management from experience gained through remote monitoring of cardiovascular implantable electronic devices (CIEDs), such as pacemakers and implantable cardioverter-defibrillators (ICDs) (Varma 2010). A wealth of data garnered from many studies over the last 10-15 years have confirmed the benefits of remote technology-assisted follow-up and established it as standard of care (Varma 2013; Slotwiner 2015). However, results of remote monitoring of CIEDs may not be immediately generalizable to mHealth. For instance, the former is restricted to those with cardiac disease (largely arrhythmias and heart failure (HF)), that is, a group already defined as patients. The care pathways for CIED remote monitoring are also well defined, with billing and reimbursement in place in the United States and many other parts of the world. In comparison, mHealth differs: It is widely available in the form of consumer products that penetrate most sectors of society, including individuals without formal medical diagnoses; it may be applied to a wider group of medical conditions; data can be self-monitored rather than assessed by healthcare professionals (HCPs); and reimbursement models are not mature. Indeed, some heart rhythm tracking capabilities may be indirectly acquired in products purchased for different goals and then subsequently used for self-monitoring. Conversely, in the medical space, applications are largely not prescribed by HCPs, often lack validation for disease management use cases, and care pathways remain varied or poorly defined. Nevertheless, if properly implemented, the intersection of these two communities opens up a broad spectrum of opportunities, extending from population screening and surveillance for undiagnosed disease to longitudinal disease management, and importantly, engaging patients in their own cycle of care, allowing much health care to be asynchronous and virtualized. Its value and degree of integration will depend on different healthcare systems in different countries.
Table 1  mHealth-based modalities for arrhythmia monitoring

|                      | Signal acquisition and visualization | ECG duration | Signal storage and transmission | Indications/Populations tested | Advantages | Limitations |
|----------------------|--------------------------------------|--------------|---------------------------------|--------------------------------|------------|-------------|
| ECG-based devices    |                                      |              |                                 |                                |            |             |
| Handheld             | External sensors; Single or multilead ECG on demand; Display in-screen ECG or screen of PC/laptop/smartphone, after transmission or real-time ECG analysis available | Intermittent recording: 10 sec to 2 min | Built-in memory Bluetooth WiFi | Palpitations AF screening | Easy to use Low cost | Short ECG duration |
| wearable patches     | Built-in electrodes Patch attached to the skin | Continuous recording up to 14 days | Built-in memory with post hoc analysis, or Bluetooth transmission with real-time analysis in selected devices | Low-risk patients with palpitations and syncope AF screening | Continuous longer-term ECG recording; Built-in alarm button High patients, compliance; Patients can affix at home Water-resistant Continuous long-term recording; Built-in alarm button; High patients’ acceptance and adherence; Multiparameter evaluation; Can be used as monitoring and treating device (WCD) | Single-channel ECG Skin irritation |
| biotextiles          | Electrodes/sensors embedded into biotextile—vests, belts Single or multichannel | Continuous recording up to 30 days | Built-in memory Real-time Bluetooth transmission | Low-risk patients with palpitations and syncope AF screening | Widely available Long-life possibility of intermittent recording | Limited availability Movement artifacts |
| smartphone-based     | External sensors attached to mobile phone Single/ multilead ECG Real-time ECG on smartphone’s screen or PC/laptop after transmission | Intermittent recording up to 30 sec Patient activated | Built-in memory Real-time or post hoc transmission | Low-risk patients with palpitations AF screening | Widely available Long-life possibility of intermittent recording | Intermittent recording Single-channel |
| smartwatch-based     | Built-in sensors | Intermittent recording Patient activated | Built-in memory Real-time or post hoc transmission | Low-risk patients with palpitations AF screening | Widely available Long-life possibility of intermittent recording | Intermittent recording Single-channel |
| Non-ECG-based        |                                      |              |                                 |                                |            |             |
| Photoplethysmography (PPG) | HR from changes in reflectance of the tissue blood volume of a skin surface | Intermittent patient activated in smartphones Continuous measurement of HR in smartwatches and wristbands | Built-in memory Real-time or post hoc transmission | Low-risk patients with palpitations AF screening HR measurement during physical activity | Widely available | Irregular heart-presumed AF |
| Oscillometry         | BP monitors with HR measurement | Intermittent recording during BP measurement | Built-in memory Post hoc transmission | HR assessment Opportunistic AF screening | Widely available | Irregular heart-presumed AF |
| Video recording      | Camera from smartphones, TVs | Patient activated Continuous recording in prespecified time frame | Real-time or post hoc transmission | Low-risk patients with palpitations AF screening Undiagnosed falls | Can use existing cameras from household goods | Irregular heart-presumed AF |

Abbreviations: AF = atrial fibrillation; BP = blood pressure; HR = heart rate; WCD = wearable cardioverter-defibrillator.
mHealth has value only if the acquired information leads to decisions that improve outcome. This requires a clear path of information flow and actionability. Moreover, all stakeholders need to be aware of the logistical chain (so that everyone knows what to expect) and responsibilities clearly defined (possibly including device vendors). Similarly, actions taken based on the monitored information should be transparent to all stakeholders. For example, for a patient who records and transmits an irregular heart rhythm via a wearable device, a designated decision process should be followed to confirm whether the rhythm is atrial fibrillation (AF) or not, whether confirmation by another diagnostic test is required, how that is arranged, and finally what therapy should be implemented and in what reasonable time frame? Clearly, there are risks of increasing cost from medical testing and provoking anxiety in consumers—who by virtue of seeking a medical verification become patients. Again, CIED experience sets a precedent. Studies that have shown improved outcome with telemonitoring succeeded when integrated into a clear logistical framework for a specific use case of disease management (e.g., IN-TIME for remote monitoring in patients receiving cardiac resynchronization therapy, CardioMEMS) (Abraham 2011, Hindricks 2014, Varma 2013). Replicating this with mHealth creates challenges for healthcare providers and goes far beyond the technological capabilities of the monitoring and transmission equipment. Implementation will require defined aims and fundamental changes to existing workflows and responsibilities. Such changes are always difficult. Apart from the organizational issues required to achieve such changes, reimbursement may drive or hinder such changes in the workplace. Awareness of these factors has been heightened by the SARS-CoV-2 pandemic, during which telemedicine solutions have been advocated to reduce patient contact with healthcare providers yet continue healthcare delivery (Varma 2020).

In view of the rapid technological development and popularity of wearable and other mobile devices, and the need for analysis and planning of the mHealth infrastructure, ISHNE (International Society for Holter and Noninvasive Electrocardiology), HRS (Heart Rhythm Society), EHRA (European Heart Rhythm Association), and APHRS (Asia Pacific Heart Rhythm Society), recognized the need for this collaborative statement. The aim of this document is to define state-of-the-art mHealth technologies and their application in arrhythmia management and explore future directions for clinical application. As such, the scope of the document encompasses discussion of the different mHealth technologies currently available or in development; the acquisition of health-related data; the applications of such data, including disease identification and management; clinical trials; the patient perspective; and the issues that must be addressed in the future to permit useful application of mHealth technologies. Additionally, discussion is extended to mHealth facilitation of those comorbidities increasingly recognized to influence arrhythmia management (e.g., obesity and sleep apnea) that are becoming the responsibility of heart rhythm professionals (Chung 2020).

References Section 1

Abraham WT, Adamson PB, Bourge RC, Aaron MF, Costanzo MR, Stevenson LW, ... Yadav JS. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: A randomised controlled trial. Lancet 2011;377:658–666. https://doi.org/10.1016/S0140-6736(11)60103-3.

Chung MK, Eckhardt LL, Chen LY, Ahmed HM, Gopinathannair R, Joglar JA, ... Trulock KM. American Heart Association Electrocardiography and Arrhythmias Committee and Exercise, Cardiac Rehabilitation, and Secondary Prevention Committee of the Council on Clinical Cardiology; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular and Stroke Nursing; and Council on Lifestyle and Cardiometabolic Health. Lifestyle and Risk Factor Modification for Reduction of Atrial Fibrillation: A Scientific Statement from the American Heart Association. Circulation 2020;141:e750–e772. https://doi.org/10.1161/CIR.0000000000000748.

Hindricks G, Taborsky M, Gilksom M, Heinrich U, Schumacher B, Katz A, ... Soegaard P. IN-TIME study group. Implant- based multiparameter telemonitoring of patients with heart failure (IN-TIME): A randomised controlled trial. Lancet 2014;384:583–590.

Slotwiner DJ, Varma N, Akar JG, Annaas G, Beardsall M, Fogel RJ, Yu CM. HRS Expert Consensus Statement on remote interrogation and monitoring for cardiovascular implantable electronic devices. Heart Rhythm 2015;12(7):e69–e100. https://doi.org/10.1016/j.hrthm.2015.05.008.

Turakhia MP, Desai SA, Harrington RA. The outlook of digital health for cardiovascular medicine: challenges but also ex- traordinary opportunities. Journal of the American Medical Association Cardiol 2016;1:743–744.

Varma N, Epstein AE, Irinpen A, Schweikert R, Love C. Efficacy and safety of automatic remote monitoring for implantable cardioverter-defibrillator follow-up. Circulation 2010;122:325–332.

Varma N, Ricci RP. Telemedicine and cardiac implants: What is the benefit? European Heart Journal 2013;34:1885–1895. https://doi.org/10.1093/eurheartj/ehs388.

Varma N, Marrouche NF, Aguinaga L, Albert CM, Arbelo E, Choi JI,... Varosy PD. HRS/EHRA/APHRS/LAHRS/ACC/AHA worldwide practical guidance for telehealth and arrhythmia monitoring during and after a pandemic. Journal of the American College of Cardiology 2020;76:1363–1374. https://doi.org/10.1016/j.jacc.2020.06.019.

https://www.fcc.gov. https://www.fcc.gov/generic/live-questions-you-can-ask-your-doctor-about-digital-health#.hbl.

World Health Organization. mHealth New horizons for health through mobile technologies. Switzerland. 2011. Available at: https://www.who.int/goe/publications/goe_mhealth_web.pdf.

World Health Organization. mHealth: Use of appropriate digital technologies for public health. Switzerland. 2018. Available at: https://apps.who.int/gb/ewha/pdf_files/WHA71/A71_20-en.pdf?ua=1.

2. mHealth Technologies

Dedicated applications and sensors, within or adjunctive to mobile communication devices, enable users to monitor, collect, and share physiologic and health data. Their applications range from diagnostic, decision support, disease management, evaluation of medication adherence, and for educational and clinical research purposes (Figure 1). They synergize naturally with arrhythmia evaluation and extend management to associated comorbidities and lifestyle.

Applications to arrhythmias:

- Diagnostic
  a. Evaluate patients with symptoms suggestive of arrhythmias
b. Assess patients’ response to both pharmacological and invasive treatment of arrhythmias.

- Screening
  a. Increasing emphasis on AF.

2.1. Ambulatory ECG monitoring
This is the cornerstone diagnostic method, and the choice of technique and time frame depend on whether symptoms (e.g., palpitations, syncope) are present and how often they occur (Figure 2). Since the XXI century has become the era of the AF epidemic, the emphasis has shifted to screen for asymptomatic patients at high risk of developing AF or in those with cryptogenic stroke, to enable early treatment with the hope of preventing stroke and other serious complications. Novel tools expand the time window in which information can be gathered and overcome existing limitations with traditional methods, that is, intermittent physical examination or ECG for the detection of a largely asymptomatic arrhythmia.

- Conventional ambulatory ECG devices with “continuous” or “intermittent” recording abilities (e.g., Holter, mobile cardiac telemetry (MCT)) increase the diagnostic yield for suspected arrhythmias, but limitations such as inadequate duration of monitoring, insufficient sensitivity or specificity for AF detection, cost, and patient discomfort and inconvenience remain important implementation barriers. Further details on these conventional systems are available in a prior expert consensus statement (Steinberg 2017).

- Implantable loop recorders (ILRs) continuously monitor cardiac rhythm, similar to traditional external loop recorders, but only record an ECG shortly before and after activation by either the patient or by an automated algorithm. The total monitoring period is limited only by battery longevity (ca. 2-5 years). Newer devices have dedicated algorithms resulting in increased interest in their use for AF detection, especially after cryptogenic stroke.

Several approved ILR devices are available (Musat 2018, Sakhi 2019, Tomson 2015), and several studies have been performed to evaluate the diagnostic accuracy of these devices (Ciconte 2017, Hindricks 2010, Mittal 2016, Nolker 2016, Sanders 2016). Since ILRs are invasive and costly, some functions may shift to mHealth.

2.2. New mHealth-based modalities for arrhythmia monitoring
These can be divided into technologies that:

- Record ECG tracings (single or multilead, in intermittent or continuous format, of various durations).
use non-ECG techniques such as pulse photoplethysmography (PPG).

mHealth tools permit indefinite monitoring and widen application to a range of conditions and patient populations. There has been rapid development and integration of diagnostic sensors into consumer devices such as smartwatches, fitness bands, and smartphones. However, validation of their notified data (or underlying algorithms) and mechanisms for professional review (as established for CIEDs and MCTs) are scant, if at all (See Section 7). This is open to risks of not detecting significant events and/or overtreating—for example, false-positive episodes of AF—if not confirmed by expert physicians.

2.2.1. ECG-based
Among these, handheld and patch systems have undergone the most extensive validation.

2.2.1.1. Handheld devices
Several stand-alone handheld devices operate without additional hardware. These devices with two or three ECG electrodes on either side generate short, 30 sec to 1 minute, single or multilead ECG recordings. Some of them display ECG tracings on a monitor. Most of these devices are equipped with dedicated automatic algorithms for detection of arrhythmias and usually focus on AF. Recognition of AF is usually based on the analysis of RR interval irregularity. The devices can store ECG tracings, which can be uploaded to a computer for review and are usually available for physicians via web-based platforms. Studies across diverse populations have documented the diagnostic accuracy of handheld devices in detection of AF by short-term rhythm monitoring (Desteghe 2017, Doliwa 2009, Hendrikx 2014, Kaasenbrood 2016, Poulsen 2017, Svennberg 2017, Tavernier 2018, Tieleman 2014, Vaes 2014) (Table 2).

References Table 2

| Reference | Title |
|-----------|-------|
| Bumgarner JM, Lambert CT, Hussein AA, Cantillon DJ, Baranowski B, Wolski K, … Tarakji KG. Smartwatch algorithm for automated detection of atrial fibrillation. Journal of the American College of Cardiology 2018;71:2381–2388. https://doi.org/10.1016/j.jacc.2018.03.003. | |
| Chan PH, Wong CK, Poh YC, Pun L, Leung WW, Wong YF, … Siu CW. Diagnostic performance of a smartphone-based photoplethysmographic application for atrial fibrillation screening in a primary care setting. Journal of the American Heart Association 2016;5:e003428. https://doi.org/10.1161/JAHA.116.003428. | |
| Cooke G, Doust J, Sanders S. Is pulse palpation helpful in detecting atrial fibrillation? A systematic review. The Journal of Family Practice 2006;55:130–134. | |
| Doliwa PS, Frykman V, Rosengvist M. Short-term ECG for out of hospital detection of silent atrial fibrillation episodes. Scandinavian Cardiovascular Journal 2009; 43:163–168. | |
| Kearley K, Selwood M, Van den Brul A, Thompson M, Mant D, Hobbs FR, Fitzmaurice D, Heneghan C. Triage tests for identifying atrial fibrillation in primary care: A diagnostic accuracy study comparing single-lead ECG and modified BP monitors. BMJ Open 2014;4:e004565. | |
| Device                      | Author                  | n   | Setting                              | Comparator                          | Sensitivity (%) | Specificity (%) | Requires ECG confirmation |
|-----------------------------|-------------------------|-----|--------------------------------------|-------------------------------------|-----------------|------------------|--------------------------|
| **Handheld devices**        |                         |     |                                      |                                     |                 |                  |                          |
| Pulse palpation             | Cooke, 2006             | 2385| Meta-analysis                        | 12-lead ECG                         | 94              | 72               | +                        |
| Zenicor                     | Doliwa, 2009            | 100 | Outpatient cardiology clinic         | 12-lead ECG interpreted by cardiologist | 96              | 92               |                          |
| MyDiagnostick               | Tieleman, 2014          | 192 | Outpatient cardiology clinic         | 12-lead ECG interpreted by cardiologist | 100             | 96               |                          |
| Omron HCG-801               | Kearley, 2014           | 999 | Primary care practices               | 12-lead ECG interpreted by cardiologist | 94.4            | 94.6             |                          |
| Merlin ECG                  | Kearley, 2014           | 999 | Primary care practices               | 12-lead ECG interpreted by cardiologist | 93.9            | 90.1             |                          |
| **Smartphone ECG device**   |                         |     |                                      |                                     |                 |                  |                          |
| AliveCor Kardia Mobile      | Lau, 2013               | 204 | Recruited patients                  | 12-lead ECG interpreted by cardiologist | 98              | 97               | +                        |
| Smartphone device PPG       |                         |     |                                      |                                     |                 |                  |                          |
| CardioRhythm iPhone         | Chan, 2016              | 1013| Primary care clinic                  | Single-lead AliveCor ECG            | 93              | 98               | +                        |
| PULSE-SMART App             | McManus, 2016           | 219 | Patients undergoing cardioversion   | 12-lead ECG or 3-channel telemetry | 97              | 94               | +                        |
| **Smartwatch ECG**          |                         |     |                                      |                                     |                 |                  |                          |
| FibriCheck App              | Proesmans, 2019         | 223 | Patients undergoing cardioversion   | 12-lead ECG                         | 95              | 97               | +                        |
| KardiaBand automated algorithm | Bumgarner, 2018        | 112 | Patients undergoing cardioversion   | 12-lead ECG                         | 93              | 84               |                          |
| **Blood pressure device**   |                         |     |                                      |                                     |                 |                  | +                        |
| Microlife                   | Wiesel 2009             | 405 | Cardiology outpatients              | 12-lead ECG                         | 95, 97 for one or 3 measurements, respectively | 86, 89 for one or 3 measurements, respectively | +                         |
address the needs of active patients. These vests and elastic bands adapt easily to patients’ movements that is particularly important for those performing physical activities that might be limited by the presence of wires. These biomedical devices capture the electrocardiographic signal via electrodes integrated into the garment that enables noninvasive acquisition of ECG signal up to 30 days. Single/multilead selection (up to full 12-leads) and event activation are available. ECG signals can be stored in memory cards and analyzed afterward as well as transmitted in real time via Bluetooth to a smartphone (and from there to a cloud-based platform), along with other signals including accelerometer and global positioning system (GPS). Other than ECG, some devices provide data on activity intensity, respiratory function, and sleep quality. Automatic analysis with manual verification is possible. Several systems for ECG monitoring based on electrodes incorporated into garments have been introduced into market. Some of them acquire signal from chest belts. Maintaining power presents a challenge. These systems have been tested in athletes, in patients with cryptogenic stroke, and in those with pacemaker-detected AHRE (Eliot 2019, Eysenck 2019, Fabregat 2014, Feito 2019, Pagola 2018).

The wearable cardioverter-defibrillator transmits 2-channel ECG data to an online patient management database allowing for remote monitoring of high-risk patients. Recent incorporation of heart sound evaluation that may predict HF decompensation will be tested in a prospective trial (HEARTIT-Reg trial ClinicalTrials.gov Identifier: NCT03203629).

2.2.1.4. Smartphone and smartwatch-based devices

More recently, nonwearable solutions coupled with the smartphone have emerged. These devices (Table 2 and Varma 2020) allow the user to perform a “spot check” single-lead ECG strip, usually of up to 30 seconds or longer by placing a finger of each hand on the two electrodes, usually located on the phone case or external card (Figure 3). The ECG electrical signal is transmitted wirelessly to a smartphone with an integrated interpretation app. The tracings can be reviewed on the smartphone, electronically stored, or transmitted for review by the user’s provider if desired. These have been directed largely to AF.

Automated algorithms can label the recording as “Possible AF” on the basis of criteria for the presence and absence of a P wave and the irregularity of the RR interval; “Normal” or “Sinus Rhythm” and “Unreadable” when the detector indicates there was too much interference for an adequate recording, whether from too much movement, or poor contact between the electrodes and the patient’s skin. Several versions of the AliveCor’s automated algorithms have been evaluated (Chan 2016, Chan 2017, Desteghe 2017, Lowres 2014, Tarakji 2015), and the device has been tested as a screening tool in at-risk populations.
In Apple watch, the algorithm is effective when the heart rate is between 50 and 150 bpm, there are no or very few abnormal beats, and the shape, timing, and duration of each beat is considered normal for the patient (Figure 4).

Sensitivity and specificity depend on the software (which can be calibrated to higher sensitivity or higher specificity), the population studied (e.g., elderly have more tremor and/or difficulty in holding the device leading to more unreadable tracings), and the prevalence of AF in the population. It indicates that use of such device always requires proper evaluation for every intended use case. There is also an accessory band for a smartwatch to allow ECG recording. The single-lead ECG with automatic AF detection is recorded by touching the band’s integrated sensors that transmit data to a watch application. Recently, a new 6-lead case has been developed, allowing for 30 second recording of all 6 limb leads by touching each of the three electrodes. Also the QT interval may be derived from this (https://cardiacrhythmnews.com/kardiamobile-6l-can-be-used-to-measure-qt-duration-in-covid-19-patients/ (Chung 2015, Garabelli 2016). Information is limited; however, on how parameters such as QTc measured on a single- (or limited number) lead ECGs can reliably substitute for 12-lead ECG information. In one study, QT was underestimated by smartphone single-lead ECG (Koltowski 2019). Preliminary data indicate ability for ST monitoring for ischemia (Figure 3, Section 4.1).

Such devices may be used by clinicians as a point-of-care device to obtain an interpretable rhythm strip in place of a 12-lead ECG. In addition, patients may use these devices for ad hoc or routine evaluation of their rhythm in a home environment. The ECG data can be instantaneously transmitted for automated interpretation with the ability of the consumer to request a physician overread for a surcharge.

- **Limitations**

  a. Single-lead devices, particularly when used by an active person who may not be recumbent, relaxed, or still, may lead to substantial electrical or motion artifact. Noise-free tracing may be more difficult for older patients or those with physical limitations (tremor, stroke, etc).

  b. Although the interpretation algorithms typically have received regulatory oversight, these algorithms can frequently misclassify rhythms, calling sinus rhythm AF and vice versa, which could lead to potential harm without confirmation by a clinician. For example, in a recent study of a consumer ECG device to detect AF, a third of ECGs were unclassifiable by the device but could be classified by experts (Bumgarner 2018). Therefore, some devices have limitations placed on them for diagnostic assessment. For example, the Apple Watch is unable to assess the ECG for AF if the heart rate is above 150 or below 50 bpm (https://www.apple.com/healthcare/docs/site/Apple_Watch_Arrhythmia_Detection.pdf) and is cleared by the U. S. Food and Drug Administration (FDA) only for use in persons without a diagnosis of AF (Figure 4) (https://support.apple.com/en-us/HT208931, accessed January 2, 2020) (See Section 6).

  c. For consumer watches, ECG diagnosis is considered a prediagnostic pending medical verification and not designed to be acted on without clinician review.

  d. ECG classification of other arrhythmias (premature ventricular complexes (PVCs), premature atrial complexes (PACs), ventricular tachycardia (VT) is currently unavailable.

Figure 3  ECG mobile applications. Left—fingertip recordings; Right—card pressed to the chest.
2.2.2. Non-ECG-based

2.2.2.1. Photoplethysmography

Consumer devices such as smartphones and smartwatches require accessories and often extra cost for conversion into rhythm monitoring tools. In contrast, the PPG technologies allow for the detection of arrhythmias using hardware already present on most consumer devices (smartwatches and fitness bands) through a downloadable application. PPG is an optical technique that can be used to detect AF by measuring and analyzing a peripheral pulse waveform. Using a light source and a photodetector, the pulse waveform can be measured by detecting changes in the light intensity, which reflects the tissue blood volume of a skin surface such as the fingertips, earlobe, or face (Conroy 2017, McManus 2013). An automated algorithm can subsequently analyze the generated pulse waveform to detect AF. PPG avoids the instability and motion artifacts of ECG sensors and can be passively and opportunistically measured.

This technology has been applied for use with smartphones using the phone’s camera to measure a fingertip pulse waveform. Rapid irregularly conducted AF may produce variable pulse pressures that challenge detection (Choi 2017). The PPG technology has also been incorporated in smartwatches to measure heart rate and rhythm (Dorr 2019, Guo 2019). Some have developed prototypes of a band that includes a single-channel ECG, multi-wavelength PPG, and tri-axial accelerometry recording simultaneously at 128 Hz (Nemati 2016), and others use a deep-neural network based on PPG sensors to detect AF (https://www.mobihealthnews.com/content/study-apple-watch-paired-deep-neural-network-detects-atrial-fibrillation-97-percent-accuracy; http://www.mrhythmstudy.org). If PPG or optical sensors and detection algorithms can match the performance of ECG-based rhythm assessment, delivery of AF care may be expected to change substantially and drive a radical departure from relying on an office or ambulatory ECG for ascertainment of AF.

2.2.2.2. Oscillometry

Blood pressure (BP) measurements can be erratic when the pulse is irregular. This characteristic is utilized by automatic oscillometric BP monitors that derive heart rhythm regularity algorithmically (Chen 2017). Automated BP monitors have been used for opportunistic AF detection. Studies have shown that six devices from two manufacturers were reliable with sensitivities and specificities greater than 85% (Kane 2016). These studies suggested that BP devices with embedded algorithms for detecting arrhythmias show promise as screening tools for AF, comparing favorably with manual pulse palpation. Such capability could be added to continuous BP recording devices (Kario 2016). One device identifies possible AF when at least two of three consecutive
measurements show pulse irregularity. Several studies addressed the diagnostic accuracy (Chan 2017, Chen 2017, Gandolfo 2015, Kearley 2014, Marazzi 2012, Sergiog 2009, Wiesel 2009, Wiesel 2014) and the feasibility of this device as a screening tool (Chan 2017, Omboni 2016, Wiesel 2017).

The following have undergone preliminary study:

2.2.2.3. Mechanocardiography
Mechanocardiography uses accelerometers and gyroscopes to sense the mechanical activity of the heart. The accuracy of this technology to detect AF using a smartphone’s built-in accelerometer and gyroscope sensors was assessed in a proof of concept study (Jaakkola 2018). A smartwatch (Sony Experia) was placed on the chest in supine patients to detect micro movements of the chest. Possibly, carrying this device in a pocket may have utility but is likely to be confounded by movement (e.g., walking) artifacts.

2.2.2.4. Contactless video plethysmography
Noncontact video monitoring of respiration and heart rate have been developed less than 15 years ago (Takano 2007, Verkruysse 2008). In 2014, a pioneering article described the concept of contactless video-based detection of AF (Coudere 2015). Deep learning of a video of a person’s face can identify AF by examining irregularity of pulsatile facial perfusion (Yan 2018). It is a monitoring technique extracting the photoplethysmographic-like signals from a standard digital RGB video recording of the human skin and specifically of an individual’s face. The videoplethysmographic signal describes the absorption peak of ambient light by the hemoglobin from the facial skin. Several studies have been performed to develop a method that is sensitive enough to detect each cardiac pulse and provide insights into variability on pulse on a beat-to-beat basis. The HealthKam works using HUE color space from video cameras (Dautov 2018, Tsouri 2015) and can easily be integrated to any portable computer device with a camera (smartphone, tablet, etc.). By using mobile devices with cameras, the deployment of the technology is easy and scalable since it does not require the use and distribution of any physical devices. Such a system may change the approach to AF screening, which currently is only 1 patient at a time. High-throughput AF detection from multiple patients concurrently using a single digital camera and a pretrained deep convolutional neural network (DCNN) was feasible in a pilot study (Yan 2020).

Limitations
One requirement for these technologies is steady focus: Thus moving subjects present a challenge. It is important to avoid recording, sending, or communicating any video of the patient thus protecting privacy and dignity.

Video-based technologies in telemedicine have raised a new set of societal and ethical concerns that are being continuously re-evaluated such as during the COVID-19 pandemic. Issues regarding privacy, confidentiality, and legal and ethical obligation to treat are crucial factors to be considered when these technologies are deployed at larger scale (Turakhia 2019).

2.2.2.5. Smart speakers
There are preliminary reports on using commodity smart devices to identify agonal breathing (Chan 2019, Wang 2019). Identification of abnormal heart rate patterns may be made possible by converting smart speakers into a sonar device with emission of in-audible frequencies sound waves and receiving them to detect motion. These are not in consumer domain but potentially have wide scalability.

References Section 2
Ciccone G, Saviano M, Giannelli L, Calovic Z, Baldi M, Ciacco C, … Pappone C. Atrial fibrillation detection using a novel three-vector cardiac implantable monitor: The atrial fibrillation detection study. Europace 2017;19:1101–1108. https://doi.org/10.1093/europace/euw181.
Hindricks G, Pokushalov E, Urban L, Taborsky M, Kuck KH, Lebedev D, … Purërferltn H. XPECT Trial Investigators. Performance of a new leadless implantable cardiac monitor in detecting and quantifying atrial fibrillation: Results of the XPECT trial. Circulation Arrhythmia and Electrophysiology 2010;3:141–147. https://doi.org/10.1161/circep.109.1078758.
Mittal S, Rogers J, Sarkar S, Koehler J, Warman EN, Tomson TT, Passman RS. Real-world performance of an enhanced atrial fibrillation detection algorithm in an implantable cardiac monitor. Heart Rhythm 2016;13:1624–1630. https://doi.org/10.1016/j.hrthm.2016.05.010.
Musat DL, Milstein N, Mittal S. Implantable loop recorders for cryptographic stroke (plus real-world atrial fibrillation detection rate with implantable loop recorders). Cardio Electrophysiology Clinics 2018;10:111–118. https://doi.org/10.1016/j.ccep.2017.11.011.
Nölker G, Mayer J, Boldt L-H, Seidl K, Yan driel V, Massa T, … Lewalter T. Performance of an implantable cardiac monitor to detect atrial fibrillation: Results of the DETECT AF study. Journal of Cardiovascular Electrophysiology 2016;27:1403–1410. https://doi.org/10.1111/jce.13089.
Sakhi R, Thuns DAMJ, Szili-Torok T, Yap SC. Implantable cardiac monitors: Current indications and devices. Expert Review of Medical Devices 2019;16:45–55. https://doi.org/10.1080/17434440.2018.1557046.
Sanders P, Purërferltn H, Pokushalov E, Sarkar S, Di Bacco M, Maus B, Dekker LR. Reveal LINQ Usability Investigators. Performance of a new atrial fibrillation detection algorithm in a miniaturized implantable cardiac monitor: Results from the Reveal LINQ Usability Study. Heart Rhythm 2016;13:1425–1430. https://doi.org/10.1016/j.hrthm.2016.03.005.
Steinberg JS, Varma N, Cygankiewicz I, Aziz P, Balsam P, Baranchuck A, … Piotrowicz R. ISHNE-HRS expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry. Annals of Noninvasive Electrocardiology 2017;22(3):e122447. https://doi.org/10.1111/anec.12447.
Tomson TT, Passman R. The Reveal LINQ implantable cardiac monitor. Expert Review of Medical Devices 2015;12:7–18. https://doi.org/10.1586/17434440.2014.93099.
Varma N, Marrouche NF, Aguinaga L, Albert CM, Choi JI, Varosy PD. HRS/EHRA/APHRS/AJRCC/AHA worldwide practical guidance for telehealth and arrhythmia monitoring during and after a pandemic. Journal of the American College of Cardiology 2020;76:1363–1374. https://doi.org/10.1016/j.jacc.2020.06.019.
Desteghe L, Raymackers Z, Lutin M, Vijn J, Dilling-Boer D, Koopman P, … Heidbuchel H. Performance of handheld electrocardiogram devices to detect atrial fibrillation in a cardiology and geriatric ward setting. Europace 2017;19:29–39. https://doi.org/10.1093/europace/euw025.
Doliva PS, Frykman V, Rosenqvist M. Short-term ECG for out of hospital detection of silent atrial fibrillation episodes. Scandinavian Cardiovascular Journal 2009; 43:163–168. https://doi.org/10.1080/14017430802593435.

Hendriks T, Rosenqvist M, Wester P, Sandstrom H, Hornsten R. Intermittent short ECG recording is more effective than 24-hour Holter ECG in detection of arrhythmias. BMC Cardiovascular Disorders 2014;14:41. https://doi.org/10.1186/1471-2261-14-41.

Kassenbrood F, Hollander M, Rutten FH, Gerhards LJ, Hoes AW. Tielenman RG. Yield of screening for atrial fibrillation in a primary care with a hand-held, single-lead electrocardiogram device during influenza vaccination. Euroacep 2016;18:1514–1520. https://doi.org/10.1038/europace.2016.292.

Poulsen MB, Binici Z, Dominquez H, Soja AM, Krause C, Hornnes AH, ... Overgaard K. Performance of short ECG recordings twice daily to detect paroxysmal atrial fibrillation in stroke and transient ischemic attack patients. International Journal of Stroke 2017;12:192–196. https://doi.org/10.1177/1747493016696883.

Svensen E, Strids M, Engdahl J, Al-Khalili F, Friberg L, Frykman V, Rosenqvist M. Safe automatic one-lead electrocardiogram analysis in screening for atrial fibrillation. European 2017;19:1449–1453. https://doi.org/10.1038/europace.2016.286.

Tavernier R, Wolf M, Katarina V, Philips T, Huys R, Taghii P, ... Duytschaever M. Screening for atrial fibrillation in hospitalised geriatric patients. Heart. 2018;104:588–593. https://doi.org/10.1136/heartjnl-2017-311981.

Tielenman RG, Plantinga Y, Rinkes D, Bartels GL, Posma JL, Cator R, ... Houben RP. Validation and clinical use of a novel diagnostic device for screening of atrial fibrillation. Euroacep 2014;14:1291–1295. https://doi.org/10.1038/europace.2014.057.

Vaes B, Stalpaert S, Tavernier K, Thaels B, Lapere D, Mullens W, Depre G, ... The diagnostic accuracy of the MyDiagnostiek to detect atrial fibrillation in primary care. BMC Family Practice 2014;15:113. https://doi.org/10.1186/1471-2296-15-113.

Barrett PM, Komatireddy R, Haaser S, Topol S, Sheard J, Encina SJ, Topol EJ. Combination of wearable sensors and mobile applications to screen for atrial fibrillation using iPhone ECG in pharmacies. The SEARCH-AF study. Thyromosis and Haemostasis 2014;111:1167–1176. https://doi.org/10.1161/tha.114.003231.

Kolotowski L, Balsam P, Glowerczyńska R, Rokicki JK, Peller M, Maksym J, ... Grabowski M. Kardia Mobile applicability in clinical practice: A comparison of Kardia Mobile and standard 12-lead electrocardiogram records in 100 consecutive patients of a tertiary cardiovascular care center. Cardioiology Journal 2013. https://doi.org/10.5603/CJ.a2013.0001. Jan 15. Online ahead of print.

Tarakji KG, Wazni OM, Callahan T, Kanj M, Hakim AH, Wolski K, ... Lindsay BD. Using a novel wireless system for monitoring patients after the atrial fibrillation ablation procedure: the iTransmit study. Heart Rhythm 2015;12:554–559. https://doi.org/10.1016/j.hrthm.2014.11.015.

Varma N, Marrouche NF, Aguinaga L, Albert CM, Arbelo E, Choi J, ... Varosy PD. HRS/EHRA/APHRS/AHRS/ACC/AHA worldwide practical guidance for telehealth and arrhythmia monitoring during and after a pandemic. Journal of the American College of Cardiology 2020;76:1363–1374. https://doi.org/10.1016/j.jacc.2020.06.019. https://supportapple/en/HT208931.

https://apple.com/healthcare/doc/site/apple/applewatch/arrhythmia/detection

https://cardiachron lynews.com/kardiamobile-6l-can-be-used-to-measure-qt-duration-in-covid-19

2.2.1.2.

Rosenberg MA, Samuel M, Thosani A, Zimetbaum PJ. Use of a noninvasive continuous monitoring device in the management of atrial fibrillation: A pilot study. Pacing and Clinical Electrophysiology 2013;36:328–333. https://doi.org/10.1111/j.1540-8159.2013.007390.

Stelhik J, Schmalffuss C, Bozkurt B, Nativi-Nicolau J, Koomson E, Parwani P, Chohan J, ... The performance of QT interval readings in normal sinus rhythm between a smartphone heart monitor and a 12-Lead ECG for healthy volunteers and inpatients receiving sotalol or dofetilide. Journal of Cardiovascular Electrophysiology 2016;27:827–832. https://doi.org/10.1111/jc.13265.

Doliwa PS, Frykman V, Rosenqvist M. Validity and reliability of the hexoskin wearable 2.2.1.3. Doliwa PS, Frykman V, Rosenqvist M. Short-term ECG for out of hospital detection of silent atrial fibrillation episodes. Scandinavian Cardiovascular Journal 2009; 43:163–168. https://doi.org/10.1080/14017430802593435.

Eckstein J. The AppleWatch as a diagnostic tool: TheSEARCH-AF study. Journal of the American College of Cardiology Clinical Electrophysiology 2019;5:199–208. https://doi.org/10.1016/j.jcellectroph.2019.10.005.

Chen A, Shiu H. Photoplethysmographic sampling frequency: Pilot assessment of how low can we go to analyze pulse rate variability with reliability? Physiological Measurement 2017;38:586–600.

Dörn M, Nothdurft V, Brasier N, Bosshard E, Djurdjevic A, Gross S, ... Eckstein J. The WATCH AF trial: SmartWatches for detection of atrial fibrillation. Journal of the American College of Cardiology Clinical Electrophysiology 2019;5:199–208. https://doi.org/10.1016/j.jacep.2018.10.006.

McManus DD, Chong JW, Soni A, Saczynski JS, Esa N, Napolitano C, ... Chon KH. PULSE-SMART: Pulse-based arrhythmia discrimination using a novel application for the detection of an irregular pulse using an iPhone 4S in patients with atrial fibrillation. Heart Rhythm 2013;10:315–319. https://doi.org/10.1016/j.hrthm.2012.12.001. PMC3698570.

McManus DD, Chong JW, Soni A, Saczynski JS, Esa N, Napolitano C, ... Chon KH. PULSE-SMART: Pulse-based arrhythmia discrimination using a novel application for the detection of an irregular pulse using an iPhone 4S in patients with atrial fibrillation. Pilot study of Crypto-AF registry. International Journal of Cardiology 2018;251:45–50. https://doi.org/10.1016/j.ijcard.2017.10.063.

Papageorge MJ, Juega J, Eshel L, Sushotzki A. CryptoAF investigators. Yield of atrial fibrillation detection with Textile Wearable Holter from the acute phase of stroke: Pilot study of Crypto-AF registry. International Journal of Cardiology 2018;251:45–50. https://doi.org/10.1016/j.ijcard.2017.10.063.

2.2.1.4. Bungarner JM, Lambert CT, Hussein AA, Cantillon DJ, Baranowski B, Wolski K, ... Tarakji KG. Smartwatch al- gorithm for automated detection of atrial fibrillation. Journal of the American College of Cardiology 2018;71:2381–2388. https://doi.org/10.1016/j.jacc.2018.03.003.

Chan PH, Wong CK, Poh YC, Pan L, Leung WW, Wong YF, ... Siu CW. Diagnostic performance of a smartphone-based photoplethysmographic application for atrial fibrillation screening in a primary care setting. Journal of the American Heart Association 2016;5(7):e003428. https://doi.org/10.1161/JAHA.116.003428.

Chung EH, Guise KD. QTC intervals can be assessed with the AliveCor heart monitor in patients on dofetilide for atrial fibrillation. Journal of Electrocardiology 2015; 48:8–9. https://doi.org/10.1016/j.jelecot.2014.10.005.

Destaeghe L, Raymaekers L, Mulin V, Vigen J, Dilling-Boer D, Koopman P, ... Heidbuchel H. Performance of handheld electrocardiogram devices to detect atrial fibrillation in a cardi-ology and geriatric ward setting. European 2017;19:29–39. https://doi.org/10.1038/europace.euw025.

Garabelli P, Stavrakis S, Albert M, Koomson E, Parwani P, Chohan J, ... Po S. Comparison of QT interval readings in normal sinus rhythm between a smartphone heart monitor and a 12-Lead ECG for healthy volunteers and inpatients receiving sotalol or dofetilide. Journal of Cardiovascular Electrophysiology 2016;27:827–832. https://doi.org/10.1111/jc.13265.
Varma et al. 2021 ISHNE/HRS/EHRA/APHRS Collaborative Statement: Digital Medicine and Arrhythmia Management

2.2.2.2.

Chan PH, Wong CK, Pun L, Wong YF, Wong MM, … Siu CW. Head-to-head comparison of the AliveCor heart monitor and microlife WatchBP office AFB for atrial fibrillation screening in a primary care setting. Circulation 2013;135:110–112. https://doi.org/10.1161/CIRCULATIONAHA.112.107256.

Kane SA, Blake JR, McAuley PJ, Langley F, Sims AJ. Opportunistic detection of atrial fibrillation using blood pressure monitors: A systematic review. Open Heart 2016;3:e003632.

Kario K. Evidence and perspectives on the 24-hour management of hypertension: Hemodynamic biomarker-initiated ‘anticipation model’ for zero cardiovascular event. Progress in Cardiovascular Diseases 2016;59:262–281. https://doi.org/10.1016/j.pcad.2016.04.001.

Kearley K, Selwood M, Van den Bruel A, Thompson M, Mant D, Hobbs FR, … Hengsang C. Triage tests for identifying atrial fibrillation in primary care: A diagnostic accuracy study comparing single-lead ECG and modified BP monitors. British Medical Journal Open 2014;4:e004565. https://doi.org/10.1136/bmjopen-2013-004565.

Marazzi G, Iellamo F, Lombardo M, Pelliccia F, Righi D, … Rosano G. Comparison of Microlife BP A200 Plus and Omron M6 blood pressure monitors to detect atrial fibrillation in hypertensive patients. Advances in Therapy 2012;29:64–70. https://doi.org/10.1007/s12325-011-0087-0.

Omboni S, Verberk WJ. Opportunistic screening of atrial fibrillation by a smartphone using facial pulsatile photoplethysmography. Journal of Clinical Hypertension 2016;19:1148–1151. https://doi.org/10.1111/jch.13081.

Gandolfo C, Balestrino M, Bruno C, Finocchi C, Reale N. Validation of a simple method for atrial fibrillation screening in patients with stroke. Neurological Sciences 2015;36:1675–1678. https://doi.org/10.1007/s10072-015-2231-0.

Kearley K, Selwood M, Van den Bruel A, Thompson M, Mant D, Hobbs FR, … Rea T, Gollakota S, Sunshine JE. Contactless Infant Monitoring Using White Noise. https://sites.google.com/a/waterstreet.ucsf.edu/spark-solutions/fi.

Wolf 1991 – 65 years, … Boriani 2005 –). 2.2.2.3.

Jaakkola J, Jaakkola S, Lahdenoja O, Hurnanen T, Koivistoo T, Pankaala M, … Siu CW. Head-to-head comparison of the AliveCor heart monitor and microlife WatchBP office AFB for atrial fibrillation screening in a primary care setting. Circulation 2013;135:110–112. https://doi.org/10.1161/CIRCULATIONAHA.112.107256.

Kim SW, Kang HS, Cho WH, Kim SH, Jeong MG, Kim HW, … Kario K. Evidence and perspectives on the 24-hour management of hypertension: Hemodynamic biomarker-initiated ‘anticipation model’ for zero cardiovascular event. Progress in Cardiovascular Diseases 2016;59:262–281. https://doi.org/10.1016/j.pcad.2016.04.001.

Kearley K, Selwood M, Van den Bruel A, Thompson M, Mant D, Hobbs FR, … Hengsang C. Triage tests for identifying atrial fibrillation in primary care: A diagnostic accuracy study comparing single-lead ECG and modified BP monitors. British Medical Journal Open 2014;4:e004565. https://doi.org/10.1136/bmjopen-2013-004565.

Wiesel J, Arbesfeld B, Schechter D. Comparison of the Microlife blood pressure monitor with the Omron blood pressure monitor for detecting atrial fibrillation. The Journal of Clinical Hypertension 2015;2015:12:195–201.

Dastov R, Savur C, Tsouri G. On the Effect of Face Detection on Heart Rate Estimation in Videoplethysmography. IEEE Western New York Image and Signal Processing Workshop (WNYISPW). https://doi.org/10.1109/wnyispw.2018.8576439.

Takano C, Ohya Y. Heart rate measurement based on a time-lapse image. Medical Engineering & Physics - Journal 2007;29:853–857.

Tsouri GR, Li Z. On the benefits of alternative color spaces for noncontact heart rate measurements using standard red-green-blue cameras. Journal of Biomedical Optics 2015;20:48002.

Turakhia MP. Diagnosing With a Camera From a Distance—Proceed Cautionously and Responsibly. JAMA Cardiology 2020;5(1):107. https://doi.org/10.1001/jamacardiol.2019.4572.

Verkruysse W, Sivasand LO, Nelson JS. Remote plethysmographic imaging using ambient light. Optics Express 2008;16:21343–21445.

Yan BP, Lai WHS, Chan CKY. Au ACK, Freedman B, Poh YC, Poh MZ. High-throughput, contact-free detection of atrial fibrillation from video with deep learning. Journal of the American Medical Association Cardiology 2020;5:105–107. https://doi.org/10.1001/jamacardiol.2019.4004.

Yan BP, Lai WHS, Chan CKY, Chan SC, Chan LH, Lam KM. … Poh MZ. Contact-free screening of atrial fibrillation by a smartphone using facial pulsatile photoplethysmographic signals. Journal of the American Heart Association 2018;9(7):e008585. https://doi.org/10.1161/JAHA.118.008585.

2.2.2.5.

Chan J, Rea T, Gollakota S, Sunshine JE. Contactless cardiac arrest detection using smart devices. NPJ Digital Medicine 2019;2:52. https://doi.org/10.1038/s41746-019-0128-7.

Wang, A., Sunshine, J. E., & Gollakota, S. Contactless infant monitoring using white noise. https://homes.cs.washington.edu/~gshyam/Papers/whitenoise.pdf

3. mHealth Applications for Arrhythmias

Typically, most patients with palpitations and dizziness are evaluated using the various technologies reviewed in Section 2.1 (Steinberg 2017). Devices capable of recording at least one ECG lead allow the interpreting clinician to distinguish between wide and narrow-complex rhythms, bradycardia, and tachycardia, and thus distinguish between the various causative rhythms. Smart devices may be useful in pediatric patients (Grolpper 2018).

3.1. Atrial fibrillation

The disease is often intermittent and asymptomatic, which may delay diagnosis (McCabe 2015, Strickberger 2005, Verma 2013), lead to incorrect estimation of AF burden (Boriani 2015, Garimella 2016), and pose management and sensor technologies have the potential for early identification of AF, opening up opportunities for screening, which then can be tied to evidence-based management. These may be directed to several broad groups: for screening the general population or managing the already diagnosed, for following responses to treatment, and increasingly to managing comorbidities and lifestyle modification (See Section 4) (Figure 5). mHealth mechanisms may facilitate understanding the relation between AF burden, its progression, and cardiovascular risk (Wong 2018).

3.1.1. Undiagnosed atrial fibrillation identification

Classical epidemiological data point to the notion that early identification of AF has the potential to improve morbidity and possibly mortality. (1) AF is associated with a 5-fold increased risk of stroke (Wolf 1991) and doubled mortality (Kirchoff 2016); (2) The prevalence of undiagnosed AF is at least 1.5% for patients > 65 years (Orchard, 2018); (3)
In about a quarter of all AF-related strokes, the stroke is the first manifestation of the arrhythmia (Friberg 2014) while other AF patients present first with congestive HF; (4) Stroke risk is independent of symptoms (Xiong 2015); (5) Diagnosis often requires repeated or prolonged ECG monitoring; and (6) Oral anticoagulants (OACs) are highly effective in reducing the risk of cardioembolic stroke, mortality, and possibly dementia in the setting of AF (Ding 2018, Friberg 2018).

Atrial fibrillation identification depends on factors having to do with the arrhythmia itself, that is the combination of AF prevalence and density (Charitos 2012), and factors associated with detection such as the frequency and duration of monitoring and diagnostic test performance (Ramkumar 2018). Several studies including patients with variable stroke risk factors have used mHealth technologies to identify undiagnosed AF (Tables 2 and 3), but these may require gold-standard ECG confirmation.

Accuracy
The positive predictive value of an AF event will differ according to pretest probability of AF in a given population (e.g., those with an established diagnosis or one or more risk factors). This is especially relevant to “healthy consumers.” Many technologies to identify AF are readily available directly to those without defined disease and are not deployed as individual or public health interventions. Rather, consumers who possess these technologies, such as smartwatches or smartphone-connected ECG recorders, opt into the use of these technologies. Therefore, consumer-driven AF identification is not the same as healthcare-initiated AF screening. AF identification by these devices requires confirmation, since these AF screening tools have variable specificity (Table 2), raising the potential of a high false-positive rate in a low-prevalence population, and risks of unnecessary treatment.

There have been almost 500 studies assessing accuracy of mHealth devices for AF detection, as described in recent systematic reviews (Giebel 2019, Lowres 2019, O’Sullivan 2020). Their capabilities varied according to technologies utilized, settings, and study populations. Two large-scale screening trials were reported recently (See Section 6).

Outcomes
No large outcome trial of screen detected AF and hard endpoints of stroke and death has been conducted as yet.

Although an incidental diagnosis of AF seems to be associated with increased risk of stroke and protection by OAC therapy (Freedman 2016, Martinez 2014, Tsivgoulis 2019), clinical trials to determine any benefit for opportunistically detected AF have not yet been completed but are underway (Gudmundsdottir 2019, Steinhubl 2018, Svennberg 2015, Heartline study https://www.heartline.com). This effort addresses the concern that AF detected by screening may identify inherently lower-risk patients so that efficacy of anticoagulation (and its risk/benefit ratio) requires recalibration. This is necessary prior to issuance of any recommendations. (Currently, no consensus exists yet on how to treat these arrhythmias, even in those with high CHADS-VASc scores).

The European and American guidelines do recommend opportunistic screening for early identification of undiagnosed AF in patients aged ≥65 years (Freedman 2016, January 2019, Kirchhof 2016). On the other hand, the U. S. Preventive Services Task Force has presently given an “insufficient” recommendation for systematic screening for AF with electrocardiograms (Jonas 2018).
| Device                  | Author, year   | Setting                        | Inclusion criteria                                                                 | N   | Mean age (yrs) | Duration of monitoring       | New AF detection (%) |
|-------------------------|----------------|--------------------------------|------------------------------------------------------------------------------------|-----|----------------|-------------------------------|---------------------|
| Handheld ECG device     | Zenicor SL     | Norway systematic              | Age 63-65 yrs, CHADS-VaSC ≥ 2 (M) or ≥ 3 (F)                                      | 1510| 64             | 10 sec Twice daily for 2 weeks| 0.9%                |
|                         | Zenicor SL     | Sweden systematic              | Age 75 to 76 yrs                                                                   | 7173| 75             | 10 sec Twice daily for 2 weeks| 3.0%                |
|                         | Zenicor SL     | Sweden systematic              | Age 75 to 76 yrs, CHADS2 risk score ≥ 2                                           | 403 | 75             | 10 sec Twice daily for 2 weeks| 7.4%                |
|                         | Zenicor SL     | Sweden systematic              | Age 75-76 yrs + NTproBNP ≥ 125 ng/l                                              | 3766| 75             | 10 sec Twice daily for 2 weeks| 4.4%                |
|                         | Zenicor SL     | Sweden Postdischarge           | Recent ischemic stroke/TIA and no prior AF                                         | 249 | 72             | 10 sec                         | 4.8%                |
|                         | My Diagnostick | Sweden                               | Influenza vaccination                                                              | 676 | 74             | 1 min                          | 1.6%                |
|                         | My Diagnostick | Geriatric ward                  | Geriatric                                                                          | 252 | 84             | Daily 1 min during hospitalization (median 5) | 13%                |
| ECG Patch               | ZioPatch iRhythm| STUDY-AF                       | M, age ≥ 65 yrs and ≥ risk factors                                                | 75  | 69             | Two weeks continuous           | 5.3%                |
|                         | ZioPatch iRhythm| National health plan members    | Age ≥ 75 yrs or M ≥ 55/F ≥ 65 yrs + risk factors                                  | 2659| 72             | Continuous 4 weeks             | 2.4%                |
|                         | Zio XT Patch   | ARIC study                      | No prior AF                                                                        | 386 | 79             | Continuous 2-4 weeks           | 2.5% (2 weeks) 4% (4 weeks) |
|                         | Zio Patch      | Multi-Ethnic Study of Atherosclerosis | No prior AF                                                     | 804 | 75             | Continuous 2-4 weeks           | 4% (AF/AFL)        |
| Smartphone ECG-based    | AliveCor Kardia Mobile SL | Australia Pharmacy Opportunistic Study                                      | Age ≥ 65 years                                                                  | 1000| 76             | 30 sec                         | 1.5%                |
|                         | AliveCor Kardia Mobile SL | Hong Kong Outpatient clinic     | Age ≥ 65 years or HTN/diabetes                                                   | 1013| 68             | 30 sec                         | 0.5%                |
|                         | AliveCor Kardia Mobile SL | UK Randomized trial             | Age ≥ 65 years                                                                  | 1001| 73             | 30 sec Twice weekly for 1 year | 3.8%                |
|                         | AliveCor Kardia Mobile SL | Hong Kong Outpatient            | Age ≥ 65 yrs or HTN                                                              | 1013| 68             | 30 sec                         | 0.5%                |
| Smartphone device PPG-based| Huawei wristband (Honor Band 4) or Huawei Watch | General population across China        | Age > 18 yrs                                                                  | 187,912| 35                     | ≥ 14 days                        | 0.23%               |
|                         | Huawei wristband (Honor Band 4) or Huawei Watch | General population across USA       | Age > 22 yrs                                                                  | 419,297| 41                     | Median 117 days                    | 0.52% irregular heart rhythm |
References Table 3

Berger T, Lyngbakken MN, Bøle-Hansen H, Brynildsen J, Pervez MO, Aagaard EN, ... Tveit A. Prevalence of atrial fibrillation and cardiovascular risk factors in a 63–65 years old general popula- tion cohort: The Akerhus Cardiac Disease Examination (ACE) 1950 Study. BMJ Open 2018;8:e021704.

Chan PH, Wong CK, Poh YC, Pun L, Leung WW, Wong YF, ... Sia CW. Diagnostic performance of a smartphone-based photoplethysmographic application for atrial fibrillation screening in a primary care setting. Journal of the American Heart As-
sociation 2016 Jul 21;5(7):e003428. https://doi.org/10.1161/JAHA.116.003428.

Doliwa R, Sobocinski P, Anggadjieh RE, Frykman Kul K, von Arbin M, Wallén L, Rosenqvist M. Improved screening for silent atrial fibrillation after ischaemic stroke. European 2012;2012(14):1112–1116. https://doi.org/10.1093/europace/eur431.

Engdahl J, Andersson L, Mürskaya M, Rosenqvist M. Stepped screening of atrial fibrillation in a 75-year-old population: Implications for stroke prevention. Circulation 2013;127:930–937.

Guo Y, Wang H, Zhang H, Liu T, Liang G, Xia Y, ... Lipp GYH. MAFa II Investigators. Mobile photoplethysmographic technology to detect atrial fibrillation. Journal of the American College of Cardiology 2019;74:2365–2375. https://doi.org/10.1016/j.jacc.2019.08.019.

Halcos JP, Wareham K, Cardew A, Gilmore M, Barry JP, Phillips C, Gravenor MB. Assessment of Remote heart rhythm monitoring using the Alivecor heart monitor to screen for atrial fibrillation: The REHHARSE-AF Study. Circulation 2017;136:1784–1794. https://doi.org/10.1161/CIRCULATIONAHA.117.030583.

Heckbert SR, Austin TR, Jensen PN, Floyd JS, Psaty BM, Soliman EZ, Krommal RA. Yield and consistency of arrhythmia detection with patch electrocardiographic monitoring: The Multi-Ethnic Study of Atherosclerosis. Journal of Electrocardiology 2018;51:997–1002. https://doi.org/10.1016/j.jelectrocard.2018.07.027.

Kaasenbrood F, Hollander M, de Bruijn SHM, Dolmans CPE, Tieleman RG, Hoes AW, Rutten FH. Opportunistic screening versus usual care for diagnosing atrial fibrillation in general practice: A cluster randomized controlled trial. British Journal of General Practice 2020;70(695):e427–e433. https://doi.org/10.3399/bjgp20X708161.

Kemp Gudmundsdottir K, Fredriksson T, Svemberg E, Al-Khalifi F, Friberg L, Frykman V, ... Engdahl J. Stepwise mass screening for atrial fibrillation using N-terminal B-type natriuretic peptide: The STROKEAST II study. European 2020;2020:22:24–32. https://doi.org/10.1093/europace/euz255.

Louters N, Neubeck L, Salkeld G, Kraaij J, McLauchlan AJ, Redfearn J, ... Freedman SB. Feasibility and cost-effectiveness of stroke prevention through community screening for atrial fibrillation using iPhone ECG in pharmacies. The SEARCH-AF study. Thrombosis & Haemostasis 2014;111:1167–1176. https://doi.org/10.11601/h4-03-0231.

Perez MV, Mahaffey KW, Hedlin H, Rumf seld JS, Garcia A, Ferris T, ... Turakhia MP. Large-scale assessment of a swatchwatch to identify atrial fibrillation. New England Journal of Medicine 2019;381:1909–1917. https://doi.org/10.1056/NEJ-
M1901183.

Rooney MR, Soliman EZ, Lutsesy PL, Norby FL, Loehr LR, Mosley TH, ... Chen LY. Prevalence and characteristics of subclinical atrial fibrillation in a community- dwelling elderly populat-ion. Circulation: Arrhythmia and Electrophysiology 2019;12(10):e007390. https://doi.org/10.1161/CIRCEP.119.007390.

Steinhubl SR, Waalen J, Edwards AM, Ariniello LM, Mehta RR, Ebner GS, ... Rosenqvist M. Improved screening for silent atrial fibrillation in high-risk individuals. Journal of the American Heart Association 2018;51:997–1002. https://doi.org/10.1016/j.jelectrocard.2018.07.027.

Svensberg E, Engdahl J, Al-Khalifi F, Friberg L, Frykman V, Rosenqvist M. Mass screening for untreated atrial fibrillation: The STROKEAST study. Circulation 2015;131:2176–2184.

Tavernier R, Wolf M, Kataria V, Philips T, Huys R, Taghi J, ... Duytschaever M. Screening for atrial fibrillation in hospital-ised geriatric patients. Heart 2018;104:588–593. https://doi.org/10.1136/heartjnl-2017-313981.

Tieleman MG, Plantinga Y, Rinkes I, Bartels GL, Posma JL, Cator R, Hofman C, Houben RP. Validation and clinical use of a novel diagnostic device for screening of atrial fibrillation. European 2014;16:1291–1295.

Turakhia MP, Ullal AJ, Hoang DD, Than CT, Miller JD, Friday KJ, ... Heidenreich PA. Feasibility of extended ambula-tory electrocardiogram monitoring to identify si- lent atrial fibrillation in high-risk patients: The Screening Study for Undiagnosed Atrial Fibrillation (STUDY-AF). Clinical Cardiology 2015;2015(30):285–292. https://doi.org/10.1002/clc.22387.

3.1.2. Targeted identification in high-risk individuals

Cryptogenic stroke/TIA

Up to one-third of ischemic strokes is attributed to AF mediated embolism to the brain (Hannon 2010). Further, the risk of recurrent thromboembolism is high if AF is left undetected and untreated (Furie 2012, Kolominsky-Rabas 2001). Hence, prolonged monitoring for AF post-stroke has been recommended in recent guidelines (January 2019, Kirchhof 2016, Schnabel 2019). Detection of AF poststroke depends not only on the monitoring device used and the duration of the monitoring period, but also on stroke type and patient selection; thus, the results of AF detection have been heterogeneous (Kishore 2014, Sanna 2014, Zungsontiporn 2018). A meta-analysis showed that a stepwise approach to AF detection in poststroke patients led to AF detection in 23.7% of patients (Sposato 2015), while a combined analysis of two randomized and two observational studies showed a 55% reduction in recurrent stroke following prolonged cardiac monitoring (Tsivgoulis 2019). However, the optimal AF duration threshold for initiating anticoagulation is currently unknown and may be lower in a poststroke population compared to those with fewer cardiovascular risk factors (Kaplan 2019).

The risk of undiagnosed AF and other sources of thrombosis has been considered high in embolic strokes of unknown source (ESUS), prompting studies that evaluated whether empiric NOAC therapy is more effective than antiplatelet therapy without a requirement of AF detection. Two of these studies, NAVIGATE ESUS (Hart 2018) and RESPECT-ESUS (Diener 2018), have not shown a reduction in recurrent stroke in patients receiving NOACs. It should be emphasized that the mere detection of AF after ESUS is not necessarily proof of positive causation. A third study is ongoing, including patients with suggested atrial myopathy (enlarged atria, increased levels of NTproBNP, or enlarged P waves) (Kamel 2019).

These findings underscore the need for AF detection prior to initiation of OAC therapy in patients with cryptogenic stroke, ESUS, or ischemic stroke of known origin, and mHealth devices can ease the process of detection (Zungsontiporn 2018). The threshold of AF burden may very well differ in patients who have had a suspected cardi-omebolic event and those who have not (Kaplan 2019).

Other high-risk individuals

The key to making AF identification feasible, efficient and clinically valuable is the selection of patients with an increased likelihood of harboring undiagnosed AF, rather than general screening in unsel ected populations. mHealth ECG recorders can facilitate frequent brief (e.g., 30 seconds) recordings over prolonged periods of time by the very ubiquity of devices (including smartphone-based apps or watches). These devices are particularly well suited to capture intermittent or nonpersistent arrhythmias; however, it is likely that frequent sampling would be necessary to capture infrequent paroxysmal AF and even daily “snapshot” ECG monitoring may miss half of AF episodes (Charitos 2012, Yano 2016). AF burden, increasingly recognized as a powerful
independent predictor of stroke (Chen 2018), though accurately measured by implanted devices (Varma 2005), cannot be readily calculated from intermittent ECG data. The use of smartwatches with passive intermittent surveillance using PPG monitoring plus ECG confirmation may be a more effective screening tool and is currently being evaluated (Heartline study https://www.heartline.com).

Formal screening with mHealth ECG recordings has yielded meaningful incidences of newly diagnosed AF, statistically greater than if diagnosis relied only on the office ECG (Table 3). The yield generally is enhanced by the presence of risk factors, such as older age and higher CHA2DS2-VASc scores. Several studies (Chan 2017, Chan 2017a, Proietti 2016) screened untargeted populations, and all yielded new AF diagnoses at a rate under 1%. By focusing on older patients (75–76 years of age) at greater risk, Swedish studies identified new AF in 3% of study participants, and up to 7.4% when additional risk factors beyond age were required (Engdahl 2013, Gudmundsdottir 2019, Svennberg 2015, Lowres et al 2019) in a patient level metanalysis found that new AF detection rate increased progressively with age from 0.34% for <60 years to 2.73% ≥85 years. Importantly, the number of subjects needed to screen to discover AF meeting indications for anticoagulation was 1089 for subjects <60 years but 83 ≥65 years.

3.1.3. Diagnostics in people with established atrial fibrillation

mHealth has important implications for the care of those already diagnosed with AF. Several key characteristics of AF can be measured with long-term continuous or near-continuous monitoring, and the information gained may provide valuable information for patient management.

Furthermore, while several studies succeeded in establishing the sensitivity and specificity of novel devices for the detection of AF, no study to date has yet evaluated the utility of an mHealth intervention in affecting clinical outcomes. The iPhone Helping Evaluate Atrial Fibrillation Rhythm through Technology (iHEART), a single-center, prospective, randomized controlled trial, and the Heartline study seek to accomplish this goal (Caceres 2019, Hickey 2016, https://www.heartline.com).

3.1.4. Atrial fibrillation therapy

Atrial fibrillation burden

Current guidelines for anticoagulation are based principally on the presence of risk factors and a diagnosis of clinical AF, regardless of AF duration, symptomatology, or burden (January 2019). This applies even if the AF has been quiescent for long periods or eliminated altogether as the result of rhythm control interventions including antiarrhythmic drugs, ablation, or risk factor modification (January 2019). However, there is increasing recognition that AF burden matters; for example, paroxysmal events have less thromboembolic risk than persistent AF (Chen 2018). This understanding has been extended during continuous monitoring from CIEDs which depict AF with high granularity, and first advanced the metrics of “AF days” and burden in terms of cumulative load (hours/day) and concentration (density of AF days) (Varma 2005). This measure is likely to be important for understanding mHealth discovered AF.

CIEDS

AF burden can be characterized as %/time monitored, longest duration, and density. Retrieved data provide an insight into natural history and associated sequelae (Healey 2012, Kaplan 2019, Van Gelder 2017, Varma 2005). This led to oral anticoagulation intervention trials to determine the ability to reduce stroke on the basis of AF duration (Lopes 2017, Martin 2015). These suggest that a threshold exists below which the risk of thromboembolic stroke is low and risk–benefit ratio may not justify chronic administration of oral anticoagulants. For instance, CIED data indicate that short subclinical AF events have lesser risk than more prolonged (and therefore more likely to be symptomatic) events (Al-Turki 2019). Device-detected, “subclinical” atrial high-rate episodes (AHRE) lasting 6 minutes to 24 hours are associated with increased stroke risk, but the absolute risk is considerably lower than expected based on risk factors alone (Glotzer 2003, Healey 2012, van Gelder 2017). Whether these require anticoagulation in high-risk individuals is the subject of ongoing studies (Kirchoff 2017, Lopes 2017, van Gelder 2017). Importantly, very short AF episodes (episodes in which both the onset and offset of AT/AF were present within a single EGM recording) were not associated with adverse outcomes (Swiryn 2016) which may be important for mHealth monitoring.

mHealth

AF detection using digital health tools offers further insights in patients without indication for implantable devices. mHealth extends AF screening to younger patients without cardiovascular disease and thromboembolic potential may be low. Those with high AF burden (defined by ≥11.4%; mean duration 11.7 hours) detected on a 14-day patch monitor had an increased thromboembolic event rate compared to those with lower AF burdens (Go 2018). There remains significant treatment variation in use of OAC, especially for device-detected AF (Perino 2019). This may be due to a large clinical uncertainty regarding the optimal cutpoint, even though observational data indicate that OAC is associated with a decreased risk of stroke for episodes > 24 hours and possibly for episodes 6-24 hours (Perino 2019).

Currently, there are no prospectively validated cutpoints or risk models that incorporate AF burden into decision-making for stroke prevention therapies.

Key knowledge gap:

- Identify characteristics (duration, episode number/density) and risk factors that justify anticoagulation for mHealth detected AF.
Rhythm and Rate control

- **Rhythm** While we await data on OAC treatment for mHealth detected AF, the finding of the arrhythmia should initiate mHealth monitoring of NSR retention, QT intervals (important for those on some antiarrhythmic drugs (Garebelli 2016), and discussion of cardiovascular risk factor modification and lifestyle changes, since AF coexists with comorbidities that may influence its occurrence and natural history (See Section 4). Thus, alcohol reduction, treatment of OSA, moderate exercise, and weight loss have been shown to reduce AF burden (Congrète 2018, Kanagalà 2003, Pathak 2015, Voskoboinik 2020).

- **Rate** While the primary goal of rate control is to minimize AF related symptoms, prolonged tachycardia can result in effort intolerance and/or tachycardia-mediated cardiomyopathy while excessively low heart rate targets may increase the risk of bradyarrhythmias that result in symptoms and device implantation. The European Society of Cardiology recommends lenient resting heart rate targets (<100-110), whereas the ACC/AHA/HRS guidelines recommend a target rate of <80 bpm. Often these targets are tailored to the individual patient based on symptoms and presence or propensity for HF. mHealth technologies can be used to assess ventricular rates during AF over long time periods and evaluate the effects of rate-control therapies (January 2019, Kirchoff 2016).

3.2. Sudden cardiac death

(See also Section 4.1 Ischemia).

Ventricular arrhythmias

The use of mHealth technology to diagnose ventricular arrhythmias lags behind its application to AF (See Section 3.1). Detection of symptomatic VT has been reported using the AliveCor cardiac monitor (AliveCor, San Francisco, USA) and SmartWatch (Ringwald 2019, Waks 2015). Sophisticated automated analysis of a 2-minute PPG recording by the camera of a commercially available smartphone (iPhone 4S, Apple) can distinguish between AF, PACs, and PVCs from sinus rhythm, with a sensitivity of 0.733 and specificity of 0.976 for PVCs (Chong 2015, McManus 2016). PVCs may challenge to PPG-based systems, as many PVCs are nonperfusing (Billet 2019). An ECG tracing is therefore essential in order to facilitate rhythm diagnosis and avoid misclassification of “slow PPG pulse rates” (bradysphygymia) simply as “bradycardia.”

Syncope

Syncope presents unique challenges for mHealth applications. While prolonged ambulatory monitoring using medical-grade devices (wearable and implantable) has been the mainstay of cardiac rhythm diagnosis during episodes of syncope, user-activated systems must either be activated by the patient during prodromal symptoms (if present and time permits) in anticipation of syncope, or else incorporate loop recording to allow postsyncope activation (Steinberg 2017). This capability is not incorporated in currently popular consumer-grade wearable devices. However, a randomized controlled trial of AliveCor versus usual care in participants presenting with palpitations or presyncope showed a faster and increased rate of detection of symptomatic arrhythmias in the intervention group, suggesting that at least in presyncope, patient-activated rhythm detection using a commercially available mHealth device is productive (Reed 2019). Rhythms reported by devices that rely on heart rates will likely require validation with a medical-grade system to provide an ECG tracing during an event to allow determination of the causative rhythm.

There is a significant overlap between transient loss of consciousness and mechanical falls due to orthostatic intolerance, neurologic, or orthopedic problems. This is particularly disabling in elderly subjects and often unnoticed (Davis 2010, Heinrich 2010). Mobile applications that combine analysis of heart rate monitoring together with fall detection, GPS positioning, video recording with display of patients’ surroundings, and the capability to send alerts either triggered by patients in case of symptoms or automatically in case of detected falls, may be useful.

Cardiac arrest

The detection and response to sudden cardiac arrest (SCA) is an area where mHealth applications may prove lifesaving. As rapid treatment for cardiac arrest has consistently been associated with improved survival, preemptive identification of at-risk persons, detection of cardiac arrests, alerting of nearby lay and professional first responders, and coaching or quality assurance in the performance of cardiopulmonary resuscitation (CPR) are ideally suited to the mHealth paradigm in societies where mobile smartphones are ubiquitous.

Prediction

It is possible that mHealth devices which continuously monitor heart rhythm and other physiologic data may be able to better predict impending SCA, even using measures which have not shown sufficient specificity or sensitivity when measured intermittently, such as heart rate variability (Lee 2016). However, such continuous monitoring is present already in CIEDs and has not yet proven to be sufficiently predictive to be clinically useful (Au-Yeung 2018). Therefore, the prediction of SCA by mHealth devices, while a tantalizing prospect, remains to be realized.

Notification and reaction

Once cardiac arrest occurs, rapid identification is essential to trigger a response by emergency responders. Wearable devices that combine physiologic monitoring, GPS, and a method of communication with emergency services such as cellular service are well positioned to provide almost instantaneous alert as well as location information (Kwon 2019, Praveen 2019). An early device using a piezoelectric sensor to detect the pulse was capable of transmitting an alert to emergency medical system or other responders when a pulse was not detected and the watch (and thus the wearer) was still (Richard 2011). Preliminary reports indicate that smart speakers in commodity smart devices may be able...
to identify agonal breath patterns for sudden cardiac death detection (Chan J 2019). Widespread diffusion of such technology to patients at elevated risk of SCA will be necessary before any potential benefits can be tested.

The ubiquity of mobile phones in society leads to more rapid notification of emergency services, and the possibility of a dispatcher gathering information from a bystander at the patient’s side and delivering instructions on care, such as CPR. This was associated with improved outcomes for a variety of emergencies (Wu 2012). Notification of lay responders in the vicinity of a cardiac arrest is also feasible with current technology. A blinded, randomized trial conducted in Stockholm, Sweden, demonstrated that such a system improved the rate of bystander CPR (Ringh 2015). However, almost 10,000 volunteers were recruited over approximately 18 months, during which 667 activations occurred, emphasizing the large resources needed and the low rate of utilization of trained volunteers, even when alerted by mobile phone.

Whether a trained or novice bystander responds, mobile devices may be further useful to provide voice (or video) instructions from a dispatcher or from the device itself. Studies of prerecorded audio, live video, and animation-based instruction have shown improvements in some aspects of CPR delivery and AED use, although technology continues to evolve (Bolle 2009, Choa 2008, Merchant 2010, You 2008). One limitation is that as such apps are unregulated, many do not convey current basic life support algorithms and may have poor usability (Kalz 2014). In addition, delay in commencing CPR and in calling emergency services due to distraction of the rescuer by using an app is a concern (Paal 2012).

Automated external defibrillator (AED) use in cardiac arrest is associated with improved survival, but AED use remains low (Weisfeldt 2010). Mobile devices have the potential to increase this by assisting with the retrieval and use of AEDs. Multiple apps have been created to locate AEDs in the vicinity of the user, although with mixed results in simulations (Sakai 2011, Hatakeyama 2018, Neves Briard 2019). Barriers include the accuracy of AED location databases, size of the user base, app interface, and the availability of multiple apps instead of a single validated regional, national, or international standard. An emerging approach to circumvent these limitations is the dispatch of an AED via a drone to the location of the cardiac arrest, which is expected to reduce time to defibrillation, especially in rural areas (Boutilier 2017). Feasibility has been demonstrated (Claesson 2017).

Clinical trial
The complete chain from activation of citizen responders was tested in the Heartrunner trial (Andelius 2020) in a region of almost 2 million inhabitants. Results showed that citizen responders arrived before emergency services 42% of out of hospital cardiac arrests, accompanied by a threefold increase in bystander defibrillation with a trend to improved 30-day survival. Results were more pronounced when emergency arrival times were longer, for example, in rural areas.

References Section 3
Gropler MR, Dalal AS, Van Hare GP, Silva JNA, Can smartphone wireless ECGs be used to accurately assess ECG intervals in pediatrics? A comparison of mobile health monitoring to standard 12-lead ECG. PLoS One 2018;13:e0204403. https://doi.org/10.1371/journal.pone.0204403.

Steinberg JS, Varma N, Cygankiewicz I, Aziz P, Balsam P, Baranchuk A, ... Piotrowski R. 2017 ISHNE-HRS expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry. Annals of Noninvasive Electrocardiology 2017;22:e12447. https://doi.org/10.1111/anec.12447.

3.1
Boriani G, Laroche C, Diemberger I, Fantechi E, Popescu MI, Rasmusson LH, ... Lip GY. Asymptomatic atrial fibrillation: clinical correlates, management, and outcomes in the EORP-AF Pilot General Registry. The American Journal of Medicine 2015;128:509–518.e2.

Garinemilla RS, Chang EH, Mounsey JP, Schwartz JD, Purcell I, Ghei AK. Accuracy of patient perception of their prevailing rhythm: A comparative analysis of monitor data and questionnaire responses in patients with atrial fibrillation. Heart Rhythm 2015;12:658–665.

McCabe PJ, Chamberlain AM, Rudy L, DeVon HA. Symptom recognition and treatment-seeking prior to diagnosis of atrial fibrillation. Western Journal of Nursing Research 2015;38:1102–1115.

Steckberger SA, Ip J, Sakena S, Curry K, Bahnson TD, Ziegler PD. Relationship between atrial tachyrhythmias and symptoms. Heart Rhythm 2005;2:125–131.

Verma A, Champagne J, Sapp J, Essebag V, Novak P, Skanes A, ... Birnie D. Discounting the incidence of symptomatic and asymptomatic episodes of atrial fibrillation before and after catheter ablation (DISCERN AF): A prospective, multicenter study. Journal of the American Medical Association Internal Medicine 2013;173:149–156. https://doi.org/10.1001/jamainternmed.2013.1561.

Wong JA, Cone D, Van Gelder I, McIntyre WF, Crijns HJ, Wang J, ... Healey JS. Progression of device-detected subclinical atrial fibrillation and the risk of heart failure. Journal of the American College of Cardiology 2018;71:2603–2611.

3.1.1
Charitos EJ, Sterie U, Ziegler PD, Balewish M, Robinson DR, Sievers HH, Hanke T. A comprehensive evaluation of rhythm monitoring strategies for the detection of atrial fibrillation recurrence: Insights from 647 continuously monitored patients and implications for monitoring after therapeutic interventions. Circulation 2012;126:806–814. https://doi.org/10.1161/CIRCULATIONAHA.112.098079.

Ding M, Qiu C. Atrial fibrillation, cognitive decline, and de mentia: An epidemiologic review. Current Epidemiology Reports 2018;5:252–261. https://doi.org/10.1007/s40471-018-0159-7.

Freedman B, Potpara TS, Lip GY. Stroke prevention in atrial fibrillation. Lancet 2016;388:806–817. https://doi.org/10.1016/S0140-6736(16)31257-0.

Freedman B, Camm J, Calkins H, Healey JS, Rosenvist M, Wang J, ... Yan BP. A Report of the AF-SCREEN International Collaboration. Circulation 2017;135:1851–1867.

Friberg L, Rosenvist M. Less dementia with oral anticoagulation in atrial fibrillation. European Heart Journal 2018;39:453–460. https://doi.org/10.1093/eurheartj/ehy369.

Friberg L, Rosenvist M, Lindgren A, Torét A, Norrving B, Asplund K. High prevalence of atrial fibrillation among patients with ischemic stroke. Stroke 2014;45:2599–2605. https://doi.org/10.1161/STROKEAHA.114.006070.

Gielb GD, Gissel C. Accuracy of mHealth devices for atrial fibrillation screening: Systematic review. JMIR Mhealth Uhealth 2019;7:e13641. https://doi.org/10.2196/13641.

Gudmundsdottir K, Fredriksson T, Svensberg E, Al-Khalili F, Friberg L, Frykman V, ... Engdal J. Stepwise mass screening for atrial fibrillation using N-terminal B-type natriuretic peptide: the STROKESTOP II study. European 2020;22:24–32. https://doi.org/10.1093/europace/euz255.

January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC, ... Yancy CW. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration With the Society of Thoracic Surgeons. Circulation 2019;140:e125–e151. https://doi.org/10.1161/CIR.0000000000006665.

Jonas DE, Kahwati LC, Yun JDY, Middleton JC, Coker-Schwimmer M, Asher GN. Screening for atrial fibrillation with electrocardiography: Evidence report and systematic review for the US preventive services task force. Journal of the American Medical association 2018;320:459–498. https://doi.org/10.1001/jama.2018.4180.

Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadesus B, ... Vardas P. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS: The Task Force for the management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the
European Heart Rhythm Association (EHRA) of the ESC. Endorsed by the European Stroke Organisation (ESO). European Heart Journal 2016;37:2893–2962. https://doi.org/10.1093/eurheartj/ehw210.

Lowres N, Olivier J, Chao TF, Chen SA, Chen Y, Diederichsen A, … Freedman B. Estimated stroke risk, yield, and number needed to screen for atrial fibrillation detected through single time screening: a multicountry patient-level meta-analysis of 141,220 screened individuals. PLoS Medicine 2019;16:e1002903. https://doi.org/10.1371/journal.pmed.1002903.

Martinez C, Katholing A, Freedman SB. Adverse prognosis of incidentally detected atrial fibrillation. A cohort study. Thrombosis and Haemostasis 2014;112:276–286.

Orchard JN, Neuback L, Freedman B, Webster R, Patel A, Gallagher R … Lowres N. Atrial fibrillation: screening, management and guideline recommended therapy (AF SMART II) in the rural primary care setting: An implementation study protocol. British Medical Journal Open 2018;8:e023130. https://doi.org/10.1136/bmjopen-2018-023130.

O’Sullivan JW, Grigg S, Crawford W, Turakhia MP, Perez M, Ingelsson E, … Ashley EA. Accuracy of smartphone cam- era applications for detecting atrial fibrillation: A systematic re- view and meta-analysis. Journal of the American Medical Association Netw Open 2020;3:e202064. https://doi.org/10.1001/jamanetworkopen.2020.2064.

Ramkumar S, Nerlick N, d’Souza D, Pol DJ, Kalman JM, Marwick TH. Atrial fibrillation detection using single lead portable electrocardiographic monitoring: A systematic review and meta-analysis. British Medical Journal Open 2018;8:e024178. https://doi.org/10.1136/bmjopen-2018-024178.

Steinhubl SR, Waalen J, Edwards AM, Amielli LM, Mehta RR, Ebner GS, … Turakhia MP. Effect of wearable continuous 24-hour patch on detection of undiagnosed atrial fibrillation: The mTePS randomized clinical trial. Journal of the American Medical Association 2018;320:146–155.

Svensen E, Engdahl J, Al-Khalifi F, Friberg L, Frykmann V, Rosenqvist M. Mass screening for untreated atrial fibrillation: THE STROKESTOP study. Circulation 2015;131:2176–2184.

Tsivgoulis G, Katsanos AH, Köhrmann M, Caso V, Perren F, Paladimos L, … Alexandrov AV. Duration of implantable cardiac monitoring and detection of atrial fibrillation in ischemic stroke patients: A systematic review and meta-analysis. Journal of Stroke 2019;21:302–311. https://doi.org/10.5853/jos.2019.01067.

Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The Framingham Study. Stroke 1991;22:983–988.

Xiong Q, Proietti M, Senos K, Lip GY. Asymptomatic versus symptomatic atrial fibril- lation: A systematic review of age/gender differences and cardiovascular outcomes. International Journal of Cardiology 2015;191:172–177. https://doi.org/10.1016/j.ijcard.2015.05.011.

https://www.heartline.com/
patients with de-vice-detected sub-clinical atrial fibrillation (ARTESIA) trial. American Heart Journal 2017;189:137–145.

Martin DT, Berson MM, Waldo AL, Watten MS, Choucri WK, Lip GY, ... Halperin JL. IMPACT investigators randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices. European Heart Journal 2015;36:1660–1668.

Pathak RK, Middeldorp ME, Meredith M, Mehta AB, Mahajan R, Wong CX, ... Sanders P. Long-term effect of goal-directed weight management in an atrial fibrillation cohort: A long-term follow-up study (LEGACY). Journal of the American College of Cardiology 2015;65:2159–2169. https://doi.org/10.1016/j.jacc.2015.03.002.

Perino AC, Fan J, Askari M, Heidenreich PA, Keung E, Raitt MH, ... Turakhia MP. Practice variation in anticoagulation prescription and outcomes after device-detected atrial fibrillation. Circulation 2019;139:2502–2512. https://doi.org/10.1161/CIRCULATIONAHA.118.038989.

Swiryn S, Orlov MV, Benditt DG, D’Maffeo JP, Lloyd-Jones D, Karst E, ... Waldo AL. Clinical implications of brief de-vice-detected atrial tachyarrhythmias in a cardiac rhythm manage-ment device population: Results from the registry of atrial tachycardia and atrial fibrillation episodes. Circulation 2016;134:1130–1140. https://doi.org/10.1161/CIRCULATIONAHA.115.020252.

Van Gelder IC, Healey JS, Crijns H, Wang J, Hohnloser SH, Gold MR, Connolly SJ. Duration of device-detected sub-clinical atrial fibrillation and occurrence of stroke in ASSERT. European Heart Journal 2017;38:1339–1344.

Varma N, Stambler B, Chan S. Detection of atrial fibrilla- tion by implanted devices with wireless data transmission capability. Pacing and Clinical Electrophysiology 2005;28(Suppl 1):S133–S136.

Voskoboinik A, Kalman JM, De Silva A, Nicholls T, Costello B, Nanayakkara S, ... Kirol P. T. Alcohol abstinence in drink-ers with atrial fibrillation. New England Journal of Medicine 2020;382:20–28. https://doi.org/10.1056/NEJMoA181759.

3.2 Andelius L, Hansen MC, Lippert FK, Karlsson L, Torp-Pedersen C, Kjar Erboll A, ... Folke F. Smartphone activation of citizen responders to facilitate defibrillation in out-of-hospital cardiac ar-rest. Journal of the American College of Cardiology 2020;76:64–73. https://doi.org/10.1016/j.jacc.2020.04.071.

Au-Yeung WM, Reinhall PG, Bardy GH, Brunston SL. Development and validation of warning system of ventricular tachyarrhythmia in patients with heart failure with heart rate variability data. PloS One 2018;13:e0207215.

Billett S, Rollin A, Mondoly P, Monteil B, Fournier P, Caruio E, ... Maury P. Hemodynamic consequences of premature ven-tricular contractions: Association of me-chanical bradycardia and postextrasystolic potenti-ation with premature ventricular contraction-induced cardiomyopathy. Heart Rhythm 2019;16:853–860.

Bolle SR, Scholl J, Gilbert B. Can video mobile phones improve CPR quality when used for dispatcher assistance during simulated cardiac arrest? Acta Anaesthesio-logica Scandinavica 2009;53:116–120.

Boultilier JJ, Brooks SC, Janmohamed A, Byers A, Buick JE, Zhan C, ... Chan TCY. Optimizing a drone network to deliver automated external defibrillators. Circulation 2017;135:2454–2465.

Claes L, Buckman A, Siegel M, Svensson L, Nordberg P, Djivar T, Hollenberg J. Time to delivery of an automated external defibrillator using a drone for simulated out-of-hospital cardiac arrests vs emergency medical services. Journal of the American Medical Association 2017;317:2332–2334.

Chan J, Rea T, Gollakota S, Sunshine JE. Contactless cardiac arrest detection using smart devices. NPJ Digital Medicine 2019;2:52. https://doi.org/10.1038/s41746-019-0128-7.

Chou M, Park J, Chung HS, Yoo SK, Shum H, Kim S. The effectiveness of cardiodi- monary resuscitation instruction: Animation versus dispatcher through a cellular phone. Resuscitation 2008;77:87–94.

Chong JW, Esa N, McNamus DD, Chen KH. Arrhythmia discrimination using a smart phone. IEEE Journal of Biomedical and Health Informatics 2018;19:815–824.

Davis JC, Robertson MC, Ashle MC, Lui-Ambrose T, Khan KM, Marra CA. Interna-tional comparison of cost of falls in older adults living in the community: A system-atic review. Osteoporosis International 2010;21:1295–1306.

Hatakeyama T, Nishiyama C, Shimamoto T, Kiyohara K, Kiguchi T, Chida L, ... Iwami T. A smartphone application to reduce the time to automated external defibril-lator delivery after a witnessed out-of-hospital cardiac arrest: A randomized simulation-based study. Simulation in Healthcare 2018;13:387–393.

Heimrich S, Rapp K, Russmann U, Becker C, König HH. Cost of falls in old age: A system-atic review. Osteoporosis International 2010;21:891–902.

Kal M, Lommer N, Felzen N, Laverman R, Tabuenca B, Specht M, Skorning M. Smartphone apps for cardiopulmonary resus-citation training and real incident support: A mixed-methods evalua-tion study. Journal of Medical Internet Research 2014; 16:e89.

Kwon JM, Lee Y, Lee Y, Lee S, Park J. An algorithm based on deep learning for pre-dicting in-hospital cardiac arrest. Journal of the American Heart Association 2018; 7:e008678. https://doi.org/10.1161/JAHA.118.008678.
Lee H, Shin SY, Seo M, Nam GB, Joo S. Prediction of ventricular tachycardia one hour before occurrence using artificial neural networks. Scientific Reports 2016; 6:32390.

McManus DD, Chong JW, Soni A, Saczynski JS, Esa N, Napolitano C, … Chon KH. PULSESMArt: Pulse-based arrhythmia discrimination using a novel smartphone application. Journal of Cardiovascular Electrophysiology 2016;27:51–57.

Merchant RM, Abella BS, Abousleme AJ, Smith TM, Long JA, Truide ME, Asch DA. Cell phone cardioptilmon- nary resuscitation: Audio instructions when needed by lay rescuers: A randomized, controlled trial. Annals of Emergency Medicine 2010; 55:538–543.

Neves Briard J, Grou-Boileau F, El Bashalty A, Spennard C, de Champlain F, Homier V. Automated external defibrillator geolocation with a mobile application, verbal assistance or no assistance: A pilot randomized simulation (AED G-MAP). Prehospital Emergency Care 2019;23:420–429.

Paal P, Pircher I, Baar T, Gruber E, Strasak AM, Herff H, … Mitterlechner T. Mobile phone-assisted basic life support augmented with a metronome. Journal of Emergency Medicine 2012;43:472–477.

Praveen Kumar D, Ampoth T, Annavarapu CSR. Machine learning algorithms for wire- less sensor networks: A survey. Information Fusion 2019;49:1–25.

Reed MJ, Grubb NR, Lang CC, O’Brien R, Simpson K, Padarenga M, … Coats T. Multi-centre randomised controlled trial of a smartphone-based event recorder alongside standard care versus standard care for patients presenting to the emergency depart- ment with palpitations and pre-syncope: The IPED (Investigation of Palpitations in the ED) study. EClinicalMedicine 2019;8:37–46.

Rickard J, Ahmed S, Barach M, Klockman B, Martin DO, Menon V. Utility of a novel watch-based pulse detection system to detect pulselessness in human subjects. Heart Rhythm 2011;8:1895–1899.

Ringu M, Rosenqvist M, Hollenberg J, Jonsson M, Fredman D, Nordberg P, … Svensson L. Mobile-phone dispatch of laypersons for CPR in out-of-hospital cardiac arrest. New England Journal of Medicine 2015;372:2316–2325.

Ringwald M, Chirch A, Bysard N. Smart watch record- ing of ventricular tachycardia: Case study. The American Journal of Emergency Medicine 2019;38(4). 849.e3–849.e5.

Sakai T, Iwami T, Kitamura T, Nishiyama C, Kawamura T, Kajino K, … Shimazu T. Effectiveness of the new “Mobile AED Map” to find and retrieve an AED: A randomized controlled trial. Resuscitation 2011;82:69–73.

Steinberg JS, Varma N, Cygankiewicz I, Aziz P, Balsam P, Baranchuk A, … Piotrowicz R. 2017 ISHNE-HRS expert consensus statement on ambulatory ECG and external cardiac moni- toring/telemetry. Annals of Noninvasive Electrocardiology 2017;22:e12447. https://doi.org/10.1111/anec.12447.

Waks JW, Fein AS, Das S. Wide complex tachycardia recorded with a smartphone car- dio rhythm monitor. Journal of the American Medical Association Internal Med- icine 2015;175:437–439.

Weisfeldt ML, Siftani CM, Ornato JP, Rea T, Aufderheide TP, Davies D, … Morrison LJ. Survival after application of auto- matic external defibrillators before arrival of the emergency medical system: Evaluation in the resuscitation out-commo nizarion popu- lation of 21 million. Journal of the American College of Cardi- ology 2010;55:1713–1720.

Wu O, Briggs A, Kemp T, Gray A, MacIntyre K, Rowley J, Willeit K. Mobile phone use for contacting emergency services in life threatening circumstances. Journal of Emergency Medicine 2012;42:291–298.

You JS, Park S, Chung SP, Park JW. Performance of cellular phones with video telephony in the use of automated external defibrillators by untrained laypersons. Emergency Medicine Journal 2008;25:597–600.

4. Comorbidities
A large proportion of arrhythmias are influenced by coexisting conditions. Their management may directly affect arrhythmia recurrence and outcome. Thus, lifestyle modifications and management of comorbid conditions (Figure 5) is becoming an objective of arrhythmia management (Chung 2020) and received a Class 1 recommendation in most recent guidelines (January 2019). mHealth has significant potential for facilitating these interventions (Figure 6).

4.1. Ischemic heart disease
Early management (e.g., primary angioplasty) of acute ischemic syndromes may reduce infarct territory and ventric- ular arrhythmias, thereby improving outcome. AF after myocardial infarction worsens prognosis (Pizzetti 2011).

At home
ST segment monitoring technology embedded in conventionally indicated ICDs when tested in a randomized cross-over study suggested a reduction in the time from the onset of ischemia to presentation to hospital (Gibson 2019, Holmes DR Jr 2019). The AngelMed Guardian system (Angel Medical Systems, Eatontown, New Jersey) is approved for use in the United States for patients with prior acute coronary syndrome (ACS) who remain at high risk for recurrent ACS. For lower-risk patients, mHealth may...
improve symptom recognition and earlier presentation, that is, “symptom-to-door time” (Moser 2006).

Wearable devices that continuously monitor physiologic data promise detection, and possibly pre-emption, of the early stages of MI, by alerting patient and/or healthcare team early. A noninvasive device consisting of a three-lead ECG linked wirelessly to a dedicated mobile device has recently been described (Van Heuverswyn 2019). Three lead ECG tracings (as well as derived augmented limb leads) can be recorded with commercially available smartwatches (Avila 2019). Limitations of this approach are the need for the patient or a bystander to possess the device or app, and be familiar with its use, before the onset of symptoms.

An emerging technology (www.heartbeam.com) uses a credit card sized device that is pressed against the user’s chest (Figure 3). It collects ECG signals using a novel 3D vector approach. The signals are sent to the cloud, where they are analyzed and compared to the patient’s asymptomatic baseline reading. A proprietary algorithm combines the signal analysis with the patient’s history and reported symptoms. This information, along with a diagnostic recommendation and ECG waveforms, is sent to the patient’s physician, who makes a final determination and informs the patient. This system is used by patients in the telehealth setting to assess whether chest pain is the result of an myocardial infarction.

Emergency teams

The next step of patient care involved transmission of ECGs by emergency responders in the field to hospitals for review and triage and was shown to result in shorter door-to-balloon time, lower peak troponin and creatine phosphokinase levels, higher postinfarction left ventricular ejection fraction, and shorter length of stay compared with control patients whose ECGs were not transmitted (Clemmensen 2010, Sanchez-Ross 2011). This paradigm has now been widely implemented. Technical factors, such as transmission failure and lack of network coverage, are the main impediments to adoption of such systems.

Post-hospital care

This is often confusing for patients, who often exhibit a poor understanding of their medications, follow-up procedures, and future appointments (Horwitz 2013; Ziaeian 2013). This contributes to frequent hospital readmissions. Mobile technologies may enable individualized contact between patients and healthcare providers. Phone calls led to a modest improvement in medication adherence in patients with coronary artery disease in one large randomized controlled trial (Vollmer 2014). Text messaging was shown to increase medication adherence and improved cardiovascular risk factors (Chow 2015; Unal 2018). Available evidence is limited by short-term follow-up and self-reported adherence (Shariful Islam 2019). Success may depend on personalized messages with tailored advice, the ability to respond to texts, timing messages to coincide with medication doses, higher frequency of messages, and the use of additional apps or websites (Park 2014). Interoperability with the EMR may facilitate this approach.

Cardiac rehabilitation

This was shown to improve health outcomes among patients with heart disease, but is underutilized. The Million Hearts Cardiac Rehabilitation Collaborative aims to increase participation rates to \( \geq 70\% \) by 2022 (Ritchey 2020). Mobile apps and linked sensors to measure heart rate, respiration rate, and exercise parameters may overcome traditional limitations of availability, cost, and convenience and be more acceptable to some patients (Zwisler 2016). A randomized controlled trial center-based and mobile rehabilitation found improved uptake, adherence, and completion with home-based cardiac rehabilitation in postinfarction patients (Varnfield 2014) (See also Section 4.2.2.).

4.2. Heart failure

Heart failure is widely prevalent, costly to manage, and degrades patient outcomes (Benjamin 2017, Albert 2019). HF may trigger AF and ventricular arrhythmias. Conversely, AF may precipitate HF. Remote monitoring of, for example, dietary and medication adherence (See Section 4.6.2), detection of arrhythmias (See Section 3), intercurrent ischemia (See Section 4.1), orthopnea, changes in heart rate, activity, and sleep (See Section 4.5) may enable remote adjustment of management to reduce emergency department visits and unplanned HF-related hospitalizations. If scalable, remote monitoring coupled with mobile communication could prove to reduce costs associated with HF.

Despite promise, most large, multicenter randomized trials failed to demonstrate improved outcomes of remote monitoring in HF patients (Table 4) (Boyne 2012, Chaudhry 2010, Dickinson 2018, Koehler 2011, Ong 2016, Takahashi 2012). Combination algorithms based on multiple parameters may be valuable (Ono 2017). One trial stands out. The TIM-HF2 trial randomized HF patients to either remote patient management plus usual care or to usual care only and were followed up for over a year (Koehler 2018). The results showed reduction in the combined endpoint of percentage of days lost due to unplanned hospitalization and all-cause mortality. However, cardiovascular mortality was similar between remote monitoring and standard care groups. Implanted devices that monitor pulmonary arterial pressure may be beneficial in select patients when used in structured programs (Dickinson 2018). The positive findings of the CHAMPION trial (CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Functional Class III Heart Failure Patients) trial and subsequent FDA approval has renewed interest in remote patient management for HF patients (Abraham 2016, Carbo 2018, Desai 2017). This requires daily download of hemodynamic data and a pre specified medical treatment plan. An app is also available which illustrates patient compliance with monitoring, alerts the
patient when transmissions are not received, shows medication reminders, and allows for medication reconciliation and titration.

References Table 4

Boyne JJ, Vrijhofd HJ, Crijns HJ, De Weerd G, Kragten J, Gorgels AP, investigators TEHAF. Tailored telemonitoring in patients with heart failure: Results of a multicentre randomised controlled trial. European Journal of Heart Failure 2012;14:791–801.

Chaudhry SI, Mattera JA, Curtis JP, Speratus JA, Herrin J, Lin Z, … Krumholz HM. Telemonitoring in patients with heart failure. New England Journal of Medicine 2010; 363:2301–2309.

Koehler F, Winkler S, Schieber M, Sechtem U, Stangl K, Böh m M, … Anker SD. Telemedical Interventional Monitoring in Heart Failure Investigators. Impact of remote telemedical management on mortality and hospitalizations in ambulatory patients with chronic heart failure: The Telemedical Interventional Monitoring in Heart Failure study. Circulation 2011;123:1873–1880.

Ong MK, Romano PS, Edgington S, Aronow HU, Auerbach AD, Black JT, … Pham M. Continuous wearable monitoring analytics predict heart failure hospitalization. Circulation 2020;131:e006513. https://doi.org/10.1161/CIRCHEARTFAILURE.119.006513.

4.2.1. Mobile technologies for managing heart failure

The concept of coupling remote monitoring and mobile cellular technologies is attractive for the HF community (Carbo 2018, Cipresso 2012). Heart rate (ECG), BP, and weight were the most frequently monitored parameters. Sensors that detect respiratory rate and pattern by detecting movement of the chest wall, via pressure, stretch, or accelerometry, may have applications in HF. Detecting breathing via microphone (sounds), change in impedance, or pulse oximetry are other possible means to monitor respiratory function. Some of these modalities could be integrated into smart clothing (Molinaro 2018).

Some trials included also alert reminders of medication use, voice messages on educational tips, video education,
and tracking of physical activity (See Section 4.6.1). Patients were mostly monitored daily and followed for an average of 6 months. A reduction was seen in HF-related hospital days (Carbo 2018). High rates of patient engagement, acceptance, usage and adherence have been reported in some trials but not others (Chaudhry 2010, Hamilton 2018).

Preliminary results using a disposable multisensor chest patch in the LINK-HF study were encouraging (Stehlik 2020), detecting precursors of hospitalization for HF exacerbation with 76% to 88% sensitivity and 85% specificity, 1 week before clinical manifestations.

4.2.2. Hybrid telerehabilitation in patients with heart failure

Exercise training is recommended for all stable HF patients (Piepoli 2011, Ponikowski 2016). Hybrid cardiac telerehabilitation is a novel approach. Telerehabilitation is the supervision and performance of comprehensive cardiac rehabilitation at a distance, encompassing: telemetry (minimally intrusive, often involving sensors), telessessment (active remote assessment), telesupport (supportive televisits by nurses, psychological support), teletherapy (actual interactive therapy), telecoaching (support and instruction for therapy), and teleconsulting and telesupervision of exercise training (Piotrowicz 2016). Various devices have been described, from heart rate monitoring (Smart 2005) and transtelephonic electrocardiographic monitoring (Kouidi 2006) to tele-ECG-monitoring via a remote device (Piotrowicz 2015) and real-time ECG and voice transtelephonic monitoring (Ades 2000).

Home-based telerehabilitation was demonstrated to be safe, effective with high adherence among HF patients. It improves physical capacity (Piotrowicz 2015) and psychological status (Piotrowicz 2016), with similar QoL improvement to standard rehabilitation (Piotrowicz 2015). The first randomized, prospective, multicenter study (TELEREH-HF) showed that hybrid telerehabilitation and telecare in HF patients was more effective than usual care in improving peak VO2, 6-minute walk distance, and QoL, although not associated with reduction of 24-month mortality and hospitalization except in the most experienced centers (Piotrowicz 2019, Piotrowicz 2019).

The recent Scientific Statement from the American Association of Cardiovascular and Pulmonary Rehabilitation, the AHA, and the ACC indicates that home-based rehabilitation using telemedicine is a promising new direction (Thomas 2019).

4.3. Diabetes

Diabetes mellitus is a strong risk factor for the development of morbidity and mortality associated with a range of cardiovascular diseases. Metabolic syndrome (elevated blood glucose and insulin resistance) acts via multiple mechanisms resultant in micro and macrovascular complications, development of autonomic neuropathy, diastolic dysfunction, renal failure, and AF. Important management goals are lifestyle changes [e.g., diet and activity: see later section] to prevent disease development and tight glycemic control, especially for type 1 diabetes mellitus which demands lifelong rigorous self-monitoring (Balakumar 2016; Donnellan 2019, Goudis 2015, Wang 2019, Wilkinson 2019, Wingerter 2019). mHealth modalities self-management was recommended recently by ESC guidelines on diabetes and cardiovascular diseases to (Cosentino 2019).

Glycemic control may reduce AF development and recurrence (Chao 2012; Chang 2014; Gu 2011, Otake 2009).

Mobile apps can facilitate self-management by reminding regular assessment of required parameters and medications to take and provide educational tools and motivational support. Regular transmission of blood glucose levels from patients to their physicians can be based on SMS, email, or diverse web-based services. Bluetooth-enabled glucose meters are frequently used (Andres 2019, Garabedian 2015). BlueStar (Welldoc, Columbia, MD), first to receive US FDA clearance for diabetes mellitus management, comes with an app which requires a physician prescription and enables patients to titrate insulin dosing by using the proprietary insulin calculator. The Freestyle LibreLink app (Abbott Laboratories, Abbott Park, IL) reads an associated continuous glucose monitoring device and displays trends (Fokkert 2017).

Stand-alone diabetes management apps have recently been reviewed (Fleming 2020). Short-term measures, such as HbA1c, may be improved by such apps in conjunction with clinical support, but many have suboptimal usability (Veazie 2018). Phone-based interventions were associated with improved glycemic control as compared to standard care (Liang 2011, Pillay 2015, Saffari 2014). Efficacy for improving glycemic control in randomized controlled trials has shown mixed results (Agarwal 2019, Quinn 2011). Meta-analyses indicate that mobile phone interventions for self-management reduced HbA1c modestly by 0.2-0.5% over a median of 6-month follow-up duration, with a greater reduction in patients with type 2 compared to type 1 diabetes (Pal 2014). A significant impact on clinical outcomes may affect healthcare expenditures by reducing the need for in-person contact with healthcare providers, preventing hospital admissions, and improving prognosis. In a retrospective study, the use of mHealth technologies was associated with a 21.9% reduction in medical spending than a control group during the first year (Whaley 2019). Key determinants to successful uptake of decision-support apps will be their user-friendliness and complexity and the delivery of electronic communications and feedback to the patient.

4.4. Hypertension

Hypertension, because of its high prevalence, provides the highest attributable risk for the development of AF (Huxley 2011).

mHealth strategies for hypertension comprise a continuum of solutions, used by consumers or healthcare providers, and includes wireless diagnostic and clinical decision-support tools, aiming to monitor health status and improve health.
outcomes. BP telemonitoring is one of the most commonly used strategies and includes remote data transmission of BP and clinical information from patients in their home or from a community setting to a central service, where they are reviewed by a managing physician for treatment adjustments. Several clinical trials have shown that BP telemonitoring might be more effective than usual care in achieving target BP (Bosworth 2011, Kim 2015, McManus 2010). A meta-analysis showed that, compared with usual care, BP telemonitoring improved office systolic BP and diastolic BP by 3.99 mm Hg (95% confidence interval (CI): 5.06–2.93; P<0.001) and 1.99 mm Hg (95% CI: −2.60 to −1.39; P<0.001), respectively (Duan 2017). BP telemonitoring nested in a more complex intervention, including additional support, as face-to-face counseling, telecounseling, education, behavioral management, medication management, and adherence contracts, led to additional and more sustainable benefit (Duan 2017, Tucker 2017).

mHealth has the potential to promote patient self-management, as a complement to the doctor’s intervention, and encourage greater participation in medical decision-making. Indeed, the TASMNTH4 unblinded randomized controlled trial showed that patients who used self-monitoring of BP to titrate antihypertensives, with or without telemonitoring, achieved better BP control than those assigned to usual care (McManus 2018). The self-monitoring group that used telemonitoring achieved lower BP quicker than the self-monitoring group not receiving telemonitoring support, but readings were not significantly different at 1 year of follow-up. Cost-effectiveness analysis suggests that self-monitoring in this context is cost-effective by NICE criteria, that is, costing well under £20,000 per QALY (Monahan 2019).

Although mHealth options may aid hypertension management, technological barriers, high costs, heterogeneity of solutions and technologies, and lack of standards challenge clinical implementation. The 2019 ESC guidelines on hypertension stress the importance of self-monitoring and underline the potential use of smartphone-based solutions. Nevertheless, they do not recommend the use of mobile apps as independent mean of BP measurements (Williams ESC/ESH guidelines 2018).

4.5. Disorders including sleep apnea (See also Heart failure Section 4.2.1)

Sleep disorders are widely prevalent and contribute to cardiovascular risk and arrhythmias, especially AF (Daghlas 2019, Hirshkowitz 2015, Mehra 2006, May 2016, May 2017), (Institute of Medicine Report: Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem), (Institute of Medicine (US) Committee on Sleep Medicine and Research/www.ncbi.nlm.nih.gov/books/NBK19961). This may be because sleep disturbance is intimately tied to circadian rhythms and sympatho-vagal balances (Burgess 1997). Standard sleep disorder diagnostics have been validated but require technical support for data acquisition and scoring.

For example, polysomnography has long been considered the gold-standard for acquisition of rich multimodal cardiovascular objective physiologic data to ascertain sleep architecture, total sleep time, and cardiorespiratory abnormalities and is primarily used for the diagnosis of obstructive sleep apnea. Actigraphy has the advantage of collecting objective data over days and nights to characterize sleep–wake patterning and provide measures of total sleep time, sleep efficiency, and sleep onset latency in addition to surrogate circadian measures. However, such tests are obtrusive and expensive.

- Treating sleep apnea may reduce AF burden (Qureshi 2015, Youssef 2018).

Consumer technology directed to sleep medicine may revolutionize the detection and treatment of sleep disorders. Since such apps are preinstalled on many smartphones, sleep tracking may be among the most widely applied facets of mHealth (Khosla 2018). Applications include mobile device applications, wearable devices, embedded devices (in the individual’s sleep environment), rings (https://bodimetrics.com/product/circul-sleep-and-fitness-ring), integration of accessory diagnostic monitoring (e.g., oximetry, ECG monitoring), and sleep therapy adherence monitoring. Several commercially available wearable devices measure total sleep time accurately, but not more detailed parameters such as sleep efficiency and different sleep stages (Mantua 2016). Preliminary data suggest that wearable devices may be capable of detecting sleep apnea with good accuracy compared to gold-standard polysomnography (Selvaraj 2014) and transform the approach to sleep disorder screening, diagnosis, and treatment. Sleep irregularity diagnosed by 7 day wrist actigraphy was linked to risk of cardiovascular events (Huang 2020). Preliminary studies indicated that use of wearables may permit behavior modifications that improve sleep quality (Berryhill 2020). In this regard, mHealth applications to sleep diagnosis and treatment promise facilitation of rhythm control.

4.6. Lifestyle (See Figure 5)

4.6.1. Physical activity

Physical activity is any bodily movement from skeletal muscle contraction to increase energy expenditure above basal level. Athletic activity varies from recreational sports to competitive events. There is a compelling evidence that regular aerobic exercise at the levels recommended by Physical Activity Guidelines Advisory Committee reduces the risk of a variety of cardiovascular conditions, including AF (Everett 2011, Mozaffarian 2008, Piercy 2018). However, the majority of the population is not engaged in physical activity at the recommended levels (Piercy 2018). Among patients with cardiovascular disease, patient activity measured automatically by ICDs correlated with survival following ICD implantation (Kramer 2015). Fitness represents an enormous market for mobile technologies and significant opportunity to improve the health of a wide range
of mHealth consumers. In 2017, over 318,000 “fitness and health” apps were available, almost double the number two years prior (IQUIVA Institute 2017). Many of these recreational apps monitor daily physical activity and support a healthy lifestyle by counting the number of steps daily, online training, and motivation coaching (McConnell 2018).

- Cardiorespiratory fitness has an inverse relationship to AF burden (Faselis 2015).
- Improvement in exercise capacity of 2 METs in overweight individuals may double freedom from AF (Pathak 2015).

Consumer-grade fitness technology includes individual fitness trackers that can stand alone, a fitness tracker that is coupled with a companion app, or an app that can be downloaded onto a smartphone, which then utilizes various features of the smartphone to measure activity and sleep. The accuracy of these measurements varies between different products and between measures within the same product (Rosenberger 2016). Furthermore, while step-counting is long established, measuring the intensity of exercise is more complex. Although fitness technology has the exciting potential to increase physical activity by promoting goal setting and providing feedback, its effectiveness in motivating positive behavioral change remains unclear (Sullivan 2017).

One cautionary tale is the study by Jakicic et al. that examined the effectiveness of a lifestyle intervention with or without a fitness tracker (Jakicic 2016). Two groups received instruction to promote physical activity and dietary restriction. Six months into the intervention, half of the participants were provided with an upper arm fitness tracker and web-based support accompanying the device. The other half logged and tracked their activity and diet on a study website. Of note, the group that wore the tracker lost less weight than the group who did not. Moreover, changes in physical activity between the two groups were not significantly different. These results cast doubt on the effectiveness of fitness trackers in promoting greater physical activity, and thus, further data are required to assess the impact of this approach (See Section 5).

**Competitive athletes**

These are a unique category. Endurance athletes may have increased AF risk (Abdulla 2009, Andersen 2013). Remote evaluation of ECG recordings may be useful in countries that perform preparticipation ECG screening (Brunetti 2014, Orchard 2019). Mobile devices and apps provide complex data which can be used as a self-monitoring tool for managing training (Aroganam 2019, Li 2016, Peake 2018, Peart 2019, Seshadri 2019). Exercise load and performance level can be accessed on a regular basis by coaches as well as athletes. Training guided by daily monitoring of HRV parameters has also been proposed, but data are limited (Coppetti 2017, Dobbs 2019, Singh 2018). Mobile devices provide the possibility of online real-time monitoring during indoor and outdoor training and competitions. Monitoring of heart rate provides both information on performance and level of training but can also provide valuable information regarding heart rhythm irregularity suggestive of arrhythmias. Any kind of paroxysmal arrhythmia related to sport participation and detected by mobile devices designed merely for heart rate assessment should trigger further cardiological evaluation. Having in mind data indicating that sports participation may be associated with higher risk of development of AF mobile devices may serve as valuable screening tool for AF detection.

Importantly, mHealth solutions enable easy access to athletes’ medical data. The latter approach can be of special interest in management of athletes’ health during competitions abroad.

### 4.6.2. Diet

In 2010, the American Heart Association promulgated “Life’s Simple 7” as a public health strategy to improve cardiovascular health with the motto: “7 Small Steps to Big Changes. It’s easy and simple. Anyone can do it. Start with one or two!” Unfortunately, research has shown that this strategy is anything but simple: virtually, no adults (<1%) are compliant with all recommendations and 42% are compliant with only 0-2 recommendations (Folsom 2011). Although there is ample evidence that weight loss and maintaining an ideal weight are beneficial in reducing AF burden and symptoms, compliance with this recommendation is poor; the reasons include among others, inability to track food intake (Abed 2013, Donnellan 2019, Pathak 2015).

- Weight loss combined with risk factor modification is a Class 1 (B-R) recommendation in treatment of AF (January 2019)
- >10% weight reduction/ target BMI <27 kg/m² reduces AF burden (Pathak 2015).

There are currently many consumer-oriented mobile phone-based applications (apps) designed for tracking food intake, but their utility for use in carbohydrate counting is limited due their design (El-Gayyar 2013). Commonly, these consumer-oriented apps require multiple steps. As an example, the user types in the food consumed and then scrolls through the search results to match with the program’s food and nutrient database. Next, after finding a matching food type, the user must estimate and enter an amount. These apps require significant user input and time burden along with high possibility of error. In addition, they are also plagued by uncertain accuracy. Recently, research has shown that nutrient calculations from leading nutrition tracking apps tended to be lower than results from using 24-hour recall with analysis by the Nutrition Data System for Research (NDSR), a research-level dietary analysis software (Griffiths 2018).

By contrast, a visual image-based app, such as the Technology-Assisted Dietary Assessment (TADA) system, directly addresses the aforementioned shortcomings (Boushey 2017, Six 2010, Zhu 2010). This is in research phase. The TADA system consists of two main
components: (1) A smartphone app that runs on either iPhones (iOS) or Android devices: the Mobile Food Record technology can be recommended or prescribed. (2) Cloud-based server that communicates with the mFR, processes, and stores the food images. Using the TADA system, a person takes a photograph of the meal they are planning to eat using their smartphone’s camera. The use of geometric models has permitted the TADA system to use a single image of a meal to estimate portion size to within 15% of the actual amount (Dounavi 2019). Hence, smartphone-based technology such as the TADA system can facilitate tracking of food intake, which in turn can potentially help with weight management.

Despite the profusion of diet and weight-related apps, and the interest in weight loss in the community, there remains a dearth of high-quality evidence that these apps are actually effective (Fang 2015). There remains a need for further evidence development before specific apps or other mHealth technology can be recommended or prescribed.

References Section 4

Chung MK, Eckhardt LL, Chen LY, Ahmed HM, Gopinathannairi R, Roglar JA, ... Trulock KM. Lifestyle and risk factor modification for reduction of atrial fibrillation: A scientific statement from the American Heart Association. Circulation 2020;141:e790–e772. https://doi.org/10.1161/CIR.0000000000000748

Horwitz LI, Moriarty JP, Chen C, Fogerty RL, Brewster UC, Kanade S, ... Ritchey MD, Maresh S, McNeely J, Shaffer T, Jackson SL, Keteyian SJ, ... Pizzetti F, Turazza FM, Franzosi MG, Barlera S, Ledda A, Maggioni AP, ... Krumholz HM. Quality of discharge practices and patient understanding at an acute coronary syndrome. Journal of the American Medical Association 2015;314:1255–1263.

Avila CO. Novel use of apple watch to 4 obtain 3-lead electrocardiogram and detect cardiac ischemia. The Permanente Journal 2019;23:19–205.

Chow CK, Redfern J, Hillis GS, Thakkar J, Santo K, Hackett ML, ... Thaiagalingam A. Effect of lifestyle-focused text messaging on risk factor modification in patients with coronary artery disease: A randomized clinical trial. Journal of the American Medical Association 2010;304:1255–1263.

Clemmensen P, Loumann-Nielsen S, Sejersten M. Telemedicine fighting acute coronary syndromes. Journal of Electrocardiology 2010;43:615–618.

Gibson CM. Implanted monitor alerting to reduce treatment delay in patients with acute coronary syndromes. Journal of Electrocardiology 2010;43:615–618.

Swinburn B, Sorensen P, weekman D, Smith DH, ... Williams A. Improving adherence to cardiovascular disease medications with automation. The American Journal of Managed Care 2014;20(S17):SP502–SP510.

Ziaein B, Arajou KL, Van Ness PH, Horwitz LI. Medication reconciliation accuracy and patient understanding of in-tended medication changes on hospital discharge. Journal of General Internal Medicine 2012;27:1513–1520.

Zwischen AD, Norton RJ, Dean SG, Dalal H, Tang LH, Wingham J, Taylor RS. Home-based cardiac rehabilitation for people with heart failure: A systematic review and meta-analysis. International Journal of Cardiovascular 2016;221:963–969.

4.2.

Abraham WT, Stevenson LW, Bourge RC, Lindenfeld JA, Baumann JM, ... Yancy CW. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration With the Society of Thoracic Surgeons. Circulation 2019;140:e125–e151. https://doi.org/10.1161/CIR.0000000000006665.

Wollmer OM, Owen-Smith AA, Tom JO, Laws R, Dittric DG, Smith DH, ... Williams A. Improving adherence to cardiovascular disease medications with automation. The American Journal of Managed Care 2014;20(S17):SP502–SP510.
Mozaffarian D, Furberg CD, Psaty BM, Siscovick D. Physical activity and incidence of atrial fibrillation in older adults - The cardiovascular health study. Circulation 2008; 118:800–807.

Orchard JJ, Neubeck L, Orchard JW, Puranik R, Raju H, Freedman B . . . Semsarian C. ECG-based cardiac screening programs: Legal, ethical, and logistical considerations. Heart Rhythm 2019;16:1584–1591.

Pathak RK, Elliott A, Middeldorp ME, Meredith M, Mehta AB, Mahajan R, . . . Sanders P. Impact of CARDIOrespiratory fitness on arrhythmia recurrence in obese individuals with atrial fibrillation: The CARDIO-FIT study. Journal of the American College of Cardiology 2015;66: 985–996. https://doi.org/10.1016/j.jacc.2015.03.002.

Peake JM, Kerr G, Sullivan JP. A Critical review of con-sumer wearable mobile applications, and equipment, for provid-ing biofeedback, monitoring stress, and sleep in physically active populations. Frontiers in Physiology 2018;9:743. https://doi.org/10.3389/fpsyg.2018.00743.

Peri DJ, Balsalobre-Fernández C, Shaw MP. Use of mobile applications to collect data in sport, health, and exercise science: A narrative review. The Journal of Strength & Conditioning Research 2019;33:1167–1177.

Piercy KL, Troiano RP, Bahrardt MA, Carlson SA, Fulton JE, Galuska DA, . . . Olson RD. The physical activity guide- lines for Americans. Journal of the American Medical Association 2018;320:2020–2028.

Rosenberger ME, Buman MP, Haskell WL, McConnell MV, Carstensen LL. Twenty-four hours of sleep, sedentary be-havior, and physical activity with nine wearable devices. Medicine and Science in Sports and Exercise 2016;4:457–465.

Seshadri DR, Li KT, Voos JE, Rowbottom JR, Altes CM, Zorman CA, Drummond CK. Wearable sensors for monitoring the internal and external workload of the athlete. North American Medical Journal 2016;2:71.

Singh N, Moneghetti KJ, Christie JW, Hadley D, Froelicher V, Plews D. Heart rate variability: An old metric with new meaning in the era of using mhealth technologies for health and exercise training guidance. Part two: Prognosis and training. Arrhythmia & Electrophysiology Review 2018;7:247–255.

Sullivan AN, Lachman ME. Behavior change with fitness technology in sedentary adults: A review of the evidence for increas-ing physical activity. Frontiers in Public Health 2017;5:209. https://doi.org/10.3389/fpubh.2017.00289.

IQVIA Institute. The growing value of digital health: Evidence and impact on human health and the healthcare system. 2017. Available at: https://www.iqvia.com/insights/the-iqvia-institute/reports/the-growing-value-of-digital-health.

4.6.2.

Abed HS, Witter t GA, Leong DP, Shirazi MG, Bahrami B, Middeldorp ME, Sanders P. Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation a random-ized clinical trial. Journal of the American Medical Association 2013;310:2050–2060.

Boushey CJ, Spoden M, Zhu FM, Delp EJ, Kerr DA. New mobile methods for dietary assessment: Review of image-assisted and image-based dietary assessment methods. The Proceedings of the Nutrition Society 2017;76:283–294.

Donnella E, Wazni O, Kanj M, Hasseini A, Banarowski B, Lindsay R, . . . Saliba W. Outcomes of atrial fibrillation ablation in morbidly obese patients following bariatric surgery compared with a nonobese cohort. Circulation: Arrhythmia and Electrophysiology 2019;12:e007598.

Donnella E, Wazni OM, Kanj M, Banarowski B, Cremer P, Harb S, . . . Saliba WI. Association between pre-ablation bariatric surgery and atrial fibrillation recurrence in morbidly obese patients undergoing atrial fibrillation ablation. Europace 2019; 21:1476–1483.

Doumani K, Tsoumani O. Mobile health applications in weight management: A systematic literature review. American Journal of Preventive Medicine 2019;56:894–903.

El-Gayar O, Timsina P, Nawar N, Eid W. Mobile applica-tions for diabetes self-management: Status and potential. Journal of Diabetes Science and Technology 2013;7:247–262.

Fang S, Liu C, Zhu F, Delp EJ, Boushey CJ. Single-view food portion estimation based on geometric models. ISM: IEEE International Symposium on Multimedia: Pro-ceedings IEEE International Symposium on Multimedia 2015;2015:385–390.

Folsom, A. R., Matsuda, H., Nettleton, J. A., Lutesey, P. L., Cushman, M., Rosamond, W. D., & Investigators, A. S. (2011). Community prevalence of ideal cardiovascular disease incidence. Journal of the American College of Cardiology, 57, 1690–1696.

Griffiths C, Harnack L, Pereira MA. Assessment of the accuracy of nutrient calculations of five popular nutrition tracking applications. Public Health Nutrition 2018; 21:1495–1502.

Pathak RK, Middeldorp ME, Meredith M, Mehta AB, Mahajan R, Sanders P. Long-term effect of goal-directed weight management in an atrial fibrillation cohort a long-term follow-up study (LEGACY). Journal of the American College of Cardiology 2015;65:2159–2169.

Six BL, Schap TE, Zhu FQM, Mariappan A, Bosch M, Delp EJ, . . . Boushey CJ. Evidence-based development of a mobile telephone food record. Journal of the American Dietetic Association 2010;110:74–79.

Zhu FQ, Bosch M, Woo I, Kim S, Boushey CJ, Ebert DS, Delp EJ. The use of mobile devices in aiding dietary assessment and evaluation. IEEE Journal of Selected Topics in Signal Processing 2010;4:756–766.

5. Patient Self-Management—Integrated Chronic Care

Generally, structured management programs inclusive of intensive patient education may improve outcomes (Hendriks 2012; Lin 2014; Angaran 2015). These may be facilitated by mHealth.

5.1. Patient engagement

mHealth offers the opportunity to reach more patients more effectively. It may promote patient engagement through ease of access and wider dissemination to regions and communities who may not access health care through traditional modes due to cost, time, distance, embarrassment/stigma, marginalized groups, health inequities, etc. In this way, mHealth may facilitate information sharing and interaction between patients and HCPs without the need for an elaborate infrastructure (Chow 2016, Walsh 2014) (Figure 6). Apps may aid HCPs to explain the condition and treatment options, utilizing videos, avatars, and individualized risk scores, enabling greater patient understanding and encouraging a two-way exchange of information to achieve a concordant decision about treatment.

Patients’ access to their own health data

A recent HRS statement advocates for transparent and secure access by patients to their digital data (Slotwiner 2019). This enables active participation and appropriate self-management. For instance, many patients with AF are interested in seeing their AF burden and physiologic data, similarly to patients with hypertension tracking their BP or patients with diabetes tracking their glucose. Recent systematic reviews of technology-based patient-directed interventions for cardiovascular disease suggest that engaging elements include self-monitoring of symptoms and measurements, daily tracking of health behaviors, disease education, reminders, and interaction with HCPs (Coorey 2018, Gandhi 2017, Park 2016, Piazza 2016). In some cardiovascular conditions, self-management (without any HCP input) improved key outcomes (Hagglund 2015, Varnfield 2014).

The model requires that patients assume responsibility and accountability for tracking conditions effectively and taking corrective measures. Possibly, this may be facilitated by data organization to present salient elements in a format comprehensible to the lay public. Active role of patients in decision-making regarding the choice of treatment has been underlined by AF clinical guidance documents. Patients with AF are encouraged to be involved in decision-taking through better understanding of their disease, which helps to improve communication between patients, their families, and doctors and improves patients’ adherence to prescribed
therapy. Two applications in AF—one for patients and the other for healthcare providers—have been developed by CATCH ME Consortium in collaboration with European Society of Cardiology (Kotecha 2018), but these have yet to be formally tested. In China, Guo and colleagues (Guo 2017) demonstrated that the mobile atrial fibrillation (mAFA) app, incorporating decision support, education, and patient engagement, significantly improved AF patients’ knowledge, medication adherence, quality of life, and satisfaction to anticoagulation compared to usual care.

Limitations should be recognized:
- Demands of self-management may be excessive for even well intentioned patients required to be facile with setting up their own medical monitoring device, assessing frequency of download, interpreting and acting on data when required, and troubleshooting. These are not trivial challenges.

5.2. Behavioral modification

Individual health status has been found to be a strong independent predictor of mortality and cardiovascular events (Runsfeld 2013).

mHealth may catalyze positive behavioral change and facilitate health care. An induced healthy-user effect was likely the basis of survival benefit among CIED patients adhering more closely to remote management (Varma 2015). mHealth may support patients with text messaging (Chow 2015) or mobile applications to remind patients of medication doses and times, as well as medical appointments (but synchronization with healthcare providers and/or EMR is generally lacking). The “just-in-time adaptive intervention” (JITAI) premise is to provide the appropriate type and amount of support to an individual at the correct time, with the ability to adjust depending on the person’s current internal and situational factors (Nahum-Shani 2018). mHealth technology is an ideal platform to facilitate JITAI by providing “real-time” personalized information, which can be utilized to inform the intervention delivered. JITAI have been widely employed for health promotion and to support behavior change, but evidence of their efficacy is limited (Gustafson 2014, Patrick 2009, Riley 2008). Timing is integral to the perception of benefit, as is receptivity to accept and use the support (Nahum-Shani 2015). Bespoke, multi-faceted mHealth tools, with motivational messages and incorporating gamification, are most engaging (Coorey 2018, Gandhi 2017, Park 2016, Piaeffi 2016).

Incorporation of gamification strategies (e.g., rewards, prizes, avatars, performance feedback, leader-boards, competitions, and social connection) into mHealth promotes patient engagement and sustains healthy behaviors (Blondon 2017, Cugelman 2013, Edwards 2016, Johnson 2016, Sardi 2017). However, a recent systematic review demonstrated that only 4% (64/1680) of English-language “top-rated” health apps incorporated ≥1 gaming feature (Edwards 2016). There are limited hypothesis-generated data for these mHealth interventions, and their efficacy in this context is as yet unmeasured. Self-regulatory behavior change techniques, such as feedback and monitoring (including self-monitoring), comparison of behavior, rewards, incentives and threats, and social support, are the most common behavior change techniques employed in gamification apps and are frequently utilized in successful non-gaming apps targeting health promotion and secondary prevention (Conroy 2014, Direito 2014, Edwards 2016). Engaging with apps involving gamification can also improve emotional well-being through feelings of accomplishment and social connectivity (Johnson 2016).

5.3. Patients as part of a community

Incorporation of a patient as part of a wider community may offer benefits. Social networking is widely used for health (Fox 2011). Online communities enable individuals to “meet,” share their experience, discuss treatment, and receive and provide support from peers, patient organizations, or HCPs (Fox 2011, Swan 2009, Swan 2012). While crowdsourcing via the Internet and social networks allows collective sharing and exchange of information from a large number of people, the integrity and accuracy of such information remains largely unvetted and as such may be unreliable (Besaleva & Weaver 2014).

5.4. Maintaining patient engagement

Sustaining healthy behaviors and minimizing intervention fatigue is paramount to long-term maintenance. Although mHealth may help to maintain motivation, available data demonstrate significant attrition with mHealth interventions targeting risk factors and chronic conditions, even when people report liking the intervention and have purchased it (Chaudhry 2010, Flores Mateo 2015, Fukuoka 2015, Morgan 2017, Owen 2015, Simblett 2018, Whitehead 2016, Endeavour Partners, Perez 2019).

A representative patient’s experience is described below:

A few years ago (2017), a friend told me about a new app that he had installed on his iPhone that would allow him to measure his heart rate through a fingertip pulse. Having an irregular heartbeat, under control through medication, I was very interested to try the new app. I thought it would provide me the opportunity to know more about myself, specifically how my heart operated under stress and at different times of day, before, during, and after physical exertion of a variety of my favorite sports and pastimes like tennis, golf, biking, and fly fishing.

At first, I was quite satisfied with the rudimentary calculations. Then, I noticed during my international business travels that the device was often down during US nighttime hours during which time I thought the ‘hosts’ were making repairs or improvements. I also noticed that there were several radically incorrect readings especially during early morning hours. It simply wasn’t performing up to the standards of more traditional monitoring devices. I found as well that the host’s increasing attempt to up-
sell to premium packages and other online health management tools became quite burdensome.

Before long, I felt almost addicted to the device and ultimately quit on it altogether. In retrospect, I believe that if I had had a proper introduction to the device by a trained medical specialist, I might have had a different expectation of this online tool, how to use it and how to interpret its data output.

Understanding the basis for health-protective behavior is vital (DuMont 2018). Many apps, including those from national heart foundations [websites], are available to support healthy lifestyle choices, but their efficacy remains largely untested or is limited by design features (i.e., small sample sizes, selection bias, etc.). Cost, service connectivity, and credibility of information sources are important factors. However, patient engagement may be jeopardized by worries about privacy and personal data security (Burke 2015, Chow 2016, Kumar 2013, Steinhaubl 2015).

Continued clinic support
The level and duration of clinic support needed will likely depend on condition monitored and goals for treatment. Reduction in compulsory routine in-clinic evaluations and reliance on continuous remote monitoring improved retention in long-term follow-up of patients with CIEDs (Varma 2014). In one HF trial, gain was related to the period of remote instruction. Whether this indicates that efficacy of the active program had peaked and stabilized or that it needed to be sustained is unclear (Varma 2020). Ideally, a training program should be finite in time but its effects durable.

5.5. Digital divide
Although mHealth is highly promising in transforming health care, it can potentially exacerbate disparities in health care along sociodemographic lines.

Older people are perceived to engage less with mHealth. A 2017 Pew Research Center survey found that 92% of 18-29 year olds and 74% of age 50-64 year olds own a smartphone (Smith 2017). However, the lack of familiarity with the technology and access to mobile devices, rather than lack of engagement per se, remain the principal barriers (Coorey 2018, Gallagher 2017, Tarakji 2018). Older users of mHealth prefer personalized information, which is clearly presented and is easy to navigate (Neubeck 2015).

There is also disparity across the educational spectrum, with smartphone usage in 57% of the population with less than high school education and 91% of the population who graduated from college.

Smartphone use differs by income, with smartphone usage in 67% of the population with income annual ≤ $30,000 and 93% of the population with income ≥ $75,000 (PRC Mobile 2018). Limited evidence from the USA suggests that, although there is some variation in the mHealth use related to ethnicity, black and Hispanic Americans are not disadvantaged (Martin 2012). mHealth permits information and apps to be tailored appropriately for language, literacy levels (including “text to speech” technology), and cultural differences to promote engagement (Coorey 2018, Neubeck 2017, Redfern 2016).

There is heterogeneity of mHealth availability among different countries (Varma 2020). Even some of the best studied and FDA and CE approved technologies described here may be currently unavailable due to regulatory or marketing rules or simply unaffordable to either individuals or healthcare systems in many other countries.

As healthcare systems leverage and incorporate smartphone-based technology in their workflow and processes, a strategy is needed in parallel to ensure that those who do not have access to smartphone-based technology will continue to receive appropriate high-quality care. This critical initiative will require consensus and action among all stakeholders including HCPs, hospital systems, insurance providers, and state and federal government agencies. Thus enabled, mHealth promises improved patient outcomes in resource-limited areas (Bhavnani 2017).

References Section 5
Angaran P, Mariano Z, Dragan V, Zou L, Atzema CL, Mangat I, Dorian P. The atrial fibrillation therapies after ER visit: Outpatient care for patients with acute AF: the AFTERR3 study. Journal of Atrial Fibrillation 2015;7:1187.
Lin, J. S., O’Connor, E. A., Evans, C. V., Senger, C. A., Rowland, M. G., & Groom, H. C. (2014). Behavioral Counseling to Promote a Healthy Lifestyle for Cardiovascular Disease Prevention in Persons With Cardiovascular Risk Factors: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force [Internet] Rockville (MD): Agency for Healthcare Research and Quality (US); U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. Report No.: 13-05179-EE-1.
Hendriks JM, de Wit R, Crijns HJ, Vrijhoef HJ, Prins MH, Pisters R, Pison LA, Blauw Y, Tieleman RG. Nurse-led care vs. usual care for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs. routine clinical care in ambulatory patients with atrial fibrillation. European Heart Journal 2013;32(21):2692–2699. https://doi.org/10.1093/eurheartj/ehs071.

5.1.
Chow CK, Ariyarathna N, Islam SM, Thilagalingam A, Redfern J. mHealth in cardiovascular health care. Heart Lung & Circulation 2016;25:802–807.
Coorey GM, Neubeck L, Mulley J, Redfern J. Effectiveness, acceptability and usefulness of mobile applications for cardiovascular disease self-management: Systematic review with meta-synthesis of quantitative and qualitative data. European Journal of Preventive Cardiology 2018;25:505–521.
Gandhi S, Chen S, Hong L, Sun K, Gong E, Li C, Yan LL, Schwalm JD. Effect of mobile health interventions on the secondary prevention of cardiovascular disease: Systematic review and meta-analysis. Canadian Journal of Cardiology 2017;33:219–231.
Guo Y, Chen Y, Lane DA, Liu L, Wang Y, Lip GYH. Mobile health technology for atrial fibrillation management integrating decision support, education and patient involvement: mAF App trial. The American Journal of Medicine 2017; 130:1388–1396.e6. https://doi.org/10.1016/j.amjmed.2017.07.003.
Haglund E, Lynga P, Frie F, Ullman B, Persson H, Melin M, Hagerman I. Patient-centred home-based management of heart failure. Findings from a randomised clinical trial evaluating a tablet computer for self-care, quality of life and effects on knowledge. Scandinavian Cardiovascular Journal 2015;49:193–199.
Kotecha D, Chua WWL, Fabritz L, Hendriks J, Casadei B, Schotten U, ... Kirchhof P. European Society of Cardiology (ESC) Atrial Fibrillation Guidelines Taskforce, the CATCH ME consortium and the European Heart Rhythm Association (EHRA). European Society of Cardiology smartphone and tablet applications for patients with atrial fibrillation and their health care providers. European 2018; 20:225–233. https://doi.org/10.1093/eurheartj/aju299.
Park JG, Beatty A, Stafford Z, Zhouley MA. Mobile phone interventions for the secondary prevention of cardiovascular disease. Progress in Cardiovascular Diseases 2016;58:639–650.
Pfaffl M, Atzema CL, Chua WWL, Kong P, and Mehta M, Redfern J. The effectiveness of mobility control of health behaviour change interventions for cardiovascular disease self-management: A systematic review. European Journal of Preventive Cardiology 2016;23:801–817.
6. Clinical Trials

mHealth may have particular impact on trials of heart rhythm disorders. Traditionally, clinical trials testing drugs and devices for arrhythmias utilized time-to-event outcomes and analyses, such as first recurrence of AF after a blanking period (Piccini 2017). Patients randomized to the control and intervention would be monitored intermittently, either with ambulatory devices and/or in-clinic visit. Such monitoring had limited sensitivity for recurrent arrhythmias, including symptomatic and asymptomatic episodes. Furthermore, time-to-first event may not accurately capture reductions in arrhythmia burden, which have also been shown to be beneficial in recent randomized trials (Andrade 2019). While CIEDs such as pacemakers and defibrillators can be leveraged for continuous monitoring (Varma 2005), these studies do not generalize to broader CIED-free populations. ILRs may have a potential role, but are costly and unless used for clinical indications, difficult to justify simply for study event ascertainment.

There are a variety of free-standing handheld ECG monitors, some of which have automated AF detection (Table 1). However, many do not have cellular or networking capability and therefore generally cannot transmit data or findings in real time. This is where smart- or mobile-connected arrhythmia and pulse detection technologies have significant promise. These may enhance detection and measurement of clinical outcomes while also allowing for remote or virtual data collection without the need for site-based study visits. Examples include remote rhythm assessment with single- or multilead ECGs from smartphone or smartwatch-based technologies and automatic ascertainment of hospitalizations using smartphone-based geofencing (Nguyen 2017). These operational enhancements, in turn, can improve participant satisfaction, reduce cost, improve study efficiency, and facilitate or expand enrollment. An example is the ongoing Health eHeart study, a site-free cardiovascular research study that leverages self-reported data, data from wearable sensors, electronic health records, and other importable “big data” to enable rapid-cycle, low-cost interventional and observational cardiovascular research (https://www. health-eheartstudy.org/).

Screening

Two recent large-scale studies highlight the potential advantages of mHealth for AF screening and treatment.

- The Apple Heart Study

This was a highly pragmatic, single-arm investigational device exemption study designed to test the performance and safety of a PPG-based irregular rhythm detection algorithm on the Apple Watch for identification of AF (Perez 2019,Turakhia 2019). The study was a siteless “bring your own device” study, such that participants needed their own compatible smartphone and watch to enroll online. All study procedures, including eligibility verification, onboarding, enrollment, and data collection, were performed via the study app, which could be downloaded from the app store. If a participant received an irregular pulse notification, then subsequent study visits were done via video conferencing to study physicians directly with the app. The study enrolled over 419,000 participants without pre-existing AF in just an eight-month period, in large part due to the pragmatic, virtual design, and easy accessibility (Figure 4). The algorithm was found to have a positive predictive value of simultaneous ECG-confirmed AF of 0.84 (Perez 2019). Only 0.5% of the enrolled population received any irregular pulse notification, but 3.2% of those age ≥ 65 years received notifications. However, only 153/450 (34%) patients had AF detected by a subsequent single ECG patches after the irregular rhythm notification was received. This may reflect the paroxysmal nature of early-stage AF rather than explicit false positives. Because the study only administered ECG patch monitoring to those with irregular rhythm notification rather than then entire cohort or to negative controls, the negative predictive value was not estimated. It should be noticed that the Apple Heart Study was in a population without diagnosed AF; test performance and diagnostic yield could be considerably different in a population with known AF, and this software is not approved for use for AF surveillance in established AF.

- The Huawei heart study

A similar study was performed using smart device-based (Huawei fitness band or smartwatch) PPG technology (Guo JACC 2019). The algorithm had been validated with over 29,485 PPG signals before commencement of the trial. More than 246,000 people downloaded the PPG screening
app, of which about 187,000 individuals monitored their pulse rhythm for 7 months. AF was found in 0.23% (slightly lower than Apple Heart, possibly due to a younger and healthier enrolled cohort). Validation was achieved in 87% (PPV >90%) compared to 34% in Apple Heart. The results indicated that this was a feasible frequent continuous monitoring approach for the screening and early detection of AF in a large population.

A significant observation was that clinical decision-support tools provided enabled management decisions, for example, almost 80% high-risk patients were anticoagulated. Subsequent enrollment into the mAFA II trial showed significantly reduced risk of rehospitalization and clinical adverse events (Guo JACC 2020). These trial results encourage incorporation of such technology effectively into the AF management pathways at multiple levels, that is, screening and detection of AF, as well as early interventions to reduce stroke and other AF-related complications.

- **Fitbit study**

Another large-scale virtual study to identify episodes of irregular heart rhythm suggestive of AF was announced by Fitbit in May 2020 (https://www.mobihealthnews.com/news/fitbit-launches-large-scale-consumer-health-study-detect-antiarrhythmic-drug-therapy such as flecainide to confirm AF, ensure no QRS widening, and confirm restoration of sinus rhythm. A similar approach has been proposed for rhythm-guided use of direct OACs in lower-risk AF patients with infrequent episodes either spontaneously or as the result of a rhythm control intervention including drugs and ablation; a randomized trial is in development (Passman 2016). The use of smartwatch-guided rate control as a treatment strategy could also be tested, as this may provide a more personalized approach rather than prior randomized trials of lenient versus strict rate control that used population level rather than personalized heart rate treatment thresholds (Van Gelder 2010).

**Questions**

- **Generalizability**

  This is key to application of results from trials. mHealth is widely available and often simple to apply and wear.

  a. Older individuals and those with low health literacy may find technologies difficult to use (5.5 Digital Divide), and this may be compounded by disease state, for example, previous stroke.

  b. Cost and service plans associated with smartphones and smartwatches may preclude their use in lower socioeconomic populations who are already under-represented in clinical trials and in many geographies.

Thus, patients who volunteer in mHealth studies in the USA are more likely to be a white/non-Hispanic, more educated, and less likely to have disease.

- **Adherence**

  mHealth-based evaluation of clinical endpoints may be confounded if adherence is low, particularly if there are no secondary means of endpoint assessments (Guo X 2017). Virtual designs may be more susceptible to the loss of participant engagement. For example, if monitoring is completely reliant upon mobile health technology and there are no traditional measures or in-person visits to assess arrhythmia, then significant missing data due to low-adherence may become a major limitation that could imperil the validity and generalizability of the findings. For example, among the 2,161 of the 419,297 that received an irregular pulse notification in the Apple Heart Study, only 945 completed a subsequent protocolled first study visit. Of these 658 ambulatory ECG patches shipped, there were only 450 with returned and analyzable data (Perez 2019).

  Development of effective strategies to increase retention and maintain high engagement remains an unmet need and is an area ripe for more research.

- **Outcomes**

  These are key to adoption and reimbursement. More specifically, the clinical and prognostic impact of new outcome measures based on mobile health technologies may not be clear.

  This is important for AF. For example, how do changes in AF burden compare to reductions in time to symptomatic sustained AF? Should AF identified on near-continuous smartwatch monitoring be considered equivalent to AF diagnosed at hospitalization or in clinic? There is a growing body of literature that the “dose” of AF burden matters for a variety of important clinical endpoints, including stroke, HF, and death (See Section 3.1.3) (Chen 2018, Glotzer 2009, Kaplan 2019, Piccini 2019, Wong 2018). Does pill-in-the-pocket DOAC treatment of PAF adequately cover the risk of stroke? Some measures remain less well studied, like the occurrence of irregularity with a wearable pulse-based monitor system, particularly without ECG confirmation.

  Since these mHealth prediagnostic or diagnostic tools may then be directly tied to initiation or termination of treatment, rigorous evaluation of clinical safety and efficacy will be required and, in some cases, warrant a combined drug-device regulatory approval.

  Despite these challenges, there is enormous potential for patients to use these technologies to self-monitor their arrhythmia treatment and extend this to manage comorbidities (See Section 4). The process of data transparency and accessibility to the patient may improve the patient’s engagement with their overall care, even if the data are not directly actionable by the patient. The restrictions to clinic access during the SARS-Cov-2 pandemic have accelerated the adoption of mHealth solutions (Varma JACC 2020). ECGs for clinical trials were recorded by smart devices and assessed at virtual
visits instead of routine in-person evaluations. In some cases, the entire management of clinical trials went online.

References Section 6
Andrade JG, Champagne J, Dubuc M, Deyell MW, Verma A, Mache L, … Khairy P. Cryoballoon or radiofrequency ablation for atrial fibrillation assessed by continuous monitoring: A random- ized clinical trial. Circulation 2019; 140:1779–1788.

Chen LY, Chung MK, Allen LA, Ezekowitz M, Furie KL, McCabe P, … Turakhia MP. Atrial fibrillation burden: moving beyond atrial fibrillation as a binary entity: A scientific statement from the American Heart Association. Circulation 2018; 137:e623–e644.

Glotzer TV, Daoud EG, Wyse DG, Singer DE, Ezekowitz MD, Hilker C, … Ziegler PD. The relationship between daily atrial tachyarrhythmia burden from implantable device diagnoses and stroke risk: The TRENDS study. Circulation: Arrhythmia and Electrophysiology 2009;2:474–480.

Guo, X., Vittinghoff, E., Olgin, J. E., Marcus, G. M., & Pletcher, M. J. (2017). Volunteer participation in the Health eHeart Study: A comparison with the US population. Science Reports 2017(7):1956. https://doi.org/10.1038/s41598-017-02232-y.

Guo Y, Wang H, Zhang H, Liu T, Liang Z, Xia Y, … Lip GYH. Mobile photoplethysmographic technology to detect atrial fibrillation. Journal of the American College of Cardiology 2019;2019(74):2365–2375. https://doi.org/10.1016/j.jacc.2019.08.019.

Guo Y, Lane DA, Wang L, Zhang H, Wang H, Zhang W, … Lip GYH. Mobile health technology to improve care for patients with atrial fibrillation. Journal of the American College of Cardiology 2020;75:1523–1534.

Kaplan RM, Koehler J, Ziegler PD, Sarkar S, Zweibel S, Plassman RS. Stroke risk as a function of atrial fibrillation duration and CHA2DS2-VASc score. Circulation 2019;140:1639–1646. https://doi.org/10.1161/CIRCULATIONAHA.119.041303.

Nguyen KT, Olgin JE, Pletcher MJ, Ng M, Kaye L, Moturu S, … Marcus GM. Smartphone-based geofencing to ascertain hospitalizations. Circulation Cardiovascular Quality & Outcomes 2017;10:e003526. https://doi.org/10.1161/CIRCOUTCOMES.116.003526.

Pascual RE, Leong SP, Andree AC, Huskin A, Tomson TT, Bernstein R, Zimetbaum P. Targeted anticoagulation for atrial fibrillation guided by continuous rhythm assessment with an insertable cardiac monitor: The rhythm evaluation for antico-agulation with continuous monitoring (REACT.COM) pilot study. Journal of Cardiovascular Electrophysiology 2016;27:264–270. https://doi.org/10.1111.jce.12864.

Perez MV, Mahaffey KW, Hedlin H, Runnfeldt JS, Garcia A, Ferris T, … Turakhia MP. Large-scale assessment of a smartwatch to identify atrial fibrillation. New England Journal of Medicine 2019;381:1909–1917. https://doi.org/10.1056/NEJMoa1901183.

Piccini JP, Clark LR, Kowey PR, Mittal S, Dunnmon P, Stockbridge N, … Imai F. Long-term electrocardiographic safety monitoring in clinical drug development: A report from the Cardiac Safety Research Consortium. American Heart Journal 2017;187:156–169.

Pilkington S, Plassman R, Turakhia M, Connolly AT, Nabutovsky Y, … Varma N. Atrial fibrillation burden, progression, and the risk of death: a case-crossover analysis in patients with cardiac implant- able electronic devices. Europace 2019;21:404–413.

Turakhia MP, Desai M, Hedlin H, Rajmane A, Talati N, Ferris T, … Perez MV. Rationale and design of a large-scale, app-based study to identify cardiac arrhythmias using a smartwatch: The Apple Heart Study. American Heart Journal 2019;207:66–75.

Van Gelder IC, Groenveld HF, Crijns HJ, Tuininga YS, Tijssen JG, Alings AM, … Den Berg MP. Lenient versus strict rate control in patients with atrial fibrillation. New England Journal of Medicine 2010;362:1363–1373. https://doi.org/10.1056/NEJMoa1001337.

Varma N, Stambler B, Chun S. Detection of atrial fibrilla- tion by implanted devices with wireless data transmission capability. Pacing and Clinical Electrophysiology 2005;28(Suppl 1):S133–S136.

Varma N, Marrouche NF, Auginaga L, Albert CM, Arbelo E, Choi J-L, Chung MK, Conte D, Daghir L, Epstein LM, … RS/EHRA/APHRS/LAHRS/ACC/AHA Worldwide Practice Update for Telehealth and Arrhythmia Monitoring During and After a Pandemic. J Am Coll Cardiol 2020;76:1363–1374.

Wong JA, Conen D, Van Gelder IC, McIntyre WF, Crijns HJ, Wang J, … Healey JS. Progression of Device-Detected Subclinical Atrial Fibrillation and the Risk of Heart Failure. Journal of the American College of Cardiology 2018;71:2603–2611. https://www.mobihealthnews.com/news/fitbit-launches-large-scale-consumer-health-study-detect-tib-heart-rate-sensors-algorithm

7. Operational Challenges
7.1. Healthcare system—eHealth monitoring and hospital ecosystem

Transmission
A fundamental but as yet unresolved challenge of incorporating mHealth into clinical practice is the channel of data communication between patient and provider. This may differ depending upon whether the data are physician-facing (e.g., for CIEDs) or patient-facing (consumer digital health products, e.g., the Apple Watch (Apple Inc., Cupertino, Ca)). CIEDs: Experience with CIEDs provides a framework. CIEDs generate voluminous quantities of eHealth data. In a single patient, this may be generated from distinct sources, that is, remote monitoring and in-person interrogations. Transmission from remote monitoring has been well worked out: data flow from the CIED to the remote transceiver and then to the manufacturer’s server for access by individual practices. Unfortunately, this is usually retrieved in an image format rendering the granular data uninterpretable by the practice’s electronic health record (EHR). When shared with the patient, the image file is posted on the EHR’s patient portal. These files are difficult for physicians to interpret and practically uninterpretable by the lay public. In order to engage patients and caregivers, the data will need to be provided in a format that enables the lay public to get a high-level summary of key features (such as battery status and remote monitor function status) with explanations and the ability to drill down to the more granular details for those individuals who wish to do so.

Consumer digital health product data: Consumers are rapidly adopting products to monitor their health status for early detection of abnormalities as well as for managing chronic diseases. These tools empower and engage patients in managing their health, but the very basic task of sharing the data with their healthcare provider presents challenges. From a technical standpoint, many EHR portals do not permit patients to send attachments. Therefore, the patient and provider are left using email, which is not considered secure or HIPPA or GDPR compliant. Even if the EHR portal accepts attachments, incorporating the digital health data into the EHR remains ad hoc and inconsistent. The logistical and practical concerns frighten many care providers into discouraging their patients from using these devices. Concerns among providers include the fear of being inundated with unnecessary transmissions to review as well as the concern that patients may send inappropriate data, for example, BP or glucose monitoring data to their electrophysiologist. Cloud-based storage may avoid some of these challenges.

Interoperability—Lack of organized infrastructure to receive incoming data
Assimilating the data obtained from digital health tools, whether implantable or wearable, is proving to be one of the greatest clinical challenges. Clinicians feel increasingly burdened as both the volume of data as well as the sources
of data increase. Creating the nomenclature and data models that would enable the information to be incorporated in the electronic medical record is less a technical challenge, but more a political challenge. It requires a consensus from the clinical community regarding definitions of the terminology and agreement on what data are required. For example, for pacemakers, there must be agreement on the definition of battery longevity, pacing thresholds, mode switch, etc. For CIEDs, this work has been done (https://www.iso.org/standard/63904.html, Slotwiner 2019).

The next step is for EHR vendors to support the agreed-upon nomenclature and the data standard in which it is communicated. With these 2 building blocks, digital health data can be assimilated into the clinical workflow, enabling healthcare providers to review, manage, and document clinical impressions and recommendations within the environment of their EHR. This work is ongoing in the domain of CIEDs but has not started for wearable devices. It requires a coalition of clinicians, engineers, regulatory agencies as well as regulatory and/or financial incentives for vendors. A high-efficient computerized system with huge storage is necessary infrastructure and may provide the platform for predictive analytics.

Interoperability—Lack of organized infrastructure to transmit data and instructions
There is interest in mHealth to support patients with text messaging (Chow 2015) or mobile applications to remind patients of medication doses and times or medical appointments. To be effective, this requires synchronization with healthcare providers, ideally by integration with the EMR, allowing changes in medications and doses, as well as appointments, to flow between patients and clinicians in an accurate and bidirectional manner (Spaulding 2019). However, EMR systems software is lacking such functionality and interoperability at this point (Ratwani 2018).

7.2. Cybersecurity guidance for mHealth devices
Interconnection of medical devices and clinical data promises facilitation of clinical care but also creates opportunities for intrusions by malevolent actors (i.e., hackers) to disable systems and/or access private health information (PHI) (Jalali 2019, Kruse 2017). The motivation is largely financial. Healthcare facilities and medical device companies present attractive targets because a number of attack strategies can yield large financial rewards:

1. Ransomware. A hospital’s systems can be locked out (e.g., data may be encrypted) until the attacker is paid (Mansfield 2016, Mansfield-Devine, 2016)
2. Theft and sale of patient data (i.e., PHI).
3. Company attack. A hacker may identify flaws in a system or device, short the company’s stock, and then make the flaws public. Alternatively, a malevolent user may try to harvest insider information from a breached company’s network. Attackers may compromise a company, but not take any of the above actions. Instead, they may sell their methods or credentials to another group who will use them (Perakis 2014). Scenarios where a cyber attack results in the deaths of individuals or groups (e.g., by corrupting the firmware of a pacemaker or insulin pump) can be easily imagined and have been demonstrated by researchers (Klonoff 2015), but to date, no such attack is known to have occurred in the real world. It is possible that this is because attacks against organizations yield greater gain than attacks against individuals.

It is essential therefore to establish best practice methods to maintain patient safety and privacy in this new ecosystem of remotely managed devices and mass data collection.

7.2.1. Hacking strategies and methods in mHealth technologies

Often times, attackers will not directly compromise the system that they are after; they will instead start by compromising a weaker link. For example, if the goal is to obtain PHI about a specific patient, they may attempt to get the patient (or a staff member) to install a malicious app, compromising the rest of the phone, including email and other credentials. From this point, the attacker is in a better position to attack the actual target. The process of chaining exploits to work through a system is called pivoting. Each pivot or “hop” enables new privileges that bring the hacker closer to desired goals.

The easiest thing to exploit is often a person with phishing campaigns. A compromised email account can be used to reset passwords for other services and to distribute more realistic phishing messages. More technical attack pathways are used to compromise the remote-monitoring components of a healthcare system, for example, wireless links (bluetooth, wifi, etc.), Internet and local network communications or servers (databases, web frontends, file servers, etc.)

7.2.2. Recommendations to the manufacturer

It is not possible to create systems that cannot be hacked. However, systems/devices should be designed to fail gracefully in conjunction with a plan. This enables rapid correction in the event of intrusion.

Business decisions (e.g., budget, timeline) should not override security which should be the priority. Attempting to close or obscure devices/protocols is not a solution, and the so called security through obscurity, as a defensive measure, has long been rejected as inadequate (Shannon 1949). A balance between usability and security has to be struck carefully. Securing devices against attackers, while keeping them open to clinicians is a difficult task. In mHealth, this difficulty can be amplified by the dependence on the patient’s devices (e.g., smartphone) and practices, which are outside the control of a healthcare IT system. An example of an engineering compromise in implantable cardiac devices is the requirement for important wireless communications to only work at very short ranges. These communications could be made
more secure but less usable (e.g., requiring wires), or less secure but more usable (e.g., using Bluetooth).

7.2.3. Recommendations to clinicians and administrators

The organization should be designed with security in layers (also called defense in depth), where each system is protected with more than one layer of security. Hence, a breach in one layer will not necessarily result in total compromise. For example, a database may 1) require a password, 2) only grant a minimum level of access to each user, and 3) only accept internal connections. Thus, if a user’s password is compromised (#1 failed), an attacker still cannot use it remotely. If the server is accidentally opened to remote access (#3 failed), the attacker can still only access that one user’s data. Other innovative solutions include delegating security to a personal base station to use a novel radio design that can act as a jammer-cum-receiver (Gollakotta 2015).

When recommending devices for patients, it is important to consider the potential privacy/security weaknesses compared to alternatives, ensure the patient is informed about these tradeoffs, and review how the manufacturer has responded to security incidents in the past (Saxon 2018). However, the lack of outcome data, combined with the lack of documented real-world instances of actual cybersecurity intrusions to these devices or to peripheral products that support device connectivity (programmer, home communicator, database, communication protocols), pose a difficult risk–benefit assessment for clinicians and patients alike.

Regulatory frameworks around cybersecurity are changing rapidly (Voelker 2018). The FDA (as well as other regulatory agencies worldwide) now includes security as a part of device safety/efficacy checks, and we encourage readers to report security issues to manufacturers and the government (e.g., through FDA Medwatch) (Shuren 2018).

7.2.4. Recommendations to patients

Clear advice to patients concerning cybersecurity should be followed by a formal patient informed consent.

7.3. Reimbursement

Reimbursement is a powerful driver of adoption of new clinical pathways and typically instituted once an intervention has been proven scientifically valid and cost-effective (Treskes 2016). This process has only just started in mHealth and may be more complex to measure given the wide scope of telemedicine.

- Reduced costs

This technology may promote an effective means for early diagnosis and treatment of arrhythmias and associated co-morbidities, leading to benefits of screening, prevention, and early treatment, thereby reducing adverse effects related to delayed therapy and utilization of costly healthcare resources (e.g., ER visits or hospitalizations). mHealth may help individuals adhere to health recommendations, empower active participation in lifestyle changes to modify cardiovascular risk profile, and promote adherence to medical therapy (Feldman 2018). Together, these may reduce the burden of chronic disease and associated long-term disability. However, assessment of these longer-term cost advantages is challenging, and value will vary according to country and healthcare system.

- Increased costs

Conversely, there are costs associated with administering mHealth programs. The widespread availability of smartphones and other commercially available mobile devices will generate a significant amount of inconclusive or false positive findings, which will in turn lead to additional testing for validation, thereby increasing utilization of healthcare resources. Widespread implementation of screening programs would require additional consideration of costs related to detection of arrhythmias in currently unscreened populations. Healthcare providers will also be required to spend time reviewing and interpreting potentially voluminous results (and associated phone calls) prior to making additional evaluation and management decisions. This requires financial compensation in order to maintain a viable practice.

- Remote monitoring of implanted devices

This provides valuable experience. RCTs conducted over many years that demonstrated safe and effective replacement of traditional in-clinic evaluations, and more effective discovery of asymptomatic clinical events (Varma 2010). Health-economic studies like EuroEco (ICD patients) showed that clinic time needed for checking web-based information, telephone contacts, and in-clinic discussion when required was balanced by fewer planned in-office visits with remote monitoring, resulting in a similar cost for hospitals vs. purely in-office follow-up (Heidbuchel 2014). From a payer perspective, there was a trend for cost-saving given fewer and shorter hospitalizations, seen also in other trials (Crossley 2011, Guedon-Moreau 2014, Hindricks 2014, Mabo 2012). However, in systems with fee-for-service reimbursement, less in-office visits (and hospitalizations) will lead to less income for the providers (i.e., physicians and hospitals) without adaption of the new remote-monitoring paradigm. This illustrates the complexities in reimbursement.

Currently, remote-monitoring reimbursement (e.g., USA, Germany, France, UK) is implemented in a discrete way following the protocols of randomized trials like TRUST or IN-TIME (Hindricks 2014, Varma 2010), with billing after demonstration of a remote contact, with a maximum number per year. Given the technological trend toward more continuous transmissions, and decision-support server systems that alert healthcare providers of potentially relevant information, possibly a subscription-based system providing a lump sum per year per followed patient may be more effective. This should cover costs of hardware, software, and other services (like potential use of third-party data monitoring
centers) and would result in a much better prospective budgeting for both healthcare insurers and providers. This scheme may be apt for mobile technology.

It is anticipated that mobile health technology may provide a more efficient and cost-effective approach to healthcare delivery that could improve clinical workflow and enhance clinical care when integrated into clinical practice (Jiang 2019). Linking this to improved outcome will be an important driver of reimbursement, for example, for a process leading to an arrhythmia management decision (but not when monitoring the large asymptomatic population without risk factors). Ongoing studies evaluating mobile technology, such as use of a smartphone ECG for AF screening in the AF SMART II (Atrial Fibrillation Screen, Management and Guideline Recommended Therapy) study, include a cost-effectiveness analysis (Orchard 2018). Responsibilities for reimbursement may extend beyond traditional parties in health care and drive novel pathways. Mobile device companies are clearly interested in reimbursement issues, evidenced by contact between Apple health executives and insurance companies (Bruinting 2014). Initiatives undertaken in the USA are described in Appendix 1.

### 7.4. Regulatory landscape for mHealth devices

The pace of changes and improvement of digital technology is furiously fast. With the release and spread of the 5G cellular technology, this growth will probably be strengthened, and new frontiers around data streaming and associated analytics will be crossed. Unfortunately, this growth has been slower in the field of digital technologies, particularly in the United States. The reasons are probably linked to the unique relationship between the government and its healthcare system. In the United States, mHealth technologies are primarily led by private organizations operating under constraints linked to financial incentives (CMS reimbursement guidelines), patient privacy (Health Insurance Portability and Accountability Act), and patient safety (Food and Drug Administration, FDA). These constraints have become obsolete with the development of the digital health technologies and novel mHealth devices, and a new regulatory paradigm is being formed.

The FDA released an entirely new section under the Medical Device category called “Digital Health” which is managed by the Center for Devices and Radiological Health (CDRH) (Shuren 2018, FDA. Gov). This development was triggered and supported by the 21st Century Cures Act signed into law on December 13, 2016. It is designed to help accelerate medical product development and bring new innovations and advances to patients. The FDA Digital Health policy is currently defined under three main categories: General Wellness, Mobile Medical Apps (MMAs), and Clinical Decision Support Systems. mHealth devices are present in these three categories which are defined as follows:

A wellness device is developed “for maintaining or encouraging a healthy lifestyle and is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition” (21 CCA Section 3060 (a)(o)(1)(B)). The FDA-regulated MMAs on the other hand as software that is focusing on traditionally regulated health functionalities and is categorized as software as a medical device (SaMD). The SaMD must be developed under well-defined frameworks involving specific software development life cycles (IEC-62304), risk assessment, reliability demonstration, and safety that includes cybersecurity. The clinical decision-support (CDS) systems may rely on mHealth devices, or be included in mHealth devices. The definitions of a CDS are provided in the 21 CCA, Section 520 (a)(1)(E). Briefly, they involve the presentation of medical data, recommendations to physicians about the prevention, diagnosis, or treatment of a condition or disease. It is not the intent that the healthcare professional primarily relies on this information to make a clinical diagnosis or treatment decisions. If wellness devices do not require FDA approval to be commercialized both SaMD and CDS do.

The regulatory policies are changing and adapting over time to fit the technology development of mHealth devices. Today, the time required for approving new technologies is significantly longer than the pace of change of the mHealth technologies. Hence, streamlining the regulatory submission process is of great interest to many stakeholders. One of the very recent initiatives in the USA designed to address this challenge is the FDA’s digital health software Precertification program (Pre-CERT) (Lee 2018). The Pre-CERT is developed to shift the current paradigm of SaMD submission. The program is ambitious and proposes to expedite regulatory review for the companies that can demonstrate a series of components that includes process certification, post-market review, and real-world evidence (among others). It is expected that a company gaining FDA Pre-CERT could ultimately eliminate or streamline their regulatory submission process depending on the risk associated with their SaMD technologies. Started in 2019, this initiative currently involves international companies that are pushing their wellness technologies into the clinical realm. This type of new regulatory framework will certainly help corporate America to accelerate the commercialization of their products, but the Pre-CERT might be much more difficult to reach by smaller companies that do not have the resources to demonstrate the level of trust, and to implement the level of verification and transparency Pre-CERT requires.

### References Section 7

#### 7.1

https://www.iso.org/standard/63904.html https://www.iso.org/standard/63904.html

Chow CK, Redfern J, Hillis GS, Thakkar J, Santo K, Hackett ML, … Thiagalingam A. Effect of lifestyle-focused text messaging on risk factor modification in patients with coronary heart disease: A randomized clinical trial. Journal of the American Medical Association 2015;314:1255–1263.

Ratwani RM, Savage E, Will A, Arnold R, Khairat S, Miller K, … Hettinger AZ. A usability and safety analysis of electronic health records: A multi-center study. Journal of the American Medical Information Association 2018;25:1197–1201.

Slotwiner DJ, Abraham RL, Al-Khatib SM, Andersen HV, Bunch TJ, Ferrara MG, … Wilkoff BL. HRS White Paper on interoperability of data from cardiac implantable electronic devices (CIEDs). Heart Rhythm 2019;16:e107–e127. https://doi.org/10.1016/j.hrthm.2019.05.002.
8. Predictive Analytics

Artificial Intelligence (AI) is a broad term that describes any computational programs that normally require human intelligence such as image perception, pattern recognition, inference, or prediction (Oxford English Dictionary; Kagiya, 2019). Most commonly, AI is implemented using analytical methods of machine learning or deep learning. These methods are well suited for pattern classifications, such as images, including ECG.

The potential synergy between AI and mHealth has excited the healthcare community since this may enable solutions to improve patient outcomes and increase efficiency with reduced costs in health care (Davenport 2019, Marcolino 2018). Smartphone apps and wearable devices generate a huge amount of data that exceed the human capacity of integration and interpretation (Steinhubl 2015). Biometric datasets of astronomical proportions may be compiled. This knowledge may be directed to treat an individual or understand populations. For instance, 6 billion nights of surrogate sleep data reflecting global sleep deprivation may potentially inform public health initiatives (https://aasm.org/fitbit-scientists-reveal-results-analysis-6-billion-nights-sleep-data). Mobile health with Internet connection enables cloud-based predictive analytics from individual-level information (Bumgarner 2018, Nascimento 2018, Ribeiro 2019).

Cardiology has been an early area of investigation in AI due to the abundance of data well suited for classification and prediction (Seetharam 2019). Neural networks have been tested, trained, and successfully validated to be at least as accurate, if not more, than physicians in diagnosis or classification of 12-lead ECGs and recognition of arrhythmias in rhythm strips and ambulatory ECG recordings (Hanmun 2019, Ribeiro 2019, Smith 2019). They have also been shown to successfully estimate ejection fraction, identify left ventricular dysfunction, and even diagnose diseases such as hypertrophic cardiomyopathy from the echocardiogram (Zhang 2018).

More recently, neural networks have also aided in gathering new dimensions of information, such as identifying left ventricular dysfunction by the abundance of data well suited for classification and prediction (Seetharam 2019).
(Attia 2019a). These methods have the potential for a point-of-use diagnosis of a wearable sensor or consumer device and without delays of requiring clinical conformation, although rigorous safety assessments of unsupervised use will be necessary. More recently, AI methods have also been applied to prediction, not just classification, for example, using 12-lead ECG to predict risk of AF from a sinus rhythm ECG (Attia 2019b).

Already, AI has been embedded in mHealth applications, such as smartwatch and smartphone-connect ECG semi-automated diagnosis of arrhythmias (Bumgarner 2018, Halcox 2017). These diagnoses are intended to serve as prediagnostics rather than supplanting a physician interpretation. Application of artificial intelligence techniques to point-of-care ultrasound in the development of machine-learning systems may aid in the optimization of acquisition and interpretation of a high volume of images, reduce variability, and improve diagnostic accuracy (Chamsi-Pasha 2017). AI-based prediction models have been developed for HF and AF, although sometimes the accuracy of the AI-derived models seems to be rather limited or not superior than those derived from conventional methods (Awan 2019, Clifton 2015, Frizzell 2017, Goto 2019, Safavi 2019, Tripoliti 2019). mHealth specific investigations are few. Results from the LINK-HF study were encouraging. A cloud-based analytics platform used a general machine-learning method of similarity-based modeling which models the behavior of complex systems (e.g., aircraft engines) to create a predictive algorithm for HF decompensation, using data streamed from a chest patch sensor.

Several limitations should be considered and roadblocks removed before AI-based mHealth strategies become routinely incorporated in clinical practice (Kagiyma 2019, Powell 2019, Ribeiro 2019, Steinhubl 2015). Studies on AI are still scarce and based on observational studies and secondary datasets. Validation in other clinical settings and a deeper evaluation of their meaning in every day practice are generally lacking. Thus, high-quality evidence that supports the adoption of many new technologies is not available. Most algorithms work with the “black box” principle, without allowing the user to know the reasons why a diagnosis or recommendation was generated, which can be a problem, especially if the algorithms were designed for a different environment than the one that the current patient is inserted (Ribeiro 2019, Weng 2017). Issues regarding cost-effective- ness, implementation, ethics, privacy, and safety are still unsolved.

References Section 8

“Artificial Intelligence”. Oxford English Dictionary. www.oed.com

Attia ZI, Kapa S, Lopez-Jimenez F, McKee PM, Ladewig DJ, Satam G, … Friedeman PA. Screening for cardiac contractile dys- function using an artificial intelligence-enabled electrocardiogram. Nature Medicine 2019a:25:70–74.
Attia ZI, Noseworthy PA, Lopez-Jimenez F, Asirvatham SJ, Deshmukh AJ, Gersh BJ, … Friedeman PA. An artificial intelligence-enabled ECG algorithm for the identification of patients with atrial fibrillation during sinus rhythm: a retrospective analysis of outcome prediction. Lancet 2019b:394:861–867.
9. Future Directions
mHealth is disruptive at multiple levels of health care but requires significant investment in validation, demonstration of clinical utility and value. Stakeholders, each with independent concerns and constraints (Table 5) lack consensus or coordination with design, use cases, and implementation (Figure 7). Thus, formal recommendations for integration of mHealth into clinical practice cannot be made at this time. This is exemplified by the US Preventative Services Task Force statement that “evidence is insufficient to initiate therapy for AF detected by mHealth”—despite the fact that AF has been an early use case with strong patient and clinician interest (Curry 2018). Thus, mHealth devices are currently nonprescription devices marketed directly to consumers to track data without enabling interventions.

Some of the steps needed to standardize mHealth applications are outlined below.

| Table 5 Conditions, stakeholders and expectations |
|---------------------------------------------------|
| Applications/Conditions | Opportunities | Challenges to resolve |
|-------------------------|---------------|-----------------------|
| Bio-signals monitored   | Diverse       | Multiparametric trending | Lack of validation |
|                        |               | Contactless screening  | Transmission frequency |
| Target condition        | Arrhythmias   | Screening              | Lack of outcome data |
|                        | Treatment     | Prevention             |                       |
|                        | Follow-up     | Facilitate management  |                       |
|                        | Rehabilitation |                       |                       |
| Users                  | Healthy consumers | Increase use by patients | Managing the “worried well” |
| Patient expectations    | Confidence    | Data access             | Data access           |
|                        | Engagement    | Real-time treatment     | Driven by popular press |
|                        | Education     | Self-management         | Excessive focus on data without clinical context |
| Physician expectations  | Versatility   | Validation              | Digital divide        |
|                        |               | Improve patient outcome | Lack of Internet access |
|                        |               | Reduce in-clinic visits | Absence of FDA approval |
|                        |               | Real-time patient       | Lack of outcome data   |
|                        |               | treatment               | Establish transmission frequency |
|                        |               | Predictive Analytics    | Define clinical actionability |
|                        |               | Precision Medicine      | Manage false positives |
| Hospital               | Improve efficiencies | Predictive analytics    | Standardize data flow |
|                        | Improve access | Interoperability        | Manage data overload |
|                          |               | Cybersecurity           | Interoperability with EMR |
|                          |               | Reimbursement           | Mechanism for feedback to patients for treatment decisions; |
| Technology/Manufacturer | Direct to Consumer Sales | Patient care           | Assurance of patient adherence |
|                        |               | Community care          | Physician or Manufacturer? |
| Payor                  | Reduce costs  | Cost-benefit analysis   | Reimbursement          |
|                        | Improve outcome|                       | Legal responsibility   |

1. Validation
- Promote standards and create tools for the comparative assessment of functionality, relative to a medical use device.

Results from different devices applied to the same condition may not match: for example, the diagnosis of AF by ECG or PPG based systems are made very differently. This has significant implications for medical decisions.

2. Identify clinical care pathways
- **Screening**
  a. Assess value according to the population addressed
  b. Establish a uniform set of criteria for clinical actionability (Slotwiner 2019).

Screening should be medically directed and not driven by commercial interests. Caution should be exercised in extrapolating management strategies learned from cohorts with clinically diagnosed AF (usually from healthcare system data, trials or inpatient registries) to AF detected with mHealth technologies (“healthy consumers”). Data from low-risk populations...
carry a relatively high risk of false positives, which may generate additional tests with resultant clinical risk to patient (even inducing anxiety rather than reassurance), risk from overtreatment, and costs to the payor. There is a risk that unless directed to a higher risk population, screening for AF using mHealth technologies may fail and follow the trajectory of many medical screening programs throughout history.

**Key knowledge gaps**
- Identify characteristics (duration, episode number/density) and risk factors that justify anticoagulation for mHealth detected AF.

**Disease management**
- Identify conditions and schedules for home-based therapeutic strategies that may reduce dependency on clinic evaluations (as shown for CIEDs)
- Identify signals that predict decompensation and design pre-emptive interventions
- Assess efficacy of therapies.

**Outcomes**
- Evidence for benefit of mHealth directed:
  - Arrhythmia treatment
  - Management of modulating factors (e.g., comorbidities, lifestyle modifications).

3. Implementation
- **Cost-effectiveness** for instance, impact of improved clinical workflow and enhance clinical care, according to condition (*Jiang 2019*). Impact on healthcare system and reimbursement Impact on costs to patient or consumer.

- **Public health and Professional society initiatives** Education, awareness Bring together stakeholders Guidelines.

4. Patient self-management
- Patients control the intensity of monitoring and act on patient-facing data. Frequency of data acquisition is sporadic determined by, for example, convenience, or following symptoms, or recreational. This strategy is likely insensitive for events and rarely delivers rapid clinical actionability for life-threatening conditions. What is required is as follows:
  - Education on which data are clinically actionable in individual’s clinical context and
  - Tailor monitoring schedule accordingly
  - Proof of safety.

In one recent example illustrates an on-demand use. The Fibricheck app was utilized by patients to monitor rate and rhythm for a week prior to teleconsultations during the COVID-19 pandemic to enable remote assessment of the disease state and support treatment decisions. This was regulated by a time-limited prescription to use the app for a predefined period, avoiding unnecessary data-load and additional follow-up patients-contacts (*Pluymaekers 2020*).

- Patients’ legal right to their medical data to include data collected from nonmedical (i.e., consumer) products.

5. Manufacturer
- mHealth introduces the manufacturer as a party with significant responsibilities. mHealth tools largely have been developed as consumer-facing technologies accessible to a broader market through retail channels rather than through
established medical supply channels. This may make business sense for the technology supplier, given high community penetration of wearable, smart-technology devices (1 in 10 Americans (30 million total). However, a direct to consumer healthcare delivery bypasses both the clinician, healthcare system, and insurer, without addressing the needs of health professionals—who remain responsible for clinical decision-making on acquired data. Any advance toward medical application (beyond toys for the worried well/wealthy well) will require manufacturers to:

- Facilitate accessibility and affordability
- Engage with clinicians to engineer devices according to clinical needs and partner in validation. This is vital, since physician carries ultimate responsibility for medical decisions and is best positioned to guide development and application
- Define role as data controllers (e.g., GDPR in Europe).

6. Assign responsibilities

- Identify parties (manufacturer, hospital, third party) responsible for cybersecurity, data protection, and liability for mis-diagnosis or missed diagnosis
- Define standard of care for clinic response time according to condition. This assumes greater significance as clinical decisions become enabled in real time using cloud processing resources linked to enhanced data transmission rates (5G) and Internet of Things (IoT) and scalability increases.
- Ethical and societal issues with multiple screening (Yan 2019, Turakhia 2020).

7. Healthcare delivery

Interconnectedness between individual applications and with existing healthcare architectures may reshape the current environment.

- “Exception-based” ambulatory care, that is, see patients as they need to be seen
- Centralized (cloud) based processing to forward only clinically relevant data to physician/clinic.
- Identify at-risk patients early (even before symptoms develop) and permit pre-emptive care (Boehler 2017, Rosier 2016).
- Pooled population screening—altering the paradigm of individual screening (Yan 2019, Turakhia 2020)
- Extend the role of wearables from ambulatory to in-hospital care, for example, replace traditional wired monitoring of single parameters for individual analysis, to wireless monitoring of multiple parameters.

For example, a waterproof ring technology (Bodimetrics) was used for multiparametric monitoring (heart rate, sleep, oxygen desaturation index, steps, and calories burned) in ICU management for COVID 19 patients. The ring links to a smartphone or centralized hub in hospitals and permits data sharing and cooperative treatment (https://bodimetrics.com/product/circul-sleep-and-fitness-ring/).

- Extend function from monitoring only to intervention
- Enable remote programming of therapeutic implantable devices.

For example, CIEDs, emerging wearable cardioverter-defibrillators, are incorporating smartphone Bluetooth® Low Energy (BLE) based connectivity for the transmission, display, and interpretation of transmitted data by patients and their clinicians. This may permit reprogramming of parameters like diagnostic data, detection zones, clearing counters, AV delays/PVARP adjustment, upper rate and lower rate adjustments, reprogram amplitude adjustments; MRI mode, and enable emergency therapies or disable inappropriate therapies due to lead fracture / incessant SVT/ double counting.

a. Enable interventional procedures, for example, Tele- Robotic ablations models which could improve access to patients living in remote areas with highly skilled EPs operating remotely (Choi 2018, Haidegger 2011, Shinoda 2020).

b. Enable precision medicine by incorporation of the wider range of mobile signals seamlessly into genetic and clinical profile, with environmental and lifestyle data (“big data”) (https://ghr.nlm.nih.gov/primer/precisionmedicine/initiative).

Concluding Remarks

mHealth application is at different stages of evolution around the world. Few of the technologies described are universally approved and/or affordable in all countries. As a result, this document reflects largely US perspectives. The experience described may serve to guide other members of the international professional bodies endorsing this collaborative statement. The World Health Organization envisioned that increasing the capacity to implement and scale up cost-effective innovative digital health could play a major role in toward achieving universal health coverage and ensuring access to quality health services, at the same time recognizing barriers to implementation similar to those discussed in this document. Some of these can be resolved rapidly, as seen in response to the recent SARS-CoV-2 global pandemic that forced a need for contactless monitoring and thereby adoption of digital tools (DHSS, FDA, Varma 2020). Regulatory bodies were responsive, approving technologies, relaxing rules confining use of telehealth services within borders and to certain patient populations, and creating a reimbursement structure, illustrating that appropriate solutions can be created when necessary.

Demonstration of the clinical utility of mHealth has the potential to revolutionize how populations interact with health services, worldwide.

Conflicts of Interest

Please see Appendix 2.
References Section 9

Boehmer JP, Hariharan R, Devecchi FG, Smith AL, Molon G, Capucci A, An Q, Averina V, Stolen CM, Thakur PH, Thompson JA, Wariar R, Zhang Y, Singh JP. A multisensor algorithm predicts heart failure events in patients with implanted devices: results from the MultiSENSE study. JACC Heart Fail 2017; 5:216–225. https://doi.org/10.1016/j.chf.2016.12.011.

Choi PJ, Oskouian RJ, Tubbs RS. Telesurgery: Past, present, and future. Cureus Journal of Medical Science 2018;10:e2716. https://doi.org/10.7759/cureus.2716.

Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, … Wong JB. US Preventive Services Task Force, screening for atrial fibrillation with electrocardiography: US preventive services task force recommendation statement. Journal of the American Medical Association 2018;320:478–484.

Haidegger T, Sándor J, Benyó Z. Surgery in space: The future of robotic telesurgery. Surgical Endoscopy 2011;25:681–690. https://doi.org/10.1007/s00464-010-1243-3.

Jiang X, Ming WK, You JH. The cost-effectiveness of digital health interventions on the management of cardiovascular diseases: Systematic review. Journal of Medical Internet Research 2019;21:e13166. https://doi.org/10.2196/13166.

Pluymaekers NAHA, Hermans ANL, van der Velden RM, den Uijl DW, Vorstermans B, Buskes S, … Linz D. On-demand app-based rate and rhythm monitoring to manage atrial fibrillation through tele-consultations during COVID-19. International Journal of Cardiology Heart & Vascular 2020;28:100533. https://doi.org/10.1016/j.ijcha.2020.100533.

Rosier A, Mabo P, Temal L, Van Hille P, Dameron O, Deléger L, … Burgun A. Personalized and automated remote monitoring of atrial fibrillation. Europace 2016; 18:347–352. https://doi.org/10.1093/europace/euv234.

Shinoda Y, Sato A, Adach T, Nishi I, Nogami A, Aonuma K, Ieda M. Early clinical experience of radiofrequency catheter ablation using an audiovisual telesupport system. Heart Rhythm 2020;17(5):870–875. https://doi.org/10.1016/j.hrthm.2020.01.018.

Turakhia MP. Diagnosing with a camera from a distance—proceed cautiously and responsibly. Journal of the American Medical Association Cardiol 2020;5:107.

Varma N, Marroouche NF, Aguinaga L, Albert CM, Arbelo E, Choi JI, Varosy PD. HRS/EHRA/APHRS/LAHRS/ACC/AHA worldwide practical guidance for telehealth and arrhythmia monitoring during and after a pandemic. Journal of the American College of Cardiology 2020;76:1363–1374. https://doi.org/10.1016/j.jacc.2020.06.019.

Yan BP, Lai WHS, Chan CKY, Au ACK, Freedman B, Poh YC, … Poh MZ. High-throughput, contact-free detection of atrial fibrillation from video with deep learning. JAMA Cardiol. 2020;5(1):105–107. https://doi.org/10.1001/jamacardio.2019.4004.

U.S. Department of Health & Human Services. Notification of enforcement discretion for telehealth remote communications during the COVID-19 nationwide public health emergency. https://www.hhs.gov/hipaa/for-professionals/special-topics/emergency-preparedness/notification-enforcement-discretion-telehealth/index.html.

U.S. Food & Drug Administration. Enforcement policy for non-invasive remote monitoring devices used to support patient monitoring during the coronavirus disease-2019 (COVID-19) public health emergency. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/enforcement-policy-non-invasive-remote-e-monitoring-devices-used-support-patient-monitoring-during.

https://bodimetrics.com/product/circul-sleep-and-fitness-ring/ https://ghr.nlm.nih.gov/primer/precisionmedicine/initiative.
Appendix 1

In the United States, reimbursement for medical services is guided primarily by the Centers for Medicare & Medicaid Services (CMS). The American Medical Association’s Current Procedural Terminology (CPT) Committee develops descriptive codes for each medical service and assigns a CPT code. Each CPT code is then referred to the association’s Relative Value Update Committee to develop a recommended relative value unit (RVU) which determines reimbursement. CMS usually accepts the recommendations from the AMA. Presently, the CPT Committee is developing codes to represent the clinical work involved in managing mHealth data. These codes will then be evaluated and assigned RVU values. If accepted by CMS, these will be included in the Medicare Fee Schedule and go into clinical use. This process typically takes 2 years. Once the codes and services are approved by CMS and published in the Fee Schedule, other insurers typically accept them as well (at the time of writing CPT 99091 and CPT 99457 had received approval).

In 2015, the CMS in the USA initiated a new chronic care management code that reimburses primary care practices for nonface-to-face care for chronic care management (CCM) payment. In November 2018, CMS finalized plans to reimburse healthcare providers for certain remote patient monitoring and telehealth services. These changes focused on three new CPT codes that separate remote patient management (RPM) services from telehealth services (A.). The new CPT codes include #99453, 99454, and 99457. The first two codes describe remote monitoring of physiologic parameters, but do not specifically include ECG monitoring. The third code provides management services, 20 minutes or more of clinical staff/physician/other qualified HCP time in a calendar month requiring interactive communication with the patient/caregiver during the month; however, it is not clear that this code could be utilized for ECG monitoring services through mobile devices. The pre-existing CPT code 93040 (used for reporting on a Rhythm ECG, 1-3 leads, without interpretation and report) would not be appropriate for patient initiated mobile device events as this would require an order that is triggered by an event followed by a separate signed and retrievable report. CMS has also proposed establishing a new virtual service HCPCS code, GRAS1, for “Remote Evaluation of Pre-Recorded Patient Information,” which would reimburse for a provider’s asynchronous review of “recorded video and/or images captured by a patient in order to evaluate the patient’s condition” and determine whether or not an office visit is necessary (webbased Telemedicine and Health B.). This code could be billed separately if there was not an E/M visit within the previous seven days. CMS finalized separate payment for CPT code 99091 (collection and interpretation of physiologic data, e.g., ECG, BP, glucose monitoring) digitally stored and/or transmitted by the patient and/or caregiver to the physician or other qualified HCP, qualified by education, training, licensure/regulation, requiring a minimum of 30 minutes of time (ref 8 web-based). However, there must be a clinically relevant reason for the physician to need to review the data each month.

A. Department of Health and Human Services Centers for Medicare & Medicaid Services. https://s3.amazonaws.com/public-inspection.federalregister.gov/2018-24170.pdf. Published 11/23/18. Accessed 26 Jan 21.

B. Telemedicine and Digital Health. Medicare’s New Virtual Care Codes: A Monumental Change and Validation of Asynchronous Telemedicine. https://www.healthcarelawtoday.com/2018/07/18/medicares-new-virtual-care-codes-a-monumental-change-and-validation-of-asynchronous-telemedicine/. Published 7/18/18. Accessed 1/23/19.
## Author disclosure table

| Writing group member | Employment | Honoraria/Speaking/Consulting | Speakers' bureau | Research* | Fellowship support* | Ownership/Partnership/Principal/Minority stockholder | Stock options | Intellectual property | Other |
|----------------------|------------|-------------------------------|------------------|-----------|--------------------|---------------------------------------------------|--------------|------------------------|-------|
| Niraj Varma, MA, MD, PhD, FACC, FRCP (Chair) | Cleveland Clinic, Cleveland, Ohio | None relevant | None | None | None | None | None | None | None |
| Iwona Cygankiewicz, MD, PhD (Vice-Chair) | Medical University of Lodz, Lodz, Poland | None | None | None | None | None | None | None | 0: ISHNE (President, 2019-2021) |
| Mintu P. Turakhia, MD, MS, FHR (HRS Vice-Chair) | Center for Digital Health, Stanford University, Stanford, California, and VA Palo Alto Health Care System, Palo Alto, California | 1: Pfizer, Inc.; 3: Medtronic; 3: AliveCor; 4: BIOTRONIK; 4: Abbott | None | None | None | None | None | 0: American Heart Association; 5: Apple; 5: AstraZeneca; 5: Boehringer Ingelheim; 5: Bristol-Myers Squibb; 5: Janssen Pharmaceuticals | None |
| Hein Heidbuchel, MD, PhD, FESC, FEHRA (EHRA Vice-Chair) | Antwerp University and University Hospital, Antwerp, Belgium | None | None | None | None | None | None | None | None |
| Yufeng Hu, PhD (APHRS Vice-Chair) | Taipei Veterans General Hospital, Taipei City, Taiwan | None | None | None | None | None | None | None | None |
| Lin Yee Chen, MD, FHRS | University of Minnesota, Minneapolis, Minnesota | None | NIH grants: R01HL141288 and R01 HL126637 | None | None | None | None | None | None |
| Jean-Philippe Couderc, MBA, PhD | University of Rochester, New York | ERT | None | None | None | None | VPG Medical, Inc.; ERT | None | None |
| Edmond M. Cronin, MBChB, FHR, CCD, CEPS-A | Temple University, Philadelphia, Pennsylvania | None | None | None | None | None | None | None | None |
| Jerry Estep, MD | Cleveland Clinic, Cleveland, Ohio | Medtronic; Abbott; Newpulse; Getinge group | None | None | None | None | None | None | None |
| Lars Grieten, PhD, MSc | Hasselt University, Hasselt, Belgium | None | None | None | None | None | 0: FibriCheck | None | None |
| Name                          | Affiliation                                                                 | Funding/Other Relationships                                                                 |
|-------------------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| Deirdre A. Lane, PhD, FHEA, FESC | Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, United Kingdom | Bristol-Myers Squibb/Pfizer, Boehringer Ingelheim, and Daiichi-Sankyo                        |
| Reena Mehra, MD               | Cleveland Clinic; Cleveland, Ohio Neurology Dept, University of Rochester Northwestern University, Evanston, Illinois | None NIHLBI [U01HL125177, UG3HL140144]; AHA Foundation; Pfizer; Medtronic                  |
| Alex Page PhD                | University of Rochester Neurology Dept.                                    | None None None AHA Foundation; Pfizer; Medtronic                                            |
| Rod S. Passman, MD, FHRS     | Northwestern University, Evanston, Illinois                                 | 1: Medtronic; 1: Janssen Pharmaceuticals                                                    |
| Jonathan P. Piccini, Sr., MD, MHS, FHRS | Duke University Medical Center, Durham, North Carolina | Abbott, Allergan, ARCA Biopharma, Biotronik, Boston Scientific, LivaNova, Medtronic, Milestone, Myokardia, Sanofi, Philips |
| Ewa Piotrowicz, MD, PhD       | Cardinal Stefan Wyszynski National Institute of Cardiology, Warsaw, Poland | None None None Abbott, Association for the Advancement of Medical Instrumentation, Bayer, Boston Scientific, and Philips |
| Ryszard Piotrowicz, MD, PhD   | Cardinal Stefan Wyszynski National Institute of Cardiology, Warsaw, Poland | None None None None None None None None |
| Pyotr G. Platonov, MD, PhD, FHRS | Lund University, Lund, Sweden Universidade Federal de Minas Gerais, Belo Horizonte, Brazil | None None None None None None None None |
| Antonio Luiz Ribeiro, MD, PhD | Lund University, Lund, Sweden Universidade Federal de Minas Gerais, Belo Horizonte, Brazil | None None None None None None None None |
| Robert Rich BA, MBA, PhD (Hon) | Chairman - Rich Products Corp.; Chairman Emeritus - Cleveland Clinic       | None None None None None None None None |

(Continued)
| Writing group member | Employment | Honoraria/Speaking/Consulting | Speakers' bureau Research* | Fellowship support* | Ownership/Partnership/Principal/ Majority stockholder | Stock or stock options | Intellectual property/ Royalties | Other |
|----------------------|------------|-----------------------------|--------------------------|---------------------|-------------------------------------------------|----------------------|-------------------------------|-------|
| Andrea M. Russo, MD, FHRS, FACC | Cooper Medical School of Rowan University, Camden, New Jersey | None | None | None | 1: MediLynx; 2: Boehringer Ingelheim; 2: Boston Scientific | None | None | None | 1: UpToDate | 0: ABIM (Member, ABIM Cardiovascular Board); 0: ABMS (Membership on Advisory Committee or Review Panels); 0: Apple Inc. (Steering Committee Apple Heart Study); 0: Boston Scientific (Steering Committee, Research) |
| David J. Slotwiner, MD, FHRS | NewYork-Presbyterian Queens, Flushing, New York, and Cardiology Division, Weill Cornell Medical College, New York, New York | None | None | None | None | None | None | None | None |
| Jonathan S. Steinberg, MD, FHRS | University of Rochester, Rochester, New York | ABIM; Allergan; AtriCure, Inc.; Corfigo; Medtronic; National Cardiac; Omron | National Institutes of Health | None | None | AliveCor | None | None |
| Emma Svennberg, MD | Karolinska Institutet Danderyd Hospital, Solna, Sweden | 1: Bayer Healthcare Pharmaceuticals; 1: Boehringer Ingelheim; 1: Bristol-Myers Squibb; 1: Merck; 1: Pfizer, Inc.; 1: Sanofi | 4: Roche Diagnostics | None | None | None | None | None |

Abbreviations: NIH = National institute of health; AHA = American Heart Association.