# Kardia

# Clinical Research & Other Supporting Literature

83 Peer-Reviewed Articles

## Table of Contents

# AliveCor®

## 1. Remote Patient Monitoring (KardiaPro)

**First real-world experience with mobile health telemonitoring in adult patients with congenital heart disease.**

This study presents the feasibility of a remote patient monitoring program in the Netherlands for managing arrhythmia, heart failure (weight) and blood pressure in symptomatic adults with congenital heart disease (CHD); the program used KardiaPro for the receipt and transfer of KardiaMobile ECG data. ECGs were assessed daily by trained nurses, under supervision of a cardiologist. Patients (median age 45; 35% male) were contacted by the treating cardiologist to adjust therapy, for surveillance or in order to provide reassurance. From June 2017 to March 2018, 55 symptomatic adult CHD patients participated; mean follow-up was 3 months and adherence was 97%. There were qualitatively fewer emergency room visits and hospitalizations (3) versus historical record (19). Serial patient-reported outcome measure (PROM) questionnaires were available for 12 patients at baseline and six patients after 6 months and showed a nonsignificant change in quality of life during telemonitoring. Nearly 75% of the 176 KardiaMobile ECGs were sinus rhythm; two patients were diagnosed with a new arrhythmia. In summary, a remote patient monitoring program featuring KardiaMobile is feasible with high adherence.

*Koole MAC, Kauw D, Winter MM, Dohmen DAJ, Tulevski, II, de Haan R, et al.*
*Neth Heart J. 2019;27(1):30-7.*

**At last, mobile health leading to a diagnosis in a young patient with congenital heart disease.**

This case report describes a woman with congenital pulmonary valve stenosis treated with balloon valvulotomy, with several years of palpitations and unrevealing Holter monitor evaluations. She was enrolled in a remote patient monitoring program in the Netherlands using KardiaPro. The woman used KardiaMobile to successfully record atrial fibrillation with intermittent bundle branch block during an episode of palpitations.

*Koole MAC, Somsen GA, Tulevski, II, Winter MM, Bouma BJ, Schuuring MJ.*
*Neth Heart J. Jan 2019.*

**A mobile one-lead ECG device incorporated in a symptom-driven remote arrhythmia monitoring program. The first 5,982 Hartwacht ECGs.**

Hartwacht Arrhythmia (HA) is a cardiac arrhythmia remote monitoring program in the Netherlands, initiated by Cardiologie Centra Nederland. This is the first evaluation of KardiaMobile in a real-world cohort of ambulatory patients for symptom-driven monitoring in that country. Between January 2017 and March 2018, 5,982 KardiaMobile ECGs from 233 participants were received, with a median of 28 ECGs per patient per year (mean age 58 years, 52% male); patients were instructed to record an ECG when they experienced palpitations or related complaints. KardiaMobile algorithms classified 59% as Normal, 22% as Possible AF, 17% as Unclassified, and 2% as Unreadable. According to the HA team, 8% of all ECGs were uninterpretable. The AF algorithm had a sensitivity of 92% and specificity of 95%; the negative predictive value (NPV) for detection of AF was high, at 98%, while the positive predictive value (PPV) was 80%, with 12% of AF ECGs being interpreted by the cardiologist as sinus rhythm. Conversely, the Normal algorithm had a high PPV, and a specificity of 91% and a sensitivity of 80%; 96% of all KardiaMobile Normal ECGs were interpreted by the cardiologist as being sinus rhythm. The authors call for a refinement in the detection of normal sinus rhythm with and without ectopy to reduce the need for manual assessment of this category of ECGs.

*Selder JL, Breukel L, Blok S, van Rossum AC, Tulevski II, Allaart CP.*
*Neth Heart J. 2019;27(1):38-45.*

## 2. Accuracy of AF Algorithm: KardiaMobile

**Accuracy of blinded clinician interpretation of single-lead smartphone electrocardiograms and a proposed clinical workflow.**

A paucity of data exists on the accuracy of primary care physicians' (PCP) interpretation of KardiaMobile ECGs compared with the device's automated diagnosis. Using 408 ECGs in 51 patients, before and after elective cardioversion, this study demonstrated variable accuracy in clinician interpretation, with a mean accuracy of 91% for the review by cardiologists, and 85% accuracy for the review by PCPs. With exclusion of Unclassified ECGs, the algorithm accuracy had a sensitivity and specificity of 100% and 95%, respectively. Accurate diagnosis of a KardiaMobile Unclassified ECG was established in 10/12 when assessed by a cardiologist, and 9/12 on review by a primary care physician. Combining the automated algorithm with cardiologist interpretation of only Unclassified traces yielded excellent results and provides an efficient, cost-effective workflow for the utilization of a smartphone-based ECG in clinical practice.

*Koshy AN, Sajeev JK, Negishi K, Wong MC, Pham CB, Cooray SP, et al.*
*Am Heart J. 2018. doi: 10.1016/j.ahj.2018.08.001.*

**Assessing the accuracy of an automated atrial fibrillation detection algorithm using smartphone technology: The iREAD Study.**

The accuracy of the KardiaMobile AF algorithm was evaluated in 52 patients admitted for antiarrhythmic drug initiation for AF. Patients performed KardiaMobile recordings immediately following twice daily 12-lead ECGs. There were 225 paired KardiaMobile and 12-lead ECG recordings. The algorithm interpretation was missing or labeled as non-interpretable in 62 (27.5%) of recordings for multiple reasons (truncated recording, noise, slow heart rate, other). When the algorithm did not provide a diagnosis, blinded electrophysiologists were able to provide interpretation in 92% of these recordings. After exclusion of non-interpretable recordings, the KardiaMobile AF algorithm had very good accuracy, with a sensitivity of 96.6% and specificity of 94% for the detection of AF when compared to physician interpreted ECGs, and a κ coefficient of 0.89. The majority of patients (93.6%) found KardiaMobile easy to use, and 59.6% noted that use lessened AF-diagnosis related anxiety. 63.8% of survey respondents preferred continued use of KardiaMobile for AF detection.

*William AD, Kanbour M, Callahan T, Bhargava M, Varma N, Rickard J, et al.*
*Heart Rhythm. August 2018. doi: 10.1016/j.hrthm.2018.06.037*

**Detection of atrial fibrillation with a smartphone camera: first prospective, international, two-centre, clinical validation study (DETECT AF PRO).**

In this prospective study of 672 patients with AF or sinus rhythm at two university hospitals in Switzerland and Germany, physician review of KardiaMobile was used as the reference for evaluation of the accuracy of a photoplethysmography (PPG) heart rhythm analysis from a smartphone camera. Less than 3% of patients had KardiaMobile recordings with poor signal quality. Additionally, the study tested the accuracy of the KardiaMobile algorithms. 18.8% of KardiaMobile recordings were labeled "unclassified," but cardiologists were able to identify the cardiac rhythm in all of these cases. The KardiaMobile AF algorithm had a sensitivity of 99.6% (95% CI 97.9-100%) and a specificity of 97.8% (95.3-99.2%).

*Brasier N, Raichle CJ, Dorr M, Becke A, Nohturfft V, Weber S, et al.*
*Europace. 2018. doi:10.1093/europace/euy176*

**Clinical validation of heart rate apps: mixed-methods evaluation study.**

Heart rate (HR) detection from a smartphone-based photoplethysmography (PPG) app (FibriCheck) was compared with the KardiaMobile ECG and the Nonin pulse oximeter. The HR (BPM, beats per minute) of 88 random subjects consecutively measured for 10 seconds with the 3 devices showed a moderate-to-strong correlation coefficient of 0.834 between FibriCheck and Nonin, 0.88 between FibriCheck and AliveCor, and 0.897 between Nonin and AliveCor. The mean HR for FibriCheck was 71 BPM, for Nonin 69 BPM, and for AliveCor 69 BPM. A single way analysis of variance showed no significant differences between the HRs as measured by the 3 devices (p=0.61). This study reports the potential utility and limitations in use of the smartphone-based PPG signal for HR detection.

*Vandenberk T, Stans J, Van Schelvergem G, Pelckmans C, Smeets CJ, Lanssens D, et al.*
*JMIR Mhealth Uhealth. 2017;5(8):e129.*

**Screening for atrial fibrillation during influenza vaccinations by primary care nurses using a smartphone electrocardiograph (iECG): a feasibility study.**

KardiaMobile was used to identify asymptomatic AF at the time of influenza vaccination in 5 practices in Sydney, Australia. Nurses used the automated algorithm to screen 973 patients aged ≥ 65 years between April-June 2015. Screening took on average 5 minutes (range 1.5 -10 minutes); abnormal recordings required additional time. Newly identified AF was found in 0.8% (8) of patients, and the overall prevalence of AF was 3.8% (37). The sensitivity and specificity of the automated algorithm for detecting AF was 95% and 99%, respectively. Screening by practice nurses was well accepted by practice staff. Key enablers were the confidence and competence of nurses and a 'designated champion' to lead screening at the practice. Barriers were practice specific, and mainly related to staff time and funding.

*Orchard J, Lowres N, Freedman SB, Ladak L, Lee W, Zwar N et al.*
*Eur J Prev Cardiol. 2016; 23(2S):13-20.*

**Feasibility and cost-effectiveness of stroke prevention through community screening for atrial fibrillation using iPhone ECG in pharmacies. The SEARCH-AF study.**

One thousand pharmacy customers (mean age 76 ± 7 years, 44% male) were screened with KardiaMobile. Newly identified AF was found in 1.5% (95% CI, 0.8-2.5%), and AF prevalence was 6.7%. The automated algorithm showed 98.5% sensitivity and 91.4% specificity for detecting AF. Using cost and outcome data from a United Kingdom study for AF screening, the incremental cost-effectiveness ratio of extending screening into the community with KardiaMobile, based on 55% warfarin prescription adherence, would be $USD4,066 per quality-adjusted life-year gained, and $USD20,695 for preventing one stroke. In summary, screening for AF with KardiaMobile is feasible and cost-effective.

*Lowres N, Neubeck L, Salkeld G, Krass I, McLachlan AJ, Redfern J, et al.*
*Thromb Haemost. 2014;111(6):1167-76.*

**iPhone ECG application for community screening to detect silent atrial fibrillation: a novel technology to prevent stroke.**

KardiaMobile was used in a community screening of 109 patients (70 in sinus rhythm and 39 in AF) soon after a 12-lead ECG had been performed. The ECGs were interpreted by two cardiologists blinded to the rhythm diagnosis, and were processed to provide an automated diagnosis of sinus rhythm or AF. Results were compared with the 12-lead ECG diagnosis by a third cardiologist. An optimized algorithm performed extremely well in the validation set with high sensitivity, specificity, overall accuracy and Kappa (95% CI) of 98% (89%–100%), 97% (93%–99%), 97% (94%–99%) and 0.92 (0.86– 0.98) respectively. This study concluded that KardiaMobile can be used to simply and rapidly record a high quality single-lead ECG to accurately detect AF, making it an ideal technology for community screening programs to detect silent AF.

*Lau JK, Lowres N, Neubeck L, Brieger DB, Sy RW, Galloway CD, et al.*
*Int J Cardiol. 2013;165(1):193-4.*

## 3. Accuracy of AF Algorithm: KardiaBand

**Automated atrial fibrillation detection algorithm using smartwatch technology.**

This study evaluated the accuracy of KardiaBand ECG and the automated AF algorithm. 100 patients (mean age 68 ± 11 yrs) with AF presenting for cardioversion (CV) were enrolled and received simultaneous 12-lead ECG and KardiaBand ECG before the procedure; if the CV was performed a post CV 12-lead ECG was then obtained along with another KardiaBand ECG. CV was canceled in 8 patients due to presentation in sinus rhythm. There were 169 simultaneous 12-lead ECG and KardiaBand ECGs. Compared to 12-lead ECG, the automated algorithm detected AF with 93% sensitivity, 84% specificity and κ coefficient 0.77. Physician-interpretation of KardiaBand ECGs demonstrated 99% sensitivity, 83% specificity and K coefficient 0.83. The automated AF algorithm on KardiaBand, when supported by physician review, can accurately differentiate AF from sinus rhythm. This technology can help screen patients prior to elective CV and avoid unnecessary procedures.

*Bumgarner JM, Lambert CT, Hussein AA, Cantillon DJ, Baranowski B, Wolski K, et al.*
*JACC. March 2018. DOI:10.1016/j.jacc.2018.03.003*

## 4. Arrhythmia Assessment

**Diagnostic accuracy of a smartphone-operated, single-lead electrocardiography device for detection of rhythm and conduction abnormalities in primary care.**

In 10 Dutch general practices, KardiaMobile ECG and AF algorithm were compared with simultaneous 12-lead ECG. Three cardiologists reviewed ECG data from 214 patients (mean age 64.1 y, 54% male). The 12-lead ECG diagnosed AF/AFL, any rhythm abnormality, and any conduction abnormality (AV block, BBB, LAD, LAFB) in 23, 44, and 28 patients, respectively. KardiaMobile ECG as assessed by the cardiologists had a sensitivity and specificity for AF/AFL of 100% (95% CI, 85.2%-100%) and 100% (95% CI, 98.1%-100%). The AF Instant Analysis algorithm identified 20 or 23 AF cases and incorrectly classified 4 cases of sinus rhythm as possible AF (sensitivity and specificity of 87.0% (95% CI, 66.4%-97.2%) and 97.9% (95% CI, 94.7%-99.4%)). KardiaMobile recordings as assessed by cardiologists had a sensitivity and specificity for any rhythm abnormality of 90.9% (95% CI, 78.3%-97.5%) and 93.5% (95% CI, 88.7%-96.7%) and for any conduction abnormality of 46.4% (95% CI, 27.5%-66.1%) and 100% (95% CI, 98.0%-100%). For conduction abnormality, the 15 false negatives were comprised of first-degree AVB (n=6), LAFB (n=8), and RBBB (n=1); on the other hand, cardiologists were able to accurately identify BBB in 13 patients' KardiaMobile ECGs. The authors concluded that in a primary care population, the KardiaMobile ECG recording showed excellent diagnostic accuracy for AF/AFL and good diagnostic accuracy for other rhythm abnormalities. The 1L-ECG device was less sensitive for left anterior fascicular block and first-degree AV block.

*Himmelreich JC, Karregat EPM, Lucassen, WAM, van Weert HCPM, de Groot JR, Handoko ML, et al.*
*Ann Fam Med. 2019;17: 403-11.*

**Rise of the smart device ECG and what it means for the general cardiologist.**

Diagnostic pathways for identification of clinically significant paroxysmal arrhythmia have historically relied on ambulatory ECG monitoring. While useful as a risk stratification tool in certain patient groups, in general, it has a limited yield for infrequent arrhythmia. This is inherently cost-inefficient, and time to diagnosis can be delayed. Smartphone-based ECG devices are now well established in the public market. However, their adoption into standard investigatory pathways is not yet widespread. Recently, the National Institute for Health and Care Excellence (NICE) published a diagnostics guidance document, which reviewed the smartphone-based devices, KardiaMobile and imPulse, with respect to atrial fibrillation (AF) detection. NICE concluded there was insufficient evidence to recommend routine adoption in primary care and recommended further research. Regardless, given the evidence that is available and their uptake by the general public, cardiologists are increasingly likely to encounter them. This article focuses on KardiaMobile as the device is currently easily available to the general public. The authors conclude there is growing evidence to support its use as a screening tool for the detection of subclinical AF in high-risk populations, but further studies are required in order to equate this benefit to stroke and mortality reduction.

*Bennett R and French A.*
*Heart. 2019.*

**NICE guidance: lead-I ECG devices for detecting symptomatic atrial fibrillation using single time point testing in primary care.**

This guidance document for the United Kingdom evaluated use of lead-I ECG devices for single time point testing of people in primary care with symptoms of atrial fibrillation and an irregular pulse. The authors concluded there is not enough evidence to recommend routine adoption of lead-I ECG devices for this use case. They recommended further research to show how using lead-I ECG affects the number of people with atrial fibrillation detected, as well the staff time needed to interpret the ECG tracings. Of note, a de novo economic model was designed to evaluate cost effectiveness, and KardiaMobile dominated all other lead-I ECG devices, costing less and producing more quality-adjusted life years [QALYs].

*National Institute for Health and Care Excellence. May 2019.*

**Multi-centre randomised controlled trial of a smartphone-based event recorder alongside standard care versus standard care for patients presenting to the emergency department with palpitations and pre-syncope: the IPED (Investigation of Palpitations in the ED) study.**

Palpitations and pre-syncope are together responsible for 300,000 annual Emergency Department (ED) attendances in the United Kingdom (UK) alone. This multicenter randomized controlled trial compared the symptomatic rhythm detection rate of KardiaMobile versus standard care alone (no planned ambulatory ECG monitoring), for 243 participants presenting to 10 emergency departments in the UK with palpitations and pre-syncope with no obvious cause evident at initial consultation. A symptomatic rhythm was detected at 90 days in 69 (n=124; 55.6%; 95% CI 46.9–64.4%) participants in the intervention group versus 11 (n=116; 9.5%; 95% CI 4.2–14.8) in the control group (RR 5.9, 95% CI 3.3–10.5; p<0.0001). Mean time to symptomatic rhythm detection in the intervention group was 9.5 days (SD 16.1, range 0–83) versus 42.9 days (SD 16.0, range 12–66; p<0.0001) in the control group. Use of KardiaMobile increased the number of patients with symptomatic rhythm detection over five-fold, to more than 55%, at 90 days. The authors recommend that KardiaMobile be considered part of on-going care to all patients presenting acutely with unexplained palpitations or pre-syncope.

*Reed MJ, Grub NR, Lang CC, O'Briend R, Simpson K, Padarenga M, et al.*
*EClinicalMedicine. Online March 3, 2019.*

**Early detection of atrial fibrillation-atrial flutter using remote patient monitoring.**

This case report presents a patient enrolled in a precision medicine study in which remote patient monitoring helped detect the presence of atrial fibrillation-atrial flutter(AFib-Flutter). A 64-year-old male with a history of ischemic heart disease used KardiaMobile after noting chest pain, and received an instant analysis of Atrial Fibrillation with a heart rate of 139 bpm. He called the paramedics and was taken by ambulance to the emergency department, where AFib-Flutter with rapid ventricular response was confirmed by 12-lead ECG, and successfully treated.

*Joung S, Dzubur E, van den Broek I, Love A, Martinez-Rubio L, Lopez M, et al.*
*J Med Cases. 2019; 10(2):31-36.*

**Wearable devices for cardiac rhythm diagnosis and management.**

In this Viewpoint, the author describes the potential utility of photoplethymographic (PPG) sensors in consumer-grade wearable devices, such as Fitbit or Apple Watch, to aid in detection of arrhythmias. He also opines that it is essential to validate abnormal PPG findings with direct electrocardiographic recordings, such as from KardiaMobile or Apple Watch series 4. The opinion piece includes a figure showing the use of KardiaMobile ECG in the lead I and lead II orientations during normal sinus rhythm and during supraventricular tachycardia (long RP tachycardia).

*Ip JE.*
*JAMA. Online Jan 2019.*

**Comparing a mobile ECG device with Holter monitoring for patients with palpitations in an urgent care setting: a preliminary study.**

This is the first study to evaluate the use of KardiaMobile in the urgent care setting. Those seeking care at urgent care centers constitute the fastest growing segment of patients in the U.S., and appropriately triaging those with palpitations will positively affect the entire American healthcare system. The purpose of this study is to compare KardiaMobile for 30 days with 24-hour Holter monitoring for the detection of symptomatic arrhythmias in an urgent care population. All Holter reports and KardiaMobile ECGs were reviewed by a general practitioner and a cardiologist. Data from the first 50 of 100 patients from 6 urgent care centers across Southern Arizona was performed. KardiaMobile was diagnostically superior to (10%) or concordant with (72%) Holter monitoring in 82% of patients. Holter monitoring was superior in 16% of patients. Arrhythmias detected included atrial and ventricular ectopy, supraventricular tachycardia, atrial fibrillation and inappropriate sinus tachycardia. This ongoing study will ultimately analyze noninferiority for diagnosis and management, perform a cost-comparison, and suggest the most effective clinical uses for KardiaMobile in an urgent care setting.

*Goel HV, Alpert JS, Shaheen MH, Jones TA, and Skinner DP.*
*American Heart Association Scientific Sessions (2018). Abstract.*

**Modified positioning of a smartphone based single-lead electrocardiogram device improves detection of atrial flutter.**

This study evaluated the use KardiaMobile in the lead II position (right hand to left leg) to improve visualization of flutter waves and clinician diagnosis of atrial flutter (AFL), compared to traditional lead-I tracings. Fifty patients were recruited (25 in sinus rhythm, 14 in AF, 11 in AFL). Lead-I AFL sensitivity was 27% for both electrophysiologists (EP), which individually improved to 73% and 55% in lead-II. KardiaMobile appropriately diagnosed lead-I AFL as unclassified in 18% of cases, compared to 55% in lead-II. Overall clinician agreement (AF, sinus rhythm and AFL) was modest utilizing lead-I position (EP1: κ=0.71, EP2: κ=0.73, p<0.001), which improved with lead-II tracings (EP1: κ=0.87, EP2: κ=0.83, both p<0.001). In summary, lead II position of KardiaMobile improves clinician diagnosis of atrial flutter.

*Rajakariar K, Koshy AN, Sajeev JK, Nair S, Roberts L, Teh AW.*
*J Electrocardiol. 2018. 51(5): 884-88.*

**ECG measurement parameters of athletes are reliable when made with a smartphone based ECG device.**

This study evaluated the between and within rater validity and reliability of KardiaMobile in recording ECG rate, rhythm, and intervals in healthy college athletes in a pre-participation screening program. First, 10 athletes' KardiaMobile ECG were reviewed by three physicians. Second, the physicians compared a 30-second simultaneous KardiaMobile and lead I from a 12-lead ECG, from 12 athletes. The between rater and between device reliability for the rate, QT interval and QRS duration parameters ranged from good to very good (intraclass correlation coefficients [ICC] = 0.667 – 0.981). The current investigation showed that the reliability of the ECG parameters measured using the smartphone technology ranged from good to very good. This paper serves as support for a technological advancement that will help advance the debate on the utility of ECG testing as part of the athletic pre-participation physical.

*Gilliland A, Timmons M, Harris JK, Petrany SM, Shepherd GS, Buchanan GS, et al.*
*Marshall J Med. 2018;4(2):61-74.*

**Diagnostic utility of real-time smartphone ECG in the initial investigation of palpitations.**

148 patients (mean age 41 years) with intermittent palpitations were asked to use KardiaMobile and record an ECG when symptomatic. Over a median period of use of 244 days, 113 patients (76.4%) made 516 symptomatic recordings. A symptom-rhythm correlation was possible for all patients who submitted recordings. Diagnoses were: sinus rhythm n=47 (41.6%), sinus tachycardia n=21 (18.6%), supraventricular/ventricular ectopics n=31 (27.4%), atrial fibrillation n=8 (7.1%), and supraventricular tachycardia n=6 (5.3%). Median time to diagnosis was nine days (range 1–287 days). In conclusion, KardiaMobile diagnosed the cause of intermittent palpitations in the majority of patients referred for evaluation.

*Dimarco AD, Onwordi EN, Murphy CF, Walters EJ, Willis L, Mullan NJ, et al.*
*Brit J Cardio. March 2018. doi:10.5837/bjc.2018.006*

**Validation of a smartphone-based event recorder for arrhythmia detection.**

This trial evaluated the diagnostic yield of KardiaMobile versus a 14-30 day external loop recorder (ELR). 38 patients were instructed to transmit ECGs via KardiaMobile and activate the ELR whenever they had symptoms. More patients had a potential diagnosis for their symptoms (i.e., at least one symptomatic recording during the entire monitoring period) with KardiaMobile than with the ELR (KardiaMobile= 34 (89.5%) vs ELR = 26 (68.4%); $\chi^2$ = 5.1, p = 0.024). In the per-protocol analysis, all 33 patients (100%) had a potential diagnosis using the KardiaMobile device, which was significantly higher compared to 24 patients (72.2%) using the ELR ($\chi^2$ = 10.4, p = 0.001). In summary, KardiaMobile is non-inferior to an ELR for detecting arrhythmias in the outpatient setting. The ease of use and portability of this device make it an attractive option for the detection of symptomatic arrhythmias.

*Narasimha D, Hanna N, Beck H, Chaskes M, Glover R, Gatewood R et al.*
*Pacing Clin Electrophysiol. March 2018. doi:10.1111/pace.13317*

**Monitoring patients with implantable cardioverter defibrillators using mobile phone electrocardiogram: case study.**

Three patients with implantable cardioverter defibrillators (ICD) used KardiaMobile; device usage and satisfaction, patient engagement, quality of life (QoL), and cardiac anxiety were assessed. Each patient used the technology approximately daily or every other day as prescribed. At the 30-day follow-up, participants recorded an average of 32 ECGs per month. At 90-day follow-up, participants recorded an average of 34 ECGs per month. Two of the three participants self-reported a significant improvement in their physical QoL from baseline to completion, while simultaneously self-reporting a significant decrease in their mental QoL. All three participants reported high levels of device acceptance and technology satisfaction.

*Kropp C, Ellis J, Nekkanti B, Sears S.*
*JMIR Cardio 2018;2(1):e5*

**Using smart technology to improve outcomes in myocardial infarction patients: rationale and design of a protocol for a randomized controlled trial, The Box.**

The aim of this randomized controlled trial is to investigate the clinical effectiveness and patient satisfaction of a smart technology intervention in patients admitted with ST elevation myocardial infarction (STEMI) or non-ST acute coronary syndrome (NST-ACS). Patients will be followed up to one year after the index event. The intervention group will take daily measurements with KardiaMobile, as well as a blood pressure monitor, weight scale, and activity tracker. Furthermore, two of four outpatient clinic visits will be replaced by electronic visits (1 and 6 months after index event). The control group will receive regular care, consisting of four outpatient clinic visits (1, 3, 6, and 12 months after index event). All patients will be asked to fill in validated questionnaires about patient satisfaction, quality of life, propensity of medication adherence, and physical activity. The primary outcome of this trial will be percentage of patients with controlled BP. In summary, this trial will investigate whether usage of smart technology can improve clinical- and cost-effectiveness of care.

*Treskes RW, van Winden LA, van Keulen N, Atsma DE, van der Velde ET, van den Akker-van Marle E, et al.*
*JMIR Res Protoc. 2017;6(9):e186*

**Alcohol consumption, sinus tachycardia, and cardiac arrhythmias at the Munich Octoberfest: results from the Munich Beer Related Electrocardiogram Workup Study (MunichBREW)**

This study prospectively associated acute alcohol consumption with cardiac arrhythmias using KardiaMobile. At the 2015 Munich Octoberfest, 3028 volunteers received a KardiaMobile ECG and breath alcohol concentration (BAC) measurements. ECGs were analyzed for cardiac arrhythmias (sinus tachycardia, sinus arrhythmia, premature atrial/ventricular complexes, atrial fibrillation/flutter) and respiratory sinus arrhythmia. Mean BAC was 0.85 +/- 0.54 g/kg. Cardiac arrhythmias occurred in 30.5% (sinus tachycardia 25.9%; other arrhythmia subtypes 5.4%). Breath alcohol concentration was significantly associated with cardiac arrhythmias overall (odds ratio (OR) per 1-unit change 1.75, 95% confidence interval (CI) 1.50-2.05; $P < 0.001$) and sinus tachycardia in particular (OR 1.96, 95%CI 1.66-2.31; $P < 0.001$). Respiratory sinus arrhythmia measuring autonomic tone was significantly reduced under the influence of alcohol.

*Brunner S, Herbel R, Drobesch C, Peters A, Massberg S, Kaab S, et al.*
*Eur Heart J. 2017. 38(35): 2641-43.*

### Supraventricular tachycardia diagnosed by smartphone ECG.

This is a case report of paroxysmal supraventricular tachycardia, unable to be diagnosed through typical evaluation with an event monitor despite several years of symptoms. Here, the patient diagnosed himself through purchase of KardiaMobile, capturing an atypical atrioventricular node re-entrant tachycardia (AVNRT). He emailed his cardiologist the tracing, which eventually led to an electrophysiology study and successful ablation procedure.

*Tabing A, Harrell TE, Romero S, Francisco G.*
*BMJ Case Rep.; published online 11 September 2017.*

### A randomized trial of pocket-echocardiography integrated mobile health device assessments in modern structural heart disease clinics.

Mobile health (mHealth) devices were used as clinical decision support tools in resource-limited areas to investigate the impact on long-term outcomes among patients with rheumatic and structural heart diseases. Patients randomized to the mHealth clinics (n=139) received, among other mHealth devices, point-of-care ECG using KardiaMobile. An initial mHealth assessment was associated with a shorter time to referral for valvuloplasty and/or valve replacement and was associated with an increased probability for valvuloplasty/valve replacement compared to standard care. Patients randomized to mHealth were associated with a lower risk of a hospitalization and/or death on follow-up (15 % vs. 28 %, adjusted hazard ratio: 0.41; 95% CI: 0.21 to 0.83; p = 0.013).

*Bhavnani SP, Sola S, Adams D, Venkateshvaran A, Dash PK, Sengupta PP, et al.*
*JACC Cardiovasc Imaging. Available online September 2017.*

### 2017 ISHNE-HRS expert consensus statement on ambulatory ECG and external cardiac monitoring/telemetry.

This consensus document by the Heart Rhythm Society describes the evolution and advancement of ambulatory ECG technology and its impact on clinical decision-making and practice. It includes a section devoted to smartphone-based ECG recording systems, highlighting the vast literature on KardiaMobile. The document describes the benefits and challenges of KardiaMobile, blurring the traditional models of prescribed device and physician interpretation, and also definitions of patient versus consumer.

*Steinberg JS, Varma N, Cygankiewicz I, Aziz P, Balsam P, Baranchuk A, et al.*
*Heart Rhythm. 2017;14(7):e55-e96.*

### Electrode placement in a smartphone ECG device to aid in the diagnosis of atrial flutter.

This case report demonstrates the use of KardiaMobile ECG to record atrial flutter waves by placing the electrodes in the right hand and on the left knee, similar to lead II of a traditional 12-lead ECG.

*Czobor P, Mehtani K, Yang SH, Goldschlager NF.*
*J Electrocardiol. 2016;49(4): 625-27.*

### Crowd-sourcing syncope diagnosis: mobile smartphone ECG apps.

This case report documents a 76-year-old gentleman with witnessed syncope. When he regained consciousness, a bystander cardiologist used KardiaMobile on the patient, which showed sinus tachycardia with complete heart block and a narrow complex escape rhythm. The patient later underwent pacemaker implantation. Although KardiaMobile is patient triggered, it can be used in syncope if applied by bystanders. The authors conclude there is a potential for widespread use of KardiaMobile to usher in a new era of democratized, crowd-sourced, syncope diagnostic capability.

*Nyotowidjojo I, Erickson RP, Lee KS.*
*Am J Med. 2016;129(4):e17-8.*

**Smartphone ECG aids real time diagnosis of palpitations in the competitive college athlete.**

Six college athletes presented to their athletic trainers complaining of palpitations during exercise. A single lead ECG was performed using KardiaMobile and sent wirelessly to the team cardiologist who con rmed an absence of dangerous arrhythmia. KardiaMobile has the potential to enhance evaluation of symptomatic athletes by allowing trainers and team physicians to make diagnoses in real-time and facilitate faster return to play.

*Peritz DC, Howard A, Ciocca M, Chung EH.*
*J Electrocardiol. 2015;48(5):896-9.*

**Diagnosing symptomatic arrhythmia via mobile phone.**

This is a case study of a 22-year old admitted to the hospital for an episode of tachycardia at a rate of 150 BPM. Upon discharge from the hospital, the patient had an exercise ECG test in attempt to provoke the arrhythmia, then wore a 24-hour ambulatory ECG, and finally was issued a patient-activated event recorder for two weeks. None of these methods captured abnormalities despite symptoms recurring approximately every three months. The patient then purchased KardiaMobile and used this device to record when symptomatic. A consultant cardiologist reviewed recordings to diagnose probable atrioventricular nodal re-entrant tachycardia. Treatment reviewed.

*Richley D, Graham A.*
*Br J Cardiac Nurs. 2015;10(3):130.*

**Living with the handheld ECG.**

This review paper discusses the evolution of the ECG and highlights the rise of digital health devices and wearable technologies. It identifies KardiaMobile as a useful tool to reduce clinic visits and lower the cost of monitoring while increasing the speed and accuracy of diagnoses. Clinical usability of KardiaMobile is described for narrow complex tachycardia in a patient with palpitations, complete heart block in a patient with intermittent giddiness, arrhythmia in a patient following catheter ablation, and AF in an asymptomatic individual.

*Mitchell AR, Le Page P.*
*BMJ Innov. 2015;0:1-3.*

**Wide complex tachycardia recorded with a smartphone cardiac rhythm monitor.**

This case report discusses the use of KardiaMobile to diagnose RVOT ventricular tachycardia in diagnosis of a 62-year old man experiencing frequent, sudden episodes of exertional near-syncope and syncope with monomorphic RVOT VT. KardiaMobile may improve diagnostic yield in patients with symptoms of palpitations, light-headedness, or near-syncope. However, the lack of adhesive electrodes and variable contact between the patient and the device can lead to superimposed noise and artifact that may, in some cases, obscure the correct electrocardiographic diagnosis. Further, the device records cardiac rhythms only upon proper activation.

*Waks JW, Fein AS, Das S.*
*JAMA Intern Med. 2015;175(3):437-9.*

**Ubiquitous wireless ECG recording: a powerful tool physicians should embrace.**

Fifty-three attendees at a computing conference (mean age 43 ±11 years, 77% male) transmitted KardiaMobile recordings weekly for eight weeks. Transmission interpretation was normal sinus rhythm (68%); sinus bradycardia or tachycardia (16%); extra atrial or ventricular systoles (2%); QRS delay (1%); and noise (13%). Symptomatic ventricular tachycardia and asymptomatic ST segment depression were detected in two participants, suggesting that early detection of abnormalities provides a window of diagnostic and therapeutic opportunity for intervention to prevent significant cardiac events. The majority of participants (82%) reported that the device was beneficial, 33% felt that they were more health conscious after participating in the study, and 88% thought that the device was transmitting accurate information. Use of the device caused 24% of subjects to reach out to see a physician for a consultation.

*Saxon LA.*
*J Cardiovasc Electrophysiol. 2013;24(4):480-3.*

# 5. Managing Patients with AF: Post-Ablation

**Recurrent atrial fibrillation/flutter detection after ablation or cardioversion using the AliveCor KardiaMobile device: iHEART results.**

This single center, randomized controlled trial evaluated the use of daily KardiaMobile recording and receipt of motivational text messages 3 times per week (the iHeart Intervention), on time to recurrent AF/AFL and time to treatment of recurrent arrhythmias in patients undergoing catheter radiofrequency ablation (RFA) or direct current cardioversion (DCCV). The study also evaluated patterns of smartphone ECG use over a 6 month period. 238 were randomized to standard of care (n=123) or the iHeart intervention (n=115). Data were collected from the KardiaMobile ECG and from the electronic health records. The likelihood of recurrence detection was greater in the intervention group (hazard ratio 1.56, 95% CI 1.06-2.30, p=0.24), and did not differ significantly for RFA and DCCV procedures. Recurrence during the first month after ablation strongly predicted later recurrence (hazard ratio = 4.53, 95% CI: 2.05-10.00, p = .0006). Time from detection of recurrent arrhythmia to treatment was shorter for the control group (HR 0.33, 95% CI 0.57-2.92, p<0.0001). The authors hypothesize longer time from detection to treatment in the intervention arm due to physicians being less likely to proceed to treatment with short (asymptomatic) AF recurrences; meanwhile the first documentation of arrhythmia in the control arm was often when they came in for treatment. Of note, there was a trend towards lower healthcare utilization (hospitalizations, ER visits) in the intervention arm. Regarding Kardia usage, 36% recorded > 180 ECGs, 56% of patients recorded at least 90 ECGs, and 75% used the device in the last 3 months of the study. In summary, KardiaMobile with motivational text messages enabled earlier detection of recurrent arrhythmias, with a trend toward less treatment and healthcare utilization.

*Goldenthal IL, Sciacca RR, Riga T, Bakken S, Baumeister M, Biviano AB, et al.*
*J Cardiovasc Electrophysiol. 2019.*

**2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation.**

This document, written by an international task force of electrophysiologists, provides updated definitions, mechanisms, and rationale for AF ablation and consensus recommendations concerning indications, strategies, techniques, and endpoints, technology and tools, and follow-up considerations for AF ablation. Specifically, it references the iTransmit study featuring KardiaMobile as an example of the use of smartphone-based ECG monitors that can be helpful for long-term intermittent surveillance after AF ablation.

*Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, et al.*
*Heart Rhythm. 2017;14(10):e275-e444.*

**Using a novel wireless system for monitoring patients after the atrial fibrillation ablation procedure: the iTransmit study.**

Fifty-five patients (mean age 60 ± 12 years) with AF undergoing ablation recorded their rhythm using KardiaMobile and a traditional transtelephonic monitor (TTM) whenever they had symptoms, or at least once a week, for 3-4 months following ablation. All were interpreted by electrophysiologists. There were 831 KardiaMobile recordings, and 7 were noninterpretable. Of the 389 simultaneous recordings with KardiaMobile and TTM, there was excellent agreement (K statistic 0.82). KardiaMobile detected sinus rhythm 97% of the time and correctly detected AF and atrial flutter 100% of the time, with 3% false-positive results. For manual review of KardiaMobile versus TTM for detection of AF, KardiaMobile had 97% specificity and 100% sensitivity. P waves could be difficult to discern, and occasionally this resulted in mislabeling sinus rhythm with atrial ectopy as AF. KardiaMobile is an alternative method for monitoring patients after AF ablation, with patients agreeing on ease of use.

*Tarakji KG, Wazni OM, Callahan T, Kanj M, Hakim AH, Wolski K, et al.*
*Heart Rhythm. 2015;12(3):554-9.*

# 6. Managing Patients with AF: Post-Cardioversion

**Detection of recurrent atrial fibrillation using novel technology.**

This is a case study of a 58-year-old patient with AF with multiple cardiac risk factors who failed to remain in normal sinus rhythm after two ablations and one cardioversion. Following a second cardioversion, the patient was given KardiaMobile for mobile monitoring of any symptomatic events. Within days, the patient began feeling symptomatic again and used his device to transmit an ECG to his healthcare provider. The novel technology led to more timely detection of recurrent AF. Since approximately one-third of patients with AF are asymptomatic, a daily ECG transmission in those who have undergone a prior cardioversion or AF ablation may prove useful in detecting silent AF.

*Hickey KT, Dizon J, Frulla A.*
*JAFIB. 2013;6(4):50-1.*

# 7. Managing Patients with AF: Monitor Symptoms and Rhythm

**Rationale and design of the Atrial Fibrillation health Literacy Information Technology Trial: (AF-LITT).**

This randomized clinical trial will implement a novel, smartphone-based intervention to address the patient experience of AF. One hundred eighty patients with AF who are receiving anticoagulation for stroke prevention will be randomized to 30 days of an embodied conversational agent and KardiaMobile, or to usual care, which includes a symptom and adherence journal. The primary endpoints are improvement in health related quality of life, and self-reported adherence to anticoagulation.

*Guhl EN, Schlusser CL, Henault LE, Bickmore TW, Kimani E, Paasche-Orlow MK, et al.*
*Contemp Clin Trials. 2017;62:153-8.*

**Evaluating the utility of mHealth ECG heart monitoring for the detection and management of atrial fibrillation and flutter in clinical practice.**

A pilot cohort from within the larger ongoing NIH randomized trial, iPhone Helping Evaluate Atrial Fibrillation Rhythm through Technology (iHEART), was evaluated to determine differences in AF/AFL recurrence rates (after undergoing treatment to restore normal rhythm) and quality-of-life over a 6-month follow-up period among 23 patients utilizing KardiaMobile on a daily basis, and 23 control patients. In the KardiaMobile group, 61% had recurrent AF/AFL versus 30% of controls (hazard ratio 2.55, 95% CI 1.06-6.11, p=0.04). Among the 13 patients with baseline and 6 month QoL assessments, significant improvements were observed in the physical functioning (p = 0.009), role physical (p = 0.007), vitality (p = 0.03), and mental health domains (p = 0.02). In summary, self-monitoring of AF is feasible using KardiaMobile, and improves self-reported quality-of-life.

*Hickey K, Biviano AB, Garan H, Sciacca RR, Riga T, Warren K, et al.*
*J Atr Fibrillation. 2017;9(5):1546.*

7. Managing
Patients
with AF: Monitor
Symptoms and
Rhythm
(Continued)

**A single-center randomized, controlled trial investigating the efficacy of a mHealth ECG technology intervention to improve the detection of atrial fibrillation: the iHEART study protocol.**

The iHEART study is a single center, prospective, randomized controlled trial. A total of 300 participants with a recent history of atrial fibrillation will be enrolled. Participants will be randomized 1:1 to receive the iHEART intervention, receiving an iPhone® equipped with a KardiaMobile and behavioral altering motivational text messages or usual cardiac care for 6 months. This will be the first study to investigate the utility of a mobile health intervention in a "real world" setting. This study will assess the impact of KardiaMobile on clinical outcomes, quality of life, quality-adjusted life-years and disease-specific knowledge.

*Hickey KT, Hauser NR, Valente LE, Riga TC, Frulla AP, Masterson Creber R, et al.*
*BMC Cardiovasc Disord. 2016;16:152.*

## 8. Diagnosing AF Early in High Risk Patients: Post-Cardiac Surgery

**Self-monitoring for atrial fibrillation recurrence in the discharge period post-cardiac surgery using an iPhone electrocardiogram.**

This study aimed to determine the feasibility of patients self-monitoring with KardiaMobile to identify recurrence of post-operative AF (POAF) in the post-discharge period following cardiac surgery. Forty-two participants with no prior history of AF, and discharged home in stable sinus rhythm, used KardiaMobile 4 times per day for 4 weeks post-discharge. Self-monitoring for POAF recurrence using KardiaMobile was feasible and acceptable, and participants felt empowered. Self-monitoring identified 24% (95% CI 12–39%) with an AF recurrence within 17 days of hospital discharge. 80% of patients with recurrence were at high enough stroke risk to warrant consideration of anticoagulation. The study concluded that KardiaMobile is a non-invasive, inexpensive, convenient and feasible way to monitor for AF recurrence in post-cardiac surgery patients. It also provides a mechanism to provide knowledge about the condition and also potentially reduces anxiety.

*Lowres N, Mulcahy G, Gallagher R, Freedman B, Marshman D, Kirkness A, et al.*
*Eur J Cardiothorac Surg. 2016;50(1):44-51.*

## 9. Diagnosing AF Early in High Risk Patients: Cryptogenic Stroke/TIA

**Smartphone electrocardiographic monitoring for atrial fibrillation in acute ischemic stroke and transient ischemic attack.**

The aim of this international multicenter study was to use KardiaMobile to identify AF in patients admitted to the hospital with stroke/transient ischemic attack, compared with 24-h Holter monitoring performed after discharge. 1056 patients had daily KardiaMobile ECG recordings while in the hospital. Patients also received standard cardiac investigations according to local institutional guidelines. Detection rates of AF was compared with Holter monitoring when available. 251 underwent Holter monitoring, generally over a 3 month period after discharge. Of the 251 patients, Holter detected AF in 7 (2.8%) and KardiaMobile detected AF in 28 (11.2%). 6 patients had AF detected on both Holter and KardiaMobile. The authors recommended that KardiaMobile could be instituted to complement local standard cardiac investigations especially when Holter monitoring was not readily available.

*Yan B, Tu H, Churilov L, Lam C, Swift C, Liu X, et al.*
*World Stroke Congress (2018). Abstract.*

9. Diagnosing
AF Early in High
Risk Patients:
Cryptogenic
Stroke/TIA
(Continued)

**Mobile phones in cryptogenic strOke patients Bringing sIngle Lead ECGs for Atrial Fibrillation detection (MOBILE-AF): study protocol for a randomised controlled trial.**

This multicenter randomized clinical trial will investigate the effectiveness of prolonged ECG monitoring with KardiaMobile for AF detection in patients with cryptogenic stroke or transient ischemic attack (TIA). One hundred patients in the intervention group will use KardiaMobile to record their ECG twice daily; 100 patients in the control group will complete a 7-day Holter monitor. The primary outcome of this study is the percentage of patients in which AF is detected in the first year after the index ischaemic stroke or TIA. Secondary outcomes include markers for AF prediction, orally administered anticoagulation therapy changes, as well as the incidence of recurrent stroke and major bleeds.

*Treskes RW, Gielen W, Wermer MJ, Grauss RW, van Alem AP, Dehnavi RA, et al.*
*Trials. 2017;18(1):402.*

## 10. Diagnosing AF Early in High Risk Patients: Screening

**Raising awareness and early detection of atrial fibrillation, an experience resorting to mobile technology centred on informed individuals.**

This study aimed to test the feasibility of an awareness event including opportunistic screening for AF and to test the reliability of KardiaMobile. During two weeks, at a community pharmacy, a nursing home, and an outpatient cardiology clinic in Portugal, individuals aged 40 years and older, without a history of atrial fibrillation, participated in a pharmacist-led detection event. Participants received a manual pulse check, provided a clinical history, and received a KardiaMobile ECG recording. ECGs highlighted as possible AF were confirmed by the cardiologist and if AF was diagnosed, they were referred to their physician. The awareness event involved 223 individuals, among which 205 were screened. Mean age was 66 years (SD=15) and hypertension was the most frequently reported (n=107; 52.2%). Mean CHAD2DS2- VASc score was 3 (SD=1.8). Cardiac irregularities were identified in 45 individuals, 14 confirmed to be new cases of AF (6.8%) by the cardiologist; detection rate varied between 1% to 13%, depending on the setting. There was one unreadable trace (0.5%). The sensitivity and specificity of the AF algorithm were 90.9% and 97.4%. The authors conclude KardiaMobile to be potentially useful for opportunistic early detection of AF, provided interprofessional collaboration is guaranteed so that suspect cases are adequately managed and in a timely way.

*Cunha S, Antunes E, Antoniou S, Tiago S, Relvas R, Fernandez-Llimos F, et al.*
*Res Social Adm Pharm. Available online 20 August 2019.*

**Screening for atrial fibrillation using a mobile, single-lead electrocardiogram in Canadian primary care clinics.**

The aim of this project was to describe the feasibility of KardiaMobile for AF screening in a large-scale, undifferentiated population. 184 Canadian primary care physicians were provided with a KardiaMobile ECG and asked to obtain a single 30-second ECG recording in all patients seen in their daily practice ≥ 65 years and not previously diagnosed with AF. Physician evaluation of KardiaMobile was measured using a Likert-scale based questionnaire. 133 physicians (72%) reported their findings and completed the survey. Over 3 months, 7585 patients were screened (42% of eligible patients). AF was detected in 471 patients (6.2%). Anticoagulation therapy was initiated in 270 patients (57%). Physicians generally reported a high perceived clinical value (94%) and ease of integration (89%) of the device. In conclusion, previously undiagnosed AF is common in older individuals attending primary care clinics. KardiaMobile appears to be an effective screening tool for AF with high physician acceptability. More research on the feasibility of such novel technologies is warranted for future consideration of integration in population-based screening programs.

*Godin R, Yeung C, Baranchuk A, Guerra P, Healey JS.*
*Canadian J Cardio. Published online April 2019.*

**The Heart Rhythm Society/American College of Physicians Atrial Fibrillation Screening and Education Initiative.**

With support from the Heart Rhythm Society (HRS) and the American College of Physicians (ACP), this initiative demonstrated the feasibility and yield, both in identifying previously undiagnosed AF and educating patients and caregivers about AF, of systematic screening events in Internal Medicine practices using a KardiaMobile ECG. Five Internal Medicine practices performed systematic screening and education of patients at higher risk for AF using KardiaMobile and a variety of educational materials. Participants were required to have at least one of the following AF risk factors: ischemic heart disease, diabetes, hypertension, congestive heart failure, chronic obstructive pulmonary disease, obesity, obstructive sleep apnea, age > 65 years old, a history of smoking, thyroid disease or female gender. Patients screened as "Unclassified" or "Possible AF" were referred for further evaluation. A total of 772 patients were screened. The average age was 65.2 + 15.4 years, and 28.2% were 75 years old or older. The majority, 521 (67.5%), were female, and 75.7% had a CHA2DS2-VASc Score > 2. Six hundred seventy (86.8%), screened as "Normal," 85 (11.0%) as "Unclassified" and 17 (2.2%) as "Possible AF." Participants demonstrated a significant knowledge deficit about stroke and AF prior to the screening events, and the majority felt that their awareness of these issues increased significantly as a result of their participation. The authors conclude that systematic screening using KardiaMobile was feasible, although with relatively modest yield of non-Normal algorithmic findings.

*Rosenfeld LE, Amin AN, Hsu JC, Oxner A, Hills MT, Frankel DS.*
*Heart Rhythm. Published online April 2019.*

**2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation.**

In this focused update of the AHA/ACC/HRS guidelines, in 7.12 Device Detection of AF and Atrial Flutter, the authors cite AliveCor research to support the following statement: "A role in screening for silent AF may also exist for remote electrocardiographic acquisition and transmission with a 'smart' worn or handheld WiFi-enabled device with remote interpretation."

*January CT, Wann LS, Calkins H, et al.*
*J Am Coll Cardiol. Jan 2019.*

**eHealth Tools to Provide Structured Assistance for Atrial Fibrillation Screening, Management, and Guideline-Recommended Therapy in Metropolitan General Practice: The AF-SMART Study**

This eHealth implementation study aimed to evaluate strategies to promote opportunistic AF screening using electronic screening prompts and improve treatment using electronic decision support (EDS) software. An electronic screening prompt appeared whenever an eligible patient's (aged ≥65 years, no AF diagnosis) medical record was opened in participating general practices. General practitioners and practice nurses offered screening using KardiaMobile ECG. Guideline-based EDS was provided to assist treatment decisions. Deidentified data were collected from practices using a data extraction tool. General practices (n=8) across Sydney, Australia, screened for a median of 6 months. A total of 1805 of 11,476 (16%) eligible patients who attended were screened (44% men, mean age 75.7 years). Screening identified 19 (1.1%) new cases of AF (mean age, 79 years; mean CHA2DS2-VASc, 3.7; 53% men). General practitioners (n=30) performed 70% of all screenings (range 1-448 patients per general practitioner). The proportion of patients with AF prescribed oral anticoagulants was higher for those diagnosed during the study: 15 of 18 (83%) for screen-detected and 39 of 46 (85%) for clinically detected, compared with 933 of 1306 (71%) patients diagnosed before the study ( P<0.001). The EDS was accessed 111 times for patients with AF and for 4 of 19 screen-detected patients.

*Orchard J, Neubeck L, Freedman B, Li J, Webster R, Zwar N, et al.*
*J Am Heart Assoc. 2019;8(1):e010959.*

**Age-and-sex stratified prevalence of atrial fibrillation in rural Western India: Results of SMART-India, a population-based screening study.**

This population-based study in India used KardiaMobile to derive age and sex-stratified AF prevalence by screening 7 participants in each of six age and sex strata (age 40-55, 56-65, 65+, and male and female) from 50 villages (2100 participants). A health worker from each village used a KardiaMobile to screen for AF on 3 separate days, and administered a questionnaire. All abnormal (AF or unclassified) ECGs were reviewed by the Indian cardiologist and AF determination confirmed by a US-based cardiac electrophysiologist. Among 2074 participants, AF was identified in 33 participants (1.6%), two-thirds on the first ECG. AF prevalence was higher among males (2.3% vs 1.0%, p = 0.03) and in older people (0.6%, 0.9%, 2.1%, 5.6%; p < 0.01). The authors conclude that the prevalence of AF observed is comparable to rates found in studies from North America and Western Europe and increases similarly with age. AF screening with KardiaMobile using village health workers in rural India is feasible and presents an opportunity for a strategy to address the stroke epidemic in India through primary prevention.

*Soni A, Karna S, Fahey N, Sanghai S, Patel H, Raithatha S, et al.*
*Int J Cardiol. Online Dec 2018.*

**Effectiveness of a nongovernmental organization-led large-scale community atrial fibrillation screening program using the smartphone electrocardiogram: An observational cohort study.**

Between November 2015 to September 2016, 11,574 Hong Kong citizens voluntarily participated in the AFinder Program, a nongovernmental organization (NGO)−led community- based AF screening program using KardiaMobile. A total of 118 screening sessions in 108 community centers was carried out by 84 trained layperson volunteers older than 50 years. Citizens with AF were contacted by telephone for completing the baseline and 9-month follow-up questionnaires. The ECG reports were mailed to those participants with AF, and they were advised to seek medical attention. Participants who had uninterpretable ECGs were advised to seek medical attention and undergo conventional ECG tests. Among all participants (9236 female citizens [79.8%]; mean age 78.6 years), KardiaMobile ECGs were interpretable in 10,735 citizens (92.8%). 244 (2.3%) had AF; a new diagnosis of AF was found in 74 participants (0.69%), with a mean CHA2DS2-VASc score of 3.9 +/- 1.5. 36 of the 74 were asymptomatic. Of 72 participants with newly diagnosed AF and indicated for oral anticoagulation, 47 sought medical attention and 17 (23.6%; 95% CI 13.8-33.4%) received oral anticoagulants. This NGO-led community-based AF screening program was effective in identifying citizens with newly diagnosed AF. However, the effectiveness of the program in subsequently leading them to receive appropriate oral anticoagulation therapy was weakened by the lack of a more structured downstream management pathway.

*Chan NY, Choy CC, Chan CK, Siu CW.*
*Heart Rhythm. 2018;15(9):1306-11.*

**Screening for atrial fibrillation is feasible in US managed care outpatient facilities.**

The purpose of this study was to evaluate the utility of screening for AF in patients presenting to Kaiser Permanente ambulatory clinics for routine care using KardiaMobile during intake. A total of 2286 patients 65 years and older were screened; mean age of the patients was 80 ± 11 years (range 65-96), 60% were males and 40% were females. AF was detected in 117 (5.1%) patients, 81 of whom had a history of AF (3.5% of the total screened). There were 36 (1.6%) patients who had undiagnosed AF, and only 2⁄36 (6%) were on anticoagulant therapy. In summary, up to 1.6% of patients 65 years and older presenting to an ambulatory clinic may have undiagnosed AF, most of whom are at significant risk of stroke (CHADsVASc score of ≥2), and would benefit from screening and treatment for AF to prevent stroke.

*Keen W, Martin J, Lopez C, Pena-Ruiz M, Antons K, Longson S, et al.*
*American Heart Association's Scientific Sessions (2017). Abstract.*

**Feasibility and acceptability of atrial fibrillation screening using a hand-held ECG device in general practice setting in Hong Kong.**

1041 patients age 65 years of age or greater were screened in 9 primary care clinics in Hong Kong using KardiaMobile. All ECGs were over-read by a cardiologist. Overall AF prevalence was 2.6%, and newly identified AF was 1.5%. Mean age of newly diagnosed AF patients was 77 years, with a mean CHA2DS2-VASc score of 3.9. Patient awareness of AF was low with 36.4% unfamiliar with AF and 63.6% unaware of the risk of AF related stroke. All patients agreed that KardiaMobile was easy to operate and willing to undergo repeated screening in future primary care visits. 86% of primary care physicians considered KardiaMobile useful for AF screening and would use it in their daily practice. At baseline, 47% of primary care physicians used CHA2D2-VASc score to assess AF related stroke risk, which increased to 71% at the end of the study.

*Chan LL, Chan SC, Yan BP.*
*Value Health. 2017;20(9):A599.*

**Assessment of remote heart rhythm sampling using the AliveCor heart monitor to screen for atrial fibrillation: the REHEARSE-AF study.**

This is the first prospective randomized trial of AF screening using a remote, handheld ECG device over an extended period of time (1 year). 1001 adults ≥ 65 years of age with a CHADS-VASc score ≥2 (mean score 3.0) were randomized to AF screening using KardiaMobile or usual care. Patients randomized to KardiaMobile acquired ECGs twice weekly over 12 months (plus additional ECGs if symptomatic). 19/500 (3.8%) patients in the KardiaMobile group were diagnosed with AF, versus 5/501 (1.0%) in the usual care group (hazard ratio, 3.9; 95% confidence interval=1.4-10.4; P=0.007) at a cost per AF diagnosis of $10,780 (£8255). There was a statistically similar number of stroke/transient ischemic attack/systemic embolic events. The majority of KardiaMobile patients were satisfied with the device, finding it easy to use without restricting activities or causing anxiety. This trial found that extended AF screening with KardiaMobile is significantly more likely to identify incident AF than usual care.

*Halcox JPJ, Wareham K, Cardew A, Gilmore M, Barry JP, Phillips C, et al.*
*Circulation. 2017;136(19):1784-94.*

**Feasibility of using mobile ECG recording technology to detect atrial fibrillation in low-resource settings.**

This study used KardiaMobile to screen 50 adults in Kenya (mean age 54 years, 66% women) attending Kijabe Hospital outpatient internal medicine or diabetes clinics; 44% had hypertension, 32% had diabetes, and 4% had stroke. ECG tracings in 4 of the 50 patients (8%) showed AF, and none had been previously diagnosed with AF. The authors concluded that KardiaMobile can be used to screen for AF in low-resource settings.

*Evans GF, Shirk A, Muturi P, Soliman EZ.*
*Glob Heart. Published online first: 13 Mar 2017. doi:10.1016/j.gheart.2016.12.003.*

**Opportunistic screening to detect atrial fibrillation in Aboriginal adults in Australia.**

This protocol is for a mixed methods study that will recruit and train Aboriginal health workers to use KardiaMobile to consecutively screen 1500 Aboriginal people aged 45 years and older. The study will quantify the proportion of people who presented for follow-up assessment and/or treatment following a non-normal screening and then estimate the prevalence and age distribution of AF of the Australian Aboriginal population.

*Gwynne K, Flaskas Y, O'Brien C, Jeffries TL, McCowen D, Finlayson H, et al.*
*BMJ Open. 2016;6(11):e013576.*

**Screening for atrial fibrillation during influenza vaccinations by primary care nurses using a smartphone electrocardiograph (iECG): a feasibility study.**

KardiaMobile was used to identify asymptomatic AF at the time of influenza vaccination in 5 practices in Sydney, Australia. Nurses used the automated algorithm to screen 973 patients aged ≥ 65 years between April-June 2015. Screening took on average 5 minutes (range 1.5 -10 minutes); abnormal recordings required additional time. Newly identified AF was found in 0.8% (8) of patients, and the overall prevalence of AF was 3.8% (37). The sensitivity and specificity of the automated algorithm for detecting AF was 95% and 99%, respectively. Screening by practice nurses was well accepted by practice staff. Key enablers were the confidence and competence of nurses and a 'designated champion' to lead screening at the practice. Barriers were practice specific, and mainly related to staff time and funding.

*Orchard J, Lowres N, Freedman SB, Ladak L, Lee W, Zwar N et al.*
*Eur J Prev Cardiol. 2016; 23(2S):13-20.*

**High burden of unrecognized atrial fibrillation in rural India: an innovative community-based cross-sectional screening program.**

Residents from 6 villages in Gujarat, India, were screened for AF using KardiaMobile. A total of 235 participants aged 50 years and older (half female) used KardiaMobile for 2 minutes on 5 consecutive days. Community health workers helped to screen participants. The prevalence of AF increased by the number of screenings, from 3.0% with 1 screening to 5.1% with 5 screenings.

*Soni A, Earon A, Handorf A, Fahey N, Talati K, Bostrom J, et al.*
*JMIR Public Health Surveill. 2016;2(2):e159.*

**Screening for atrial fibrillation in 13,122 Hong Kong citizens with smartphone electrocardiogram.**

From May 1, 2014, to April 30, 2015, adults aged 18 and above were informed by media promotion for a community-wide AF screening program in Hong Kong. A group of non-medical volunteers used KardiaMobile to screen 13,122 Hong Kong citizens (mean age 65.5 ± 13.3 years). All recordings were overread by a cardiologist within 1 month of the recording, and all participants with AF detected were referred for medical consultation. Fifty-six (0.4%) out of 13,122 KardiaMobile recordings were uninterpretable. Newly diagnosed AF was discovered in 101 (0.8%) participants. The overall prevalence for AF was 1.8% (239/13,122, 95% CI 1.6-2%). Systematic population-based ECG screening for AF with KardiaMobile was feasible and identified a proportion of Hong Kong citizens with AF that was comparable with that of contemporary US and European populations.

*Chan NY, Choy CC.*
*Heart. 2017;103(1):24-31.*

**The effectiveness of a mobile ECG device in identifying AF: sensitivity, specificity, and predictive value.**

Ninety-five patients, 29 with AF and 66 in sinus rhythm, were assessed with KardiaMobile and a standard 12-lead EKG by two physicians in clinic. For one practitioner's review, the sensitivity of KardiaMobile was 90% and the specificity was 86%; for the other practitioner, the sensitivity was 93% and the specificity was 76%. The high sensitivity of KardiaMobile suggests this test is a good 'rule-out' for AF. A positive test should be combined with a 12-lead EKG to confirm the diagnosis of AF.

*Williams, J, Pearce K, Benett I.*
*Br J Cardiol. 2015;22:70-2.*

**The efficacy of a smartphone ECG application for cardiac screening in an unselected island population.**

KardiaMobile was used to screen 954 participants aged 12-99. There were 54 (5.6%) people noted to have a potential abnormality (conduction defect, increased voltage, rhythm abnormality); of these 23 (43%) were abnormal with two confirming AF and 2 showing atrial flutter. Other abnormalities detected included atrial and ventricular ectopy, bundle branch block, and left ventricular hypertrophy. One patient with increased voltages was later diagnosed with hypertrophic cardiomyopathy. In conclusion, KardiaMobile was quick and easy to use and led to new diagnoses of arrhythmia, bundle branch block, left ventricular hypertrophy and cardiomyopathy.

*Le Page P, McLachlan H, Anderson L, Penn L, Moss A, Mitchell A.*
*Br J Cardiol. 2015;22:31-3.*

**Pharmacy-based screening for atrial fibrillation in high-risk Maori and Pacific populations**

One hundred twenty-one Maori and Pacific people age ≥ 55 years were screened for AF with KardiaMobile in New Zealand community pharmacies; if the automatic algorithm was positive, participants were referred to primary care for confirmatory 12-lead ECG. Two of the 121 participants screened had a new diagnosis of AF (1.7%), and two known AF cases appeared to not be receiving warfarin, giving a total of four people (3%) that could benefit from initiation of anticoagulation. There were 2 false positives, which were thought to occur due to incorrect handling of the device, which was corrected through further training of the pharmacists. The study determined that KardiaMobile is highly acceptable to patient populations as well as health professionals in this environment.

*Walker N, Doughty R, Parag V, Harrison J, Bennett M, Freedman B.*
*N Z Med J. 2014;127(1398):128-31.*

**iPhone ECG screening by practice nurses and receptionists for atrial fibrillation in general practice: the GP-SEARCH qualitative pilot study.**

Receptionists and practice nurses screened patients aged ≥65 years using KardiaMobile. General practitioner (GP) review was then provided during the patient's consultation. Eighty-eight patients (51% male; mean age 74.8 ± 8.8 years) were screened: 17 patients (19%) were in AF (all previously diagnosed). KardiaMobile was well accepted by GPs, nurses and patients. Receptionists were reluctant, whereas nurses were confident in using the device to explain and provide screening.

*Orchard J, Freedman SB, Lowres N, Peiris D, Neubeck L.*
*Aust Fam Physician. 2014;43(5):315-9.*

**Feasibility and cost-effectiveness of stroke prevention through community screening for atrial fibrillation using iPhone ECG in pharmacies. The SEARCH-AF study.**

One thousand pharmacy customers (mean age 76 ± 7 years, 44% male) were screened with KardiaMobile. Newly identified AF was found in 1.5% (95% CI, 0.8-2.5%), and AF prevalence was 6.7%. The automated algorithm showed 98.5% sensitivity and 91.4% specificity for detecting AF. Using cost and outcome data from a United Kingdom study for AF screening, the incremental cost-effectiveness ratio of extending screening into the community with KardiaMobile, based on 55% warfarin prescription adherence, would be $USD4,066 per quality-adjusted life-year gained, and $USD20,695 for preventing one stroke. In summary, screening for AF with KardiaMobile is feasible and cost-effective.

*Lowres N, Neubeck L, Salkeld G, Krass I, McLachlan AJ, Redfern J, et al.*
*Thromb Haemost. 2014;111(6):1167-76.*

**iPhone ECG application for community screening to detect silent atrial fibrillation: a novel technology to prevent stroke.**

KardiaMobile was used in a community screening of 109 patients (70 in sinus rhythm and 39 in AF) soon after a 12-lead ECG had been performed. The ECGs were interpreted by two cardiologists blinded to the rhythm diagnosis, and were processed to provide an automated diagnosis of sinus rhythm or AF. Results were compared with the 12-lead ECG diagnosis by a third cardiologist. An optimized algorithm performed extremely well in the validation set with high sensitivity, specificity, overall accuracy and Kappa (95% CI) of 98% (89%–100%), 97% (93%–99%), 97% (94%–99%) and 0.92 (0.86– 0.98) respectively. This study concluded that KardiaMobile can be used to simply and rapidly record a high quality single-lead ECG to accurately detect AF, making it an ideal technology for community screening programs to detect silent AF.

*Lau JK, Lowres N, Neubeck L, Brieger DB, Sy RW, Galloway CD, et al.*
*Int J Cardiol. 2013;165(1):193-4.*

## 11. Investigational Use: Accuracy of Other Algorithms*

**Sensor analytics for interpretation of EKG signals.**

Over 6,000 KardiaMobile ECGs were used by researchers at Oklahoma State University to develop machine learning models to identify normal sinus rhythm, atrial fibrillation, AV block, sinus bradycardia, and sinus tachycardia. Specifically, QT interval, PR interval, P wave interval and average HR were used as inputs for the multi-label classification models. For the binary relevance model, classification sensitivities and specificities were, for normal, 97.1% and 78.5%; for AF, 94.2% and 98.7%; for AV block, 68.4% and 99.7%; for sinus bradycardia, 42.5% and 99.7%; and for sinus tachycardia, 81.1% and 99.1%. Overall, the model had 91.1% accuracy.

*Kalgotra P, Sharda R, Hammer B, Albert D.*
*Expert Systems with Applications. Jan 2019*

## 12. Investigational Use: AF Episode Detection*

**Smartwatch performance for the detection and quantification of atrial fibrillation.**

AF burden and duration appear to be related to stroke risk. A wearable consumer electronic device could provide long-term assessment of these measures inexpensively and noninvasively. This study compares the accuracy of a research version of SmartRhythm for KardiaBand on the Apple Watch, with simultaneous recordings from an insertable cardiac monitor (ICM). The research version of SmartRhythm, a convolutional neural network, was trained on anonymized data of photoplethysmogram (PPG)-derived heart rate, activity level, and KardiaBand ECGs from 7500 AliveCor users. The network was validated on data collected in 24 patients with ICMs and a history of paroxysmal AF who simultaneously wore KardiaBand on an Apple Watch (Series 2). The primary outcome was sensitivity of SmartRhythm for AF episodes ≥1 hour. 31,348.9 hours (mean (SD), 11.3 (4.4) hours/day) of simultaneous Apple Watch and ICM recordings were obtained in 24 patients. The ICM detected 82 episodes of AF ≥1 hour while the Apple Watch was worn, with a total duration of 1127.1 hours. Of these, SmartRhythm detected 80 episodes (episode sensitivity, 97.5%) with a total duration of 1101.1 hours (duration sensitivity, 97.7%). Three of the 18 subjects with AF ≥1 hour had AF only when the watch was not being worn (patient sensitivity, 83.3%; or 100% during time worn). Positive predictive value for AF episodes was 39.9%. This proof-of-concept study found that smartwatch PPG and activity data, coupled with an investigational SmartRhythm algorithm, is highly sensitive for detection of AF episodes in an ambulatory population when compared with an ICM. Such devices, coupled with ECG data, may represent an inexpensive, noninvasive approach to long-term AF surveillance and management.

*Wasserlauf J, You C, Patel R, Valys A, Albert D, Passman R.*
*Circ Arrhythm Electrophysiol. 2019 May;12:e006834. DOI: 10.1161/CIRCEP.118.006834*

## 13. Investigational Use: As-Needed Anticoagulation for AF*

**"As Needed" nonvitamin K antagonist oral anticoagulants for infrequent atrial fibrillation episodes following atrial fibrillation ablation guided by diligent pulse monitoring: a feasibility study.**

This study assessed the feasibility of direct oral anticoagulation (DOACs) guided by pulse monitoring to detect AF. 99 patients (average age was 64 ± 8 years) were enrolled with a CHA2DS2-VASc score greater than or equal to 1 in men and greater than or equal to 2 in women, capable of pulse assessment twice daily and no AF on extended monitoring following successful AF ablation. Twelve (12%) patients used KardiaMobile twice daily because of uncertainty in their ability of detecting their pulse accurately. All patients were instructed to start DOAC if AF >1 hour or recurrent shorter episodes. Duration of DOAC use after restart was typically 2 to 4 weeks. After 30 ± 14 months (total 244 patient-years), 22 patients (22%) transitioned to daily DOAC because of noncompliance with pulse assessment or patient preference (six patients) or because of suspected or documented AF episode(s) in 16 (16%) patients. There was only one thromboembolic event (0.4%/yr of follow- up) in a patient without AF and one mild bleeding event (epistaxis).

*Zado ES, Pammer M, Parham T, Lin D, Frankel DS, Dixit S, et al.*
*J Cardiovasc Electrophysiol. Published online 2019.*

**Intermittent versus continuous anticoagulation therapy in patients with atrial fibrillation (ICARE-AF), a pilot study.**

Fifty-eight patients with paroxysmal AF and CHADS2 < 3 were randomized to intermittent anticoagulation based on daily KardiaMobile monitoring (n=29), or continuous anticoagulation with a new oral anticoagulation medication (n=29). Over a median 20 months, 20 patients in the intermittent arm failed to submit a daily ECG at least once (median 3 failed submissions). 10 patients (35%) crossed over to continuous anticoagulation, either for failure to submit an ECG for 3 days, or for progression to persistent AF. Rates of death or stroke were not different between the groups (3 vs. 1, p=0.65). Major bleeding was not different. Gastrointestinal bleeding was more frequent in the continuous group.

*Stavrakis S, Stoner JA, Kardokus J, Garabelli PJ, Po SS, Lazzara R.*
*J Interv Card Electrophysiol. 2017;48(1):51-60.*

## 14. Investigational Use: HRV*

**Impact of heart rate variability, a marker for cardiac health, on lupus disease activity.**

Decreased heart rate variability (HRV) is associated with adverse outcomes in cardiovascular diseases and has been observed in patients with systemic lupus erythematosus (SLE). This study assessed HRV in 53 SLE patients with a 5-minute KardiaMobile ECG. Baseline HRV (RMSSD, pNN50, HF power, LF/HF ratio) was inversely related to disease activity, as measured by clinical assessment and plasma cytokine levels. Changes in RMSSD between visits were inversely related to changes in the Systemic Lupus Erythematosus Disease Activity Index (p = 0.007). Changes in the LF/HF ratio between visits were also associated with plasma cytokine changes. Impaired HRV, particularly the LF/HF ratio, is associated with lupus disease activity and several cytokines related to IFN type II and TNF pathways.

*Thanou A, Stavrakis S, Dyer JW, Munroe ME, James JA, Merrill JT.*
*Arthritis Res Ther. 2016;18:197.*

**14. Investigational Use: HRV\*** (Continued)

**Heart rate variability in concussed athletes: a case report using the smartphone electrocardiogram.**

This case report describes assessment of heart rate variability in a concussed 18-year-old male collegiate football player, using KardiaMobile. Five days after his concussion, and while still symptomatic, a 5-minute ECG was obtained using KardiaMobile, at rest and after exercise on a stationary bike. The assessment was repeated 2 weeks post injury when he was symptom free. HRV analysis was performed using Kubios HRV version 2.2 (Biosignal Analytics and Medical Imaging Group, Kuopio, Finland). Exercise induces an overall decrease in HRV due to an increase in sympathetic activity and decrease in parasympathetic activity. There were expected post-exercise decreases in HRV 2 weeks post-injury, and some deviation from the expected pattern when the athlete was symptomatic 5 days post injury, suggesting some dysfunction in autonomic cardiovascular regulation when the athlete was concussed. HRV may be a promising tool, especially via wearable technologies, for the sideline assessment of concussion..

*Lai E, Boyd K, Albert D, Ciocca M, Chung EH.*
*HeartRhythm Case Rep. 2017;3(11):523-6.*

**15. Investigational Use: Cardiovascular Implantable Electronic Devices (CIEDs)\***

**Safety and compatibility of smart device heart rhythm monitoring in patients with cardiovascular implantable electronic devices.**

A total of 251 patients (59% with pacemaker, 41% with ICD, 24.3% CRT), were recruited to evaluate the safety and compatibility of KardiaMobile in patients with cardiovascular implantable electronic devices (CIED); manufacturers included Medtronic, Boston Scientific, St. Jude Medical, Biotronik, and Guidant. Electrograms from the CIED were obtained at the time of recording to assess for any electromagnetic interference introduced by KardiaMobile. There were no adverse clinical events noted at the time of recording and no changes to CIED settings. Review of all ECGs revealed no EMI introduced by KardiaMobile. Recordings were correctly interpreted in 90% of paced recordings and 94.7% of nonpaced recordings. In conclusion, KardiaMobile has an excellent safety profile when used in conjunction with most CIEDs.

*Abudan AA, Isath A, Ryan JD, Henrich MJ, Dugan JL, Attia ZI et al.*
*J Cardiovasc Electrophysiol. 2019.*

**Validation of a smartphone-based electrocardiography in the screening of QT intervals in children.**

The aim of this pilot study was to assess the reliability of KardiaMobile in the measurement of QT and corrected QT intervals in children. In all participants, ECGs from KardiaMobile (placed on the chest surface horizontally) and a standard 12-lead electrocardiograph were obtained simultaneously. Randomly selected three QT intervals and their corresponding RR intervals were measured to calculate the average corrected QT using Bazett's formula (in a blinded manner by two pediatric electrophysiologists). Of 285 transmitted tracings, 265 (93%) were of diagnostic quality; the remaining were not interpretable due to too much noise or motion artifact and unclear T-wave termination. The ages ranged from 2 months to 20.8 years (mean 9.8 years). Averaged weight was 39.7 kg (3-92 kilos). 20 patients had congenital heart disease. The mean QT intervals obtained from lead I of a 12-lead ECG and KardiaMobile were 343±40 ms and 340±41 ms, respectively. The mean corrected QT intervals were 419±28 ms and 415±33 ms, respectively. There was high correlation between the QT intervals (Pearson's correlation coefficient: 0.83 [p<0.001]) and moderate correlation between the corrected QT intervals (Pearson's correlation coefficient: 0.57 [p<0.001]); the mean heart rate was at a range (92-93 bpm) where minimal changes in heart rate substantially influence corrected QT intervals, which may explain the later result. The authors concluded that KardiaMobile can potentially be used as a practical tool to assess QT intervals in children for screening purposes.

*Karacan M, Celik N, Gul EE, Akdeniz C and Tuzcu V.*
*North Clin Istanb. 2019;6:48-52.*

**Can smartphone wireless ECGs be used to accurately assess ECG intervals in pediatrics? A comparison of mobile health monitoring to standard 12-lead ECG.**

The goal of this study was to assess the accuracy of ECG interval measurements on KardiaMobile in pediatric patients. A single center enrolled 30 pediatric outpatients, mean age 8.2 years (age range 14 days – 17 years), presenting for cardiology clinic; subjects underwent standard 12-lead ECG followed by 30-second KardiaMobile tracing. Structural heart disease and/or conduction abnormality was present in 20 patients (67%). The majority of tracings (27/30, 90%) were of diagnostic quality on first attempt. Overall, the ΔPR was 15.2±10.8ms (r = 0.86), ΔQRS was 9.6±8ms (r = 0.86), and ΔQTc was 15.6±12.7ms (r = 0.83). There were 9 patients with ΔQTc measurements >20ms with 4/9 (44%) having a conduction disorder and 2/9 (22%) having marked sinus arrhythmia. Bland-Altman method of agreement demonstrated strong agreement for QRSd and QTc. The AF algorithm reported 4/30 (13%) false positive "possible AF" diagnoses (rhythm over-read demonstrated n = 3 marked sinus arrhythmia, n = 1 sinus rhythm with aberrated PACs) resulting in a specificity of 87%. In summary, KardiaMobile produces accurate single lead ECG tracings in both healthy children and children with cardiac disease or rhythm abnormalities across the pediatric spectrum.

*Gropler MRF, Dalal AS, Van Hare GF, Avari Silva JN.*
*PLoS ONE 13 (9): e0204403. https://doi.org/10.1371/journal. pone.0204403*

## Comparison of a smartphone-based ECG recording system with a standard cardiac event monitor in the investigation of palpitations in children.

The use of KardiaMobile in 80 children with palpitations was compared to a pediatric practice's most recent 100 conventional patient-activated event monitors. Median patient age was 11 years in KardiaMobile group, compared with 10 years in the conventional group. Seventy-nine of 80 (98%) patients with a smartphone monitor sent an ECG recorded during symptoms, compared with 62/100 (62%) from the conventional group. A total of 836 ECG recordings were sent from the smartphone monitors compared with 752 from the conventional group. Eight per cent of ECG recordings in each group were of inadequate quality for analysis. Twenty of 80 (25%) patients with a smartphone monitor had documented tachyarrhythmia compared with 6/100 (6%) patients with the conventional monitor (p<0.001). On comparison with the conventional approach, the smartphone monitor outperformed with respect to diagnostic yield and patient satisfaction. The authors conclude that KardiaMobile allows simple, effective, long-term ECG event monitoring in children that is highly acceptable to the patient and parent.

*Macinnes M, Martin N, Fulton H, McLeod KA.*
*Arch Dis Child. Published Online First: 02 June 2018. doi:10.1136/archdischild-2018-314901.*

## An unusual cause of lone atrial fibrillation in a young female subject due to a rapid-cycling focal atrial trigger.

A 13-year-old female was diagnosed with lone atrial fibrillation with recurrence despite multiple cardioversions and antiarrhythmic medications. She underwent EP testing and had radiofrequency ablation of a rapidly cycling focal atrial trigger in the region of the ligament of Marshall. Catheter ablation was successful. KardiaMobile was used throughout her treatment to document recurrent atrial fibrillation and tachycardia, as well as normal sinus rhythm once the atrial focus was ablated.

*Baskar S, Attari M, Czosek RJ, Jais P, Anderson JB, Spar DS.*
*HeartRhythm Case Rep. 2018;4(6):204-8.*

## SPEAR Trial: Smartphone Pediatric ElectrocARdiogram Trial.

This study aimed to assess the usefulness of pediatric ECG tracings generated by KardiaMobile. Over a year, 20 patients with documented paroxysmal arrhythmia used KardiaMobile, generating a total of 238 tracings. 96% of tracings were of diagnostic quality for sinus rhythm, sinus tachycardia, supraventricular tachycardia, and AF. 126 patient satisfaction surveys (64% from parents) were completed. 98% of the survey responses indicated that it was easy to obtain tracings, 93% found it easy to transmit the tracings, 98% showed added comfort in managing arrhythmia by having the device, and 93% showed interest in continued use of the device after the study period ended. In summary, KardiaMobile generates tracings of diagnostic quality in children. User satisfaction was extremely positive.

*Nguyen HH, Van Hare GF, Rudokas M, Bowman T, Silva JN.*
*PLoS ONE 10(8):e0136256. Available online 2015 August.*

## A smartphone application to diagnose the mechanism of pediatric supraventricular tachycardia.

The utility of KardiaMobile to record supraventricular tachycardia (SVT) and to distinguish atrioventricular reentrant tachycardia (AVRT) from atrioventricular nodal reentrant tachycardia (AVNRT) in pediatric patients was ascertained. Tracings were obtained by placing the smartphone in three different positions on the chest. Two blinded pediatric electrophysiologists jointly analyzed a pair of sinus and tachycardia tracings in each position. 37 patients (mean age 13.7 years) were enrolled. 128 pairs of tracings were obtained, and the correct diagnosis was made in 59-73% with the three-lead positions. KardiaMobile can successfully record SVT in pediatric patients and can predict the SVT mechanism at least as well as previously published reports of Holter monitors.

*Ferdman DJ, Liberman L, Silver, ES.*
*Pediatr Cardiol. 2015;36(7):1452-7.*

## 17. Investigational Use: Potassium*

**Development and validation of a deep-learning model to screen for hyperkalemia from the electrocardiogram.**

In this original research conducted by AliveCor and Mayo Clinic, a deep learning model was trained and validated to screen for elevated potassium (hyperkalemia) from the ECG in patients with chronic kidney disease (CKD); hyperkalemia is common in this population and associated with fatal arrhythmias. A deep convolutional neural network (DNN) was trained using 1,576,581 ECGs from 449,380 patients seen at Mayo Clinic, Rochester, Minnesota, from 1994 to 2017. The DNN was trained using 2 (leads I and II) or 4 (leads I, II, V3, and V5) ECG leads to detect serum potassium levels of 5.5 mEq/L or greater, and was validated using retrospective data from the Mayo Clinic in Minnesota, Florida, and Arizona. The validation included 61,965 patients with stage 3 or greater CKD. Each patient had a serum potassium count drawn within 4 hours after their ECG was recorded. The prevalence of hyperkalemia in the 3 validation data sets ranged from 2.6% (n = 1,282 of 50,099; Minnesota) to 4.8% (n = 287 of 6,011; Florida). Using ECG leads I and II, the AUC of the deep-learning model was 0.883 (95% CI, 0.873-0.893) for Minnesota, 0.860 (95% CI, 0.837-0.883) for Florida, and 0.853 (95% CI, 0.830-0.877) for Arizona. The positive predictive value ranged from 10.1% (Minnesota) to 14.0% (Florida). Further research is warranted, but the application of artificial intelligence to the ECG may enable screening for hyperkalemia.

*Galloway CD, Valys AV, Shreibati JB, Treiman DL, Petterson FL, Gundotra VP, et al.*
*JAMA Cardiol. Published online April 2019.*

**Noninvasive blood potassium measurement using signal-processed, single-lead ECG acquired from a handheld smartphone.**

The single lead ECG from KardiaMobile was used to estimate blood potassium levels in 21 patients during hemodialysis sessions. Individualized potassium estimation models were generated for each patient. ECG-calculated potassium values were compared to blood potassium results at subsequent visits to evaluate the accuracy of the potassium estimation models. The mean absolute error between the estimated potassium and blood potassium was 0.38 ± 0.32 mEq/L (9% of average potassium level) decreasing to 0.6 mEq/L using predictors of poor signal.

*Yasin OZ, Attia Z, Dillon JJ, DeSimone CV, Sapir Y, Dugan J, et al.*
*J Electrocardiol. 2017;50(5):620-5.*

## 18. Investigational Use: Precordial Lead*

**Improved accuracy and confidence with multiple-lead recordings from a single-lead mobile electrocardiographic device.**

This study compared accuracy of a 12-lead ECG, KardiaMobile, and a 3-lead ECG−using KardiaMobile with an alligator clip to record leads II and V1−in 10 patients with either sinus rhythm with low amplitude P wave, or atrial flutter (AFL). It was hypothesized that cardiologists who interpreted the multi-lead tracings would make more accurate diagnoses. All patients were able to record their own single and 3-lead tracings. 29 cardiologists reviewed the ECGs. The single lead, 3-lead, and 12-lead ECG yielded 36.4%, 84.3%, and 97.7% agreement with the established diagnosis, respectively (P < .01 for each comparison). Overall mean confidence scores (out of a score of 5) were 2.95, 3.50, and 4.47 for single lead, 3-lead, and the 12-lead ECG, respectively (P < .01 for each comparison). Compared to a single lead KardiaMobile, the 3-lead KardiaMobile ECG significantly improved cardiologists' diagnostic accuracy and confidence in their interpretation, approaching that of a standard 12-lead ECG.

*Frisch DR, Weiss M, Dikdan SJ, Keith SW and Sarkar K.*
*Pacing Clin Electrophysiol. 2019;42:1191-1196.*

## 19. Investigational Use: QT Interval*

**Validation of a smartphone-based electrocardiography in the screening of QT intervals in children.**

The aim of this pilot study was to assess the reliability of KardiaMobile in the measurement of QT and corrected QT intervals in children. In all participants, ECGs from KardiaMobile (placed on the chest surface horizontally) and a standard 12-lead electrocardiograph were obtained simultaneously. Randomly selected three QT intervals and their corresponding RR intervals were measured to calculate the average corrected QT using Bazett's formula (in a blinded manner by two pediatric electrophysiologists). Of 285 transmitted tracings, 265 (93%) were of diagnostic quality; the remaining were not interpretable due to too much noise or motion artifact and unclear T-wave termination. The ages ranged from 2 months to 20.8 years (mean 9.8 years). Averaged weight was 39.7 kg (3-92 kilos). 20 patients had congenital heart disease. The mean QT intervals obtained from lead I of a 12-lead ECG and KardiaMobile were 343±40 ms and 340±41 ms, respectively. The mean corrected QT intervals were 419±28 ms and 415±33 ms, respectively. There was high correlation between the QT intervals (Pearson's correlation coefficient: 0.83 [$p<0.001$]) and moderate correlation between the corrected QT intervals (Pearson's correlation coefficient: 0.57 [$p<0.001$]); the mean heart rate was at a range (92-93 bpm) where minimal changes in heart rate substantially influence corrected QT intervals, which may explain the later result. The authors concluded that KardiaMobile can potentially be used as a practical tool to assess QT intervals in children for screening purposes.

*Karacan M, Celik N, Gul EE, Akdeniz C and Tuzcu V.*
*North Clin Istanb. 2019;6:48-52.*

**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.**

A group of 100 patients seen at an academic cardiology care center in Poland received a 12-lead ECG and a subsequent KardiaMobile ECG. Two cardiologists were blinded to review of rhythm and intervals. There was no statistically significant difference in arrhythmia assessment of atrial fibrillation and atrial flutter. Basic intervals measured on the 30-second KardiaMobile ECG, namely PQ, RR, and QT, were significantly shorter than those measured in the standard 10-second 12-lead ECG method (160 ms vs. 180 ms [$p < 0.001$], 853 ms vs. 880 ms [$p =0.03$] and 393 ms vs. 400 ms [$p < 0.001$], respectively).

*Koltowski L, Balsam P, Gllowczynska R, Rokicki JK, Peller M, Maksym J, et al.*
*Cardiol J. Online Jan 2019.*

**Artificial intelligence and deep neural networks can identify patients with electrocardiographically concealed long QT syndrome from the surface 12-lead electrocardiogram.**

Long QT syndrome (LQTS) is characterized by prolongation of the QT interval and is associated with increased risk of sudden cardiac death, especially if the QTc exceeds 500 ms. However, approximately 25% of patients with genetically confirmed LQTS have a normal QTc at rest. Distinguishing LQTS patients from normal is of utmost importance to correctly diagnose disease, implement simple preventative measures, and initiate prophylactic therapy if necessary. All ECGs from patients seen at Mayo Clinic's Genetic Heart Rhythm Clinic were analyzed retrospectively. Patients were included if they a) had a definitive diagnosis of LQTS (n=1048) or b) were seen because of an initial suspicion for LQTS but dismissed as normal (n=1010). A multi-layer convolutional recurrent neural network (CRNN) was used to classify patients based on a 10 second ECG using Lead I alone. The CRNN was trained using 72% of the patients and validated in the remaining 28%. When looking only at LQTS patients with a normal resting QTc value (QTc < 450ms), the QTc alone distinguished LQTS from normal with an AUC of 0.67. Here, the CRNN increased this discrimination to an AUC of 0.83. Deep neural networks were able to successfully distinguish patients with electrocardiographically concealed LQTS from those dismissed as normal. As these tools are further developed, deep neural networks and artificial intelligence could aid in the early detection and diagnosis of patients with LQTS.

*Bos JM, Attia ZI, Thome T, Albert D, Friedman PA, Ackerman MJ.*
*Heart Rhythm Scientific Sessions (2018). Abstract.*

**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.**

This study sought to evaluate the accuracy of KardiaMobile for assessing the QTc. Across 99 healthy volunteers and 25 hospitalized patients in sinus rhythm being loaded on dofetilide or sotalol, KardiaMobile QTc had good agreement with the 12-lead ECG QTc. For patients receiving QT prolonging antiarrhythmics, KardiaMobile is capable of detecting QTc prolongation, and lead I is most accurate in measuring the QTc if < 500 milliseconds.

*Garabelli P, Stavrakis S, Albert M, Koomson E, Parwani P, Chohan J, et al.*
*J Cardiovasc Electrophysiol. 2016;27(7): 827-32.*

**QTc intervals can be assessed with the AliveCor heart monitor in patients on dofetilide for atrial fibrillation.**

The feasibility of KardiaMobile tracings for QTc assessment in 5 patients receiving dofetilide was assessed. There was no significant difference between KardiaMobile QTc and standard ECG-QTc (all ± 20 msec). None of the patients required a dosage adjustment due to QT prolongation during their stay. KardiaMobile can be used to monitor the QTc in patients receiving dofetilide for AF.

*Chung EH, Guise KD.*
*J Electrocardiol. 2015;48(1):8-9.*

## 20. Investigational Use: ST Elevation*

**Smartphone ECG for evaluation of ST-segment elevation myocardial infarction (STEMI): Design of the ST LEUIS International Multicenter Study.**

This multicenter, international prospective study aims to validate an investigational KardiaMobile attachment that provides all 12 leads of a standard ECG system, and its ability to accurately assess the presence or absence of ST-elevation myocardial infarction (STEMI) in patients presenting with chest pain. The aim is to support the diagnostic utility of smartphone technology which can improve the availability of a 12-lead ECG in the diagnosis of STEMI. The study will take place over 12 months at five institutions. Approximately 60 patients will be enrolled per institution, for a total recruitment of 300 patients.

*Barbagelata A, Bethea CF, Severance HW, Mentz RJ, Albert D, Barsness GW, et al.*
*J Electrocardiol. Available online 19 October 2017.*

**Mobile digital health devices and the diagnosis in real-time of myocardial ischaemia.**

This case report describes the use of KardiaMobile during episodes of chest pain at rest in a 61-year-old man. The single-lead ECG demonstrated ST-segment elevation with intermittent ectopy, which resolved following the administration of sublingual nitroglycerin. He underwent coronary angiography which did not show significant coronary obstructive disease, so he was diagnosed with coronary artery spasm and treated with vasodilators. This case provides a demonstration of how mobile health devices can provide new insights into previously difficult to establish diagnoses.

*Joseph JP, Redwood SR.*
*QJM. 2017;110(5):309-10.*

**Smartphone ECG for evaluation of STEMI: results of the ST LEUIS Pilot Study.**

In this pilot study, a 12-lead ECG generated from electrodes attached to KardiaMobile was compared to the 12-lead ECG in evaluation of in-hospital cardiac ischemia. Six patients for whom the hospital ST elevation myocardial infarction (STEMI) was activated were evaluated. All tracings were taken prior to catheterization or immediately after revascularization while still in the catheterization laboratory. The 12-lead ECG generated from KardiaMobile had excellent correlation with the gold standard 12-lead ECG in all patients. Four out of six tracings were judged to meet STEMI criteria on both modalities as determined by three experienced cardiologists, and in the remaining two, consensus indicated a non-STEMI ECG diagnosis. This study confirmed the potential of KardiaMobile for evaluation of acute ischemia.

*Muhlestein JB, Le V, Albert D, Moreno FL, Anderson JL, Yanowitz F, et al.*
*J Electrocardiol. 2015;48(2):249-59.*

**Clinical stage of acquired immunodeficiency syndrome in HIV-positive patients impacts the quality of the touch ECG recordings.**

Patients with human immunodeficiency virus (HIV) are at higher risk for cardiac arrhythmias, which can be recorded by Kardia. However, quality of KardiaMobile ECG depends on the skin condition; drying of the skin is observed in HIV patients with lower CD4 count and as a side effect of applied pharmacotherapy. This study examined the quality of the KardiaMobile ECG signal in 263 Kenyan adults with different clinical stages of human immunodeficiency virus (HIV) infection. The recordings were made during routine check-ups at the outpatient clinics. The ECG was readable in 201 patients (76.4%) and unreadable in 62 (23.6%). The World Health Organization AIDS Clinical Staging (WACS) score > 1 was associated with OR 3.95 (95% CI 2.14-7.29, p < 0.0001) for acquiring an unreadable ECG. The authors conclude that KardiaMobile ECG accuracy is limited in HIV patients, but could be improved with moisturizing the skin before recording.

*Kaminski M, Prymas P, Konobrodzka A, Filberek P, Sibrecht G, Sierocki W, Osinska Z, Wykretowicz A, Lobodzinski S and Guzik P.*
*J Electrocardiol. 2019;55:87-90.*