iPhone® Helping Evaluate Atrial fibrillation Rhythm through Technology (iHEART) Study (NCT02731326)

IRB approval: August 15, 2020

Study Design

The iPhone® Helping Evaluate Atrial fibrillation Rhythm through Technology (iHEART) study is a single-center, prospective, randomized controlled trial (RCT) (**Figure 1**). The primary aims of the iHEART study are to: (1) Examine the efficacy of mHealth ECG technology (iHEART intervention) on the detection and treatment of recurrent AF as compared to usual cardiac care (control group); (2) Evaluate the quality-adjusted life-years (QALYs) in those in the iHEART intervention as compared to the control group between baseline and 6 months; (3) Determine the impact of behavior altering, motivational text messages on chronic cardiovascular conditions (e.g., hypertension, diabetes) and AF knowledge over 6 months. Participants are randomized to one of two groups: iHEART (intervention group) or usual care (control group). All participants enrolled will be followed for a period of 6 months. This study protocol adheres to the appropriate standards of reporting as stated in the Standard Protocol Items: Recommendations for Interventional Trials statement and facilitates the methodology of the Consolidated Standards of Reporting Trials statement for later dissemination of the results of the outlined RCT.

Study Population

Patients will be screened for eligibility (**Table 1**). Those who meet inclusion criteria will be approached for enrollment after the patient's provider agrees to the study protocol and is willing to receive and review ECG transmissions. The details of the study will be explained in English or Spanish, and patients will be given an opportunity to ask questions before signing informed consent. A copy of the consent form will be given to the patient.

Inclusion criteria will include documented AF that has been treated in the last 30 days resulting in the restoration of normal sinus rhythm. The operational definition of AF for this study will include the presence of AF captured by the AliveCor® Mobile ECG, a standard 12 lead ECG, Holter, or any other external recording mechanism that documents AF. Over a six-month period, those individuals with ≤ 7 days of AF will be considered paroxysmal, and those with greater than 7 days of continuous AF will be defined as persistent AF per the AHA/ACC/HRS guidelines. The main exclusion criteria for participants include documented permanent (chronic) AF, unwillingness to use technology and have one's clinical data collected over the study period, unwillingness to receive and read cardiovascular text messaging three times a week, and patients who have a documented medical history of cognitive impairment.

Data and Safety Monitoring

The study was approved by the Columbia University Medical Center Institutional Review Board. Participants provide written informed consent prior to enrollment and all data collection procedures are in accordance with the Health Information Portability and Accountability Act regulations.

Sample Size

A total of 300 participants with documented AF who are undergoing clinical treatment of their AF with electrical cardioversion, radiofrequency ablation and/or medical management to restore normal sinus rhythm will be enrolled. After a normal rhythm is restored, participants will be randomized to usual cardiac care (n= 150) or usual cardiac care plus the iHEART intervention (n= 150). The population will be recruited from the Columbia University Medical Center (CUMC) cardiac services and will include English and Spanish speaking participants.

Randomization
The randomization process will be performed by a random computer number generator in a one-to-one block allocation ratio. In order to achieve a balance of applicable participant characteristics in both the intervention and control groups, participants will be stratified based on age and gender.

Outcome assessments
Upon study entry, all relevant clinical data will be collected at baseline and monthly throughout six months via an electronic medical records system review. This will be used to capture and quantify cardiac outcomes in both groups. In addition, all outside medical records will be requested, and participants will be contacted monthly to capture any hospitalizations, cardiac events, or changes in therapy that may occur outside of our center and clinics. AF in the usual care group may be detected during routine follow-ups with providers, as well as during self-evaluations such as a pulse check initiated as a result of participant-reported symptoms or changes in health status. AF may also be captured by a 12-lead ECG, pulse check, or heart sound auscultation during an exam that reveals an irregular heart rhythm. Participants in the usual care group may seek medical evaluation by their providers because of a change in their health status or symptoms (shortness of breath, palpitations, fatigue), which may lead to further cardiac monitoring or testing (e.g., echocardiogram) that may reveal AF. This could include Holter monitoring (24 hour) or extended cardiac monitoring (7-30 days) that may document AF and be the basis for changes in treatments prescribed by their providers (e.g., medication changes or dosage adjustments, cardioversion). In the intervention group, AliveCor® Mobile ECG transmissions will be read daily to detect recurrence of AF or other arrhythmias. All results and any treatment changes due to mobile ECG findings will be recorded over the course of the study period.

All study participants will be asked to complete a series of questionnaires including the Atrial Fibrillation Knowledge Scale (AFKS), the Canadian Cardiovascular Society Severity in Atrial Fibrillation scale (CCS-SAF), the Atrial Fibrillation Effect on Quality of Life (AFEQT), the Control Attitudes Scale-Revised (CAS-R), the Morisky 4-item Self-Report Measure of Medication-Taking Behavior (MMAS-4), the Self-Efficacy for Appropriate Medication Use Scale (SEAMS), the Short Form Health Survey (SF-36 Quality of Life), European Questionnaire 5 Dimensions (EQ-5D), the Patient Health Questionnaire (PHQ-9), and the State Trait Anxiety Inventory (STAI). These measures will be administered to both the intervention and control groups at baseline prior to any procedures, such as a cardioversion or ablation, and again at the 6-month follow-up visit for the purpose of comparison.

Study Intervention
Participants randomized to the iHEART intervention will receive an iPhone® and cellular service plan with unlimited data/text messaging, the AliveCor® Mobile ECG, and Behavioral Altering Motivational (BAM) text messaging three times a week for six months. BAM is an in-house database that automatically sends one-way text messages to the intervention participant related to their AF, as well as two underlying cardiovascular risk factors of their choosing.

AliveCor™ Heart Monitor
The AliveCor® Mobile ECG, an FDA-approved smartphone technology, works through a free application, “Kardia.” It captures a highly sensitive (98%), specific (97%), and accurate (97%) single-lead ECG recording through two electrodes on the back of the smartphone[7]. When the application is opened, recording begins automatically when both electrodes make contact with skin (Figure 2). Transmissions are automatically uploaded to the study portal within the

AliveCor® “cloud”. All participants will receive in-person training on the use of the study equipment at enrollment. A return demonstration from the participant to the research coordinator will be required at baseline enrollment. This will include how to capture an ECG daily and in the setting of symptoms, as well as how to record any associated symptoms in the application.

All ECG images and any associated symptoms will be sent via WiFi or cellular network transmission to the AliveCor® cloud. A login will occur daily to the password-protected study database that will be stored on the AliveCor® cloud in order to review and interpret all ECG strips transmitted during the previous 24 hours. Any clinically significant arrhythmias, including AF or other arrhythmias, detected during the daily review of ECGs over the 6-month period will be immediately sent to the provider caring for the participant. The study team will ensure the provider has received the transmission, is aware of any ECG abnormalities, and will then be responsible for communicating such findings.

Smartphone

The study is innovative in its use of mHealth and widely available smartphone technology, which allows rapid two-way communication between patients and healthcare providers, rather than waiting for office or clinic visits that delay care. An FDA-approved smartphone technology is being used, the AliveCor® Mobile ECG to capture and send ECG data via WiFi or cellular network for immediate interpretation. Transmission of a normal ECG while a patient is experiencing a symptom with multiple underlying diagnoses impacts immediate triage and treatment of the symptom. The AliveCor® technology allows clinicians to correlate symptoms with heart rhythms.

Unlike previous ECG technology, the AliveCor® Mobile ECG is not worn, so it eliminates the need for adhesive ECG electrodes and skin patches placed on the chest and does not require complicated changing of leads by the subject. This is a significant improvement from previously available technology. The use of tailored cardiac behavior altering motivational (BAM) text messaging sent to an individual’s smartphone to improve AF awareness and knowledge, as well as self-management of pre-existing chronic cardiovascular conditions associated with AF will be simultaneously evaluated.

Behavior Altering Motivational (BAM) Text Messaging

BAM one-way text messages are sent to the intervention participant three times per week and pertain to their AF, as well as two underlying cardiovascular risk factors of the patient’s choosing (weight management, physical activity, hypertension, heart failure, diabetes, etc.). Starting on the day of enrollment, intervention participants will receive text messages every Wednesday related to AF management, as well as a message on Monday related to risk factor one and a message on Friday related to risk factor two. BAM text messages will be systematically selected from a bank of text messages developed through collaboration by the study team and an expert interdisciplinary panel from the American Heart Association. All messages are available in English and Spanish according to participant preference.

Control Group (Usual Care)

Participants randomized to usual care will continue their guideline-directed clinical management and follow-up as determined by their providers’ interpretation of the 2014 ACC/AHA/HRS Guideline for the Management of Patients with Atrial Fibrillation.

Study end-points

The primary endpoint is detection of recurrence of AF. Secondary endpoints include treatment changes as a result of early detection of AF recurrence, study questionnaire scores at baseline and six months, including QoL, QALYs, and improvement in cardiovascular measures (e.g., blood pressure, glucose levels) and AF knowledge from baseline to 6 months. Outcome assessors will be blinded to group allocation.

Statistical Analysis

We will define and calculate recurrent AF detection rate as the ratio of the number of recurrent AF episodes to the number of person-months of follow-ups. We will compare the difference in recurrent AF detection rate over the six-month study period between the control group and the iHEART intervention group. Analysis of the potential moderating effects of demographic factors (e.g., age, gender, etc.) as well as the difference between the groups will be performed using multivariate Poisson regression.

We will compare the time-to-treatment between the iHEART intervention group and the control group with the application of survival analysis methods. For those who are treated for recurrent AF, the time-to-treatment is the time from beginning of study to the time of treatment. Those who are not treated for recurrent AF will be censored at the end of the sixth month, or the time of death should a subject die before the sixth month. We will apply the Cox proportional hazard model to examine and test the difference in the time-to-treatment between the intervention group and control group, with the adjustment for other potential confounders (e.g., age, gender). QALYs are calculated as follows: for each month of life lived at an EQ-5D index of x, the QALYs will be x/12=0.0833x years. We will calculate QALYs during the 6-month study period for all participants by summarizing QALYs from baseline through sixth month. We will compare QALYs between the iHEART intervention group and the control group using a two-tailed independent sample t-test. To adjust for potential confounders (e.g., age, gender), multivariate linear regression models will be used. Additionally, we will compare change of quality of life (QoL) and symptoms of AF scores (AFEQT, AFKS, EQ5D and CCS-SAF scales, etc.) from baseline to 6 months between the two groups and between those with and without AF using linear mixed models (growth model).

Figure 1. Flowchart for Study Procedures

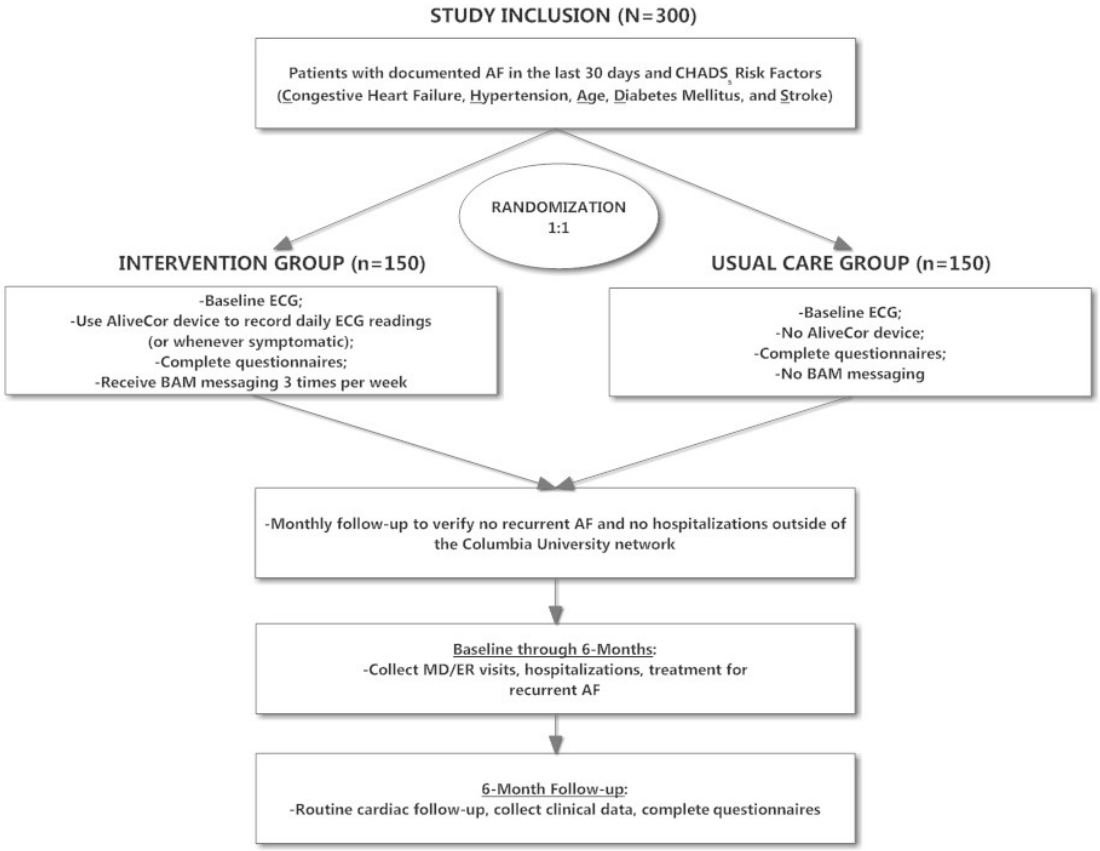

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria

- Males and females (English or Spanish speaking) age ≥ 18 years with a prior history of AF in the last 30 days that was treated and normal rhythm restored
- Already utilizes a smartphone prior to enrollment
- Ability to successfully use the AliveCor™ Heart Monitor, capture a baseline ECG, and transmit on the day of enrollment
- Demonstrated ability to receive and read text messages on the day of enrollment
- Willingness to complete the study questionnaires at baseline and 6 months

Exclusion Criteria

- Documented permanent (chronic) AF
- Unwillingness to have their clinical data collected over the study period
- Unwillingness to receive and read cardiovascular text messaging three times a week.