Study Protocol

Smartwatch Monitoring for Atrial Fibrillation After Stroke

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PULSEWATCH INVESTIGATOR STUDY PLAN

1) **Study Title**

Pulsewatch: Smartwatch Monitoring for Atrial Fibrillation After Stroke

2) **IRB Review History***

The application has never been submitted for review by an external IRB. NHLBI R01HL137734-01A1 from the NIH is funding this project.

3) **Principal Investigator**

Timothy Fitzgibbons, M.D. PhD.

4) **Objectives***

The objectives of this project are to develop a mobile device application with providers and patients that is both usable and accurate. The mobile device application will collect and extract RR interval data and use real-time algorithms for accurate detection of atrial fibrillation (AF) from mobile devices, including a smartwatch. Our central hypothesis is that a wrist-based wearable paired with a smartphone application will detect paroxysmal AF (pAF) with high sensitivity and specificity when compared to conventional cardiac monitors and will be found acceptable by stroke and cardiology patients and their providers. To accomplish this goal, our study will have two phases, a developmental phase and a testing phase. The overall objective will be accomplished by testing our central hypothesis after achieving the following specific aims:

Part I (Aim 1):

-To develop a robust and comprehensive mobile device application for analysis of heart rate interval series followed by real-time detection of paroxysmal AF and atrial flutter using our previously developed AF detection algorithm using smartwatch.

-To increase the accuracy and acceptability of our smartwatch-based pAF detection technology by involving older stroke patients and their providers in the design of the application.

Part II (Aims 2-3):

-To evaluate the performance of a smartwatch for pAF detection in stroke patients and/or to monitor patient who are at stroke risk with CHA_2DS_2-VASc score ≥ 3 by examining over 14 days the accuracy of pAF detection from Pulsewatch vs. a state-of-the-art cardiac monitoring device.

-To evaluate rates of adherence and factors associated with successful longer-term smartwatch use among up to 60 randomly selected stroke patients and/or who have a CHA_2DS_2-VASc score ≥ 3 enrolled in our 14-day validation study. These randomly selected participants will be asked to use the smartwatch/phone dyad for 30 days. We will explore the impact of smartwatch use over 30 days on patient-reported quality of life, anxiety, and self-efficacy compared up to 60 usual-care patients.

Learnings from these new objectives will support our future goal to extend monitoring periods to many months or years, surpassing the capabilities of event monitors.

5) **Background***

Atrial Fibrillation (AF) is the most common sustained dysrhythmia worldwide. Although new AF treatment strategies have emerged over the last decade, a major challenge facing clinicians and researchers is the paroxysmal, often short-lived, and frequently asymptomatic nature of AF. Given that paroxysmal and asymptomatic AF is a growing clinical and public health problem, better, less expensive, and more readily available AF detection technologies are needed. There

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is, therefore, a pressing need to develop methods for readily-accessible monitoring devices powered by accurate AF detection algorithm in order to improve patient care and reduce healthcare costs associated with treating these arrhythmias and their complications.

Novel technologies for AF detection have important clinical and research applications for AF screening and monitoring. As was emphasized by a recent National Heart, Lung and Blood Institute (NHLBI) expert panel, there is a pressing need to develop methods for accurate AF detection and easily accessible monitoring devices. To this end, we have previously developed a sensitive, real-time realizable algorithm for accurate AF detection using commercially available, clinically applicable electrocardiographic recordings. Our AF algorithm has been tested using the MIT-BIH AF database and Holter recordings, shown to be accurate, and is now commercially available in a new Holter monitor from Scottcare Corporation. We have also made improvements to the algorithm so that it can detect AF episode that is as short as 12 beats. Further, we have recently developed a software application to measure heart interval series, which can be used to detect AF in real time from pulse plethysmographic (PPG) devices. Given the ever-growing popularity of smartphones and smartwatches, our approach to AF detection using a mobile device will give patients as well as healthcare providers the opportunity to monitor these arrhythmias under a wide variety of conditions outside of the physician's office and outside of the patient's home.

Because our approach uses only standard smart device hardware (e.g., iPhone or Samsung watch), it is cost-effective, thereby leading to better acceptance and use by patients. Our mobile health for AF detection platform has the potential to markedly change the traditional delivery of healthcare, allowing for more frequent, rapid, and patient-directed AF detection. We will test the acceptability and accuracy of our smartwatch-app dyad using smart devices (a smartphone and smartwatch) to be collected from recruited stroke or transient ischemic attack survivors at risk for AF or patients with a CHA_2DS_2-VASc score of ≥ 3 at risk for a stroke or transient ischemic attack. We believe this research will result in rapid translation into innovative AF detection solutions, leading to more effective monitoring and diagnosis of these common arrhythmias. Finally, the proposed work has the potential to significantly reduce healthcare costs and enhance patient care by accurately and rapidly establishing the diagnosis of AF in at-risk groups, thereby providing clinicians with an opportunity to prevent secondary complications of these life-threatening arrhythmias.

Stroke survivors and individuals at high risk for incident stroke require cardiac monitoring for AF, the single greatest risk factor for stroke: Current American Stroke Association stroke management guidelines recommend: "For patients who have experienced an acute ischemic stroke or TIA with no other apparent cause, prolonged rhythm monitoring (≈7-14 days) for AF is reasonable" and recommended. In addition, patients with AF risk factors, including hypertension, diabetes mellitus, vascular disease, and prior episodes of AF or atrial flutter should be monitored for recurrence. This is because AF is the primary cause of ~15% of all strokes and AF recurrence and burden relate to stroke. Moreover, patients with AF, if not treated with anticoagulation therapies, tend to have larger strokes that lead to significant disability. One in 4 patients leaves the hospital without a cause of their stroke identified (cryptogenic strokes). Of the 200,000 American patients diagnosed with cryptogenic stroke yearly, 1 in 5 has paroxysmal AF identified if long-term post-discharge cardiac monitoring is used. Unfortunately, traditional in–hospital monitoring following stroke identifies AF in only ≈5% of cases and longer-term monitoring, although effective, is rarely used as it presently necessitates the implantation of an expensive invasive device (e.g., Medtronic LinQ monitor or pacemaker).

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Most existing smartphone apps can detect heart rate, but they cannot detect cardiac rhythm. AF detection algorithms used in cardiac devices and monitors are rudimentary and require the use of electrodes or invasive devices implanted underneath a patient's skin. AliveCor - a smartphone-based arrhythmia detection platform - pairs ECG electrodes with a smartphone running a proprietary app, enabling single-lead ECG and intermittent pAF monitoring. No existing algorithm for AF detection uses the combination of passive monitoring, pattern recognition, computational speed, and robust noise cancellation routines our solution employs. Additionally, although there are several smartwatches and wearables, including those from Apple, Philips, and Fitbit, that are capable of heart rate monitoring, the Samsung platform offers 3 unique advantages: 1) provides researchers with access to a secure data management system designed for research (Artikcloud), 2) allows for independent development of open-source applications, 3) has a smartwatch capable of out-of-the-box pulse monitoring.

In our new "Pulsewatch study," we propose to hone our existing smartphone app to work with a smartwatch in concert and in a manner that is accessible and usable by elders with, or at risk for, stroke with input from expert providers and patients. The app will use prompts to promote adherence to daily use of the smartwatch during the monitoring period and will prompt participants to perform a pulse check if they experience a symptom of AF.

6. Inclusion/Exclusion Criteria

Part I: Design/Development of the app-smartwatch dyad

Patient (and Caregiver) Focus Groups and Hack-a-thon (Part 1):
Inclusion: For patients: history of TIA or stroke, presenting at the UMass Memorial Medical Center (UMMMC) inpatient service or ambulatory clinic (neurology clinics and cardiovascular clinics included), age ≥ 50 years. For patient caregivers: history of caring for a family member or loved one with the inclusion criteria listed above in the last five years. For both patients and patient caregivers: able to sign informed consent, and willing to participate in a focus group and/or Hack-a-thon.

Exclusion: For both patients and patient caregivers: serious physical illness (e.g., unable to interact with a smart device, or communicate verbally or via written text) that would interfere with study participation, lacking capacity to sign informed consent, unable to read and write in English, plans to move from the area during the study period, unwilling to complete all study procedures, including attending a focus group and/or Hack-a-thon.

Provider Focus Groups and Hack-a-thon for Part 1:
Inclusion: medical provider (i.e., cardiology fellow or neurology resident, attending cardiologist, attending neurologist, stroke or cardiology nurse practitioner) at UMMMC, >3 years of experience providing care to stroke or TIA patients, willingness to complete informed consent, and willingness to participate in a focus group and/or Hack-a-thon.

Part II: Study of the app-smartwatch dyad

Inclusion: History of TIA or stroke, presenting to the inpatient UMMMC neurology service or ambulatory clinic (neurology clinic or cardiovascular medicine clinic/monitoring station), and/or has a CHA_2DS_2-VASc score ≥ 3, age ≥ 50 years, capable of signing an informed consent, willing

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and capable of using Pulsewatch (smartwatch and smartphone app) daily for up to 44 days and returning to UMMMC for up to two study visits.

A CHA_2DS_2-VASc score is a widely used and validated instrument recommended for use by cardiologists to determine stroke risk in atrial fibrillation patients. CHA_2DS_2-VASc score relates to stroke risk among individuals with AF and those free from a known diagnosis of AF. Using a CHA_2DS_2-VASc score as an inclusion criterion during screening for possible subjects will enable the study to approach patients at high risk for stroke who could benefit from continuous monitoring.

Exclusion: Major contraindication to anticoagulation treatment (i.e., major hemorrhagic stroke). Plans to move out of the area over the 44-day follow-up period. Unable to read or speak English. Unable to sign consent. Unable or unwilling to return for potential study visits (up to two over a 44-day study period). Patients with known allergies or hypersensitivities to medical grade hydrocolloid adhesives or hydrogel. Patients with life threating arrythmias who require in patient monitoring for immediate analysis. Patient with implantable pacemaker as paced beats interfere with the ECG reading.

Major contraindication to anticoagulation treatment is an exclusion due to the goal of this study, which is to help prevent secondary stroke; anticoagulation is a mainstay treatment for these patients. Therefore, if patients are unable to receive anticoagulation treatment, they are not in the ideal target population for this study.

Special Populations:
- Adults unable to consent - Will not be recruited for this study.
- Individuals who are not yet adults - Will not be recruited for this study.
- Pregnant women - Will not be recruited for this study.
- Prisoners - Will not be recruited for this study

If we struggle to enroll a sufficient number of participants using the campus and clinics outlined above, we will recruit at the stroke treatment centers or cardiology clinics at UMass Memorial - Health Alliance Hospital in Leominster, MA, and at UMass Memorial - Marlborough Hospital in Marlborough, MA. The inclusion/exclusion criteria will otherwise remain the same.

7. Study-Wide Number of Subjects*

Not a multi-site study.

8. Study-Wide Recruitment Methods*

Not a multi-site study

9. Study Timelines*

The first year to 1.5 years of the study will be focused on achieving Aim I (**Part I – design of the application**). Focus groups will be scheduled on a rolling basis over Year 1 and will be strongly influenced by the coordinator and room availability, as well as participant preference. The Hack-

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a-thon will also be scheduled at or around the end of Year 1 of the study (Spring 2019). Participants will be advised of when the event will be held.

Enrollment for Aims 2-3 (**Part II**) will begin in Year 2 and will run for 3 years. At enrollment, participants will be asked to use a cardiac monitor for 14 days and return for a study visit to evaluate device usability and accuracy. Thereafter, we will ask a randomly selected subsample to continue to use the device for an additional 30 days for a total of 44 days. We will hold additional semi-structured exit interviews for select Aim 2 intervention participants who used the Pulsewatch devices for 14 days.

The Pulsewatch study will be conducted over a 4-year period; see table below.

Study Year	1				2				3				4			
Quarter	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*	*1*	*2*	*3*	*4*
DEVELOPMENT/ENHANCEMENT (Aim 1)																
Formative patient focus groups & provider interviews	█	█														
Analysis of formative qualitative data		█	█	█												
"Hack-a-thon" Stakeholder-Agile Team Meeting																
Refine & Integrate AF, skin contact, & MNA algorithms	█	█	█	█												
EVALUATION/DEPLOYMENT (Aims 2 and 3)																
Smartwatch deployed in stroke population					█	█	█	█	█	█	█	█	█	█	█	█
Follow-up interviews/exit interview assessment of app					█	█	█	█	█	█	█	█	█	█	█	█
Data analysis														█	█	█

10. Study Endpoints*
Not only will we achieve our central hypothesis with our aims, but we will be able to complete the following endpoints as well:

Part I:
- Using focus groups, we will gain feedback on the:
  - App prototype and system as a whole
  - Role of caregivers in technology use
  - Barriers and facilitators of use
  - Preferences and usability of features
  - Enhancements to text and ambient messaging
  - Communication system design
  - Provider preferences regarding notification criteria and format
  - Potential implementation settings
  - Information display, graphical images, and message content

- Hack-a-thon endpoints will ensure developers:
  - Hear patient and provider needs
  - Obtain feedback on information display, graphical images, and message content

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Part II:

- Quantitative Endpoints: We will evaluate the performance of the application for detection of atrial fibrillation compared to a gold-standard ECG monitor. We will also evaluate adherence to the system and factors associated with adherence.
- Qualitative Interview Endpoint: Impact of app use on quality of life, anxiety, and self-activation (using our questionnaire at baseline, at the 14-day follow-up, and the 44-day follow-up). This information will be obtained from study questionnaires administered at enrollment, at the end of Aim 2 at 14 days post-enrollment, and after study completion 44 days post-enrollment, as well as from exit interviews convened with up to 30 selected participants after they use the system.

11. Procedures Involved*

Focus groups (Part 1)

Focus groups will be used to help inform the app development and will include patients, patient caregivers, and provider participants. Focus groups with patients and patient caregivers will occur together, and provider focus groups will be conducted separately. Focus groups will last for approximately 60 minutes. Qualitative data analysis will generate aggregated preferences and recommendations about smartphone application message components, user interface, reporting, alerts, and watch functions. Focus group/interview analyses will inform the Hack-a-thon and finalize the Pulsewatch design.

All participants (patients, caregivers, and providers) will be told by the study team that their feedback is appreciated and if they feel uncomfortable at any time of the focus group, they have the right to refuse to answer any question(s) and the right to opt-out of the study at any time.

Part I: Semi-structured and open-ended agendas for the focus groups and/or provider interviews have been written and are submitted as part of our application packet. Discussions will be audio-recorded and transcribed, protecting confidentiality by replacing participants' names with study IDs. Focus groups will begin with a broad description of the Pulsewatch system (including smartphone app and watch), its purpose, and general functionality. Each participant will be given a smartwatch and smartphone programmed with the Pulsewatch app and AliveCor ECG app and will be asked to use them during the focus group. In keeping with contemporary user-centric app design processes,[80,81] facilitators will interact with participants as they use the smartwatch and smartphone app. After users have time to wear the watch, perform an ECG, review their data, and use the annotator, we will invite them to ask open-ended questions to explore elements such as the following: the layout of the result and summary screens, including the graphical representation of heart rate and rhythm (e.g., bar graph, slider, stoplight, faces); alert and adherence prompts, including the number of acceptable prompts that Pulsewatch can deliver per day; opinions about personalized intervention messages (e.g., "Mr. Jones, you've not checked your ECG"); and their preferred timing.

Provider interviews will also explore what data outputs the clinicians consider ideal, along with when and how often they would want to receive them. We will conduct up to 6 focus groups with participants and up to 2 focus groups with providers as part of Part I over a 6-month period, then will pause to review the data. If there is strong consensus or saturation on key areas, we will stop.

Hack-a-thon (Part 1):

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The PI, Co-Is, 4 participants, 4 provider champions, and computer programmers and engineers from the University of Connecticut (UConn) will meet at the University of Massachusetts Medical School (UMMS) in a conference room to create the final Pulsewatch technology to be deployed in Aims 2 and 3. Modeled on "Hack-a-thons" in the software engineering industry, we will drive innovation by creating team synergy and accelerating product development. This meeting will likely occur in the Albert Sherman Center 7th floor conference room. Patient participants will receive parking vouchers and compensation. Providers will not be compensated. Light refreshments will be provided for all. The meeting will take place over a single day (8-hours) to accommodate the busy schedules of providers and participants. After the Hack-a-thon, the study team will meet to review and encode changes to the application.

The purpose of the Hack-a-thon meeting is to optimize the interactivity and usability of Pulsewatch, guided by information gleaned from focus groups. Using this format, end users (providers and patients) can suggest changes, and programmers will make modifications in real-time. Using a combination of focus groups and agile programming is an innovative as well as sound approach to designing apps. This event will be a critical aspect for Aims 2 and 3 to help develop the interface and management of the app for patients to use. At the Hack-a-thon, participants will be asked to use a prototype of the Pulsewatch app and the system, and then provide feedback on what they think of the system. Programmers will make modifications to the application in real time. While programmers are making those modifications, participants may take a break during the Hack-a-thon, and then come back at a later time during the event to see the final product.

The individuals who will be invited to this Hack-a-thon event will be participants and providers from the focus groups. At the focus groups, we will provide a fact sheet about the day-long Hack-a-thon and a contact sheet for people who may be interested in being invited. We will explain that they may accept or decline the invitation. (Please see Fact Sheet: Patient Hack-a-thon in our eIRB submission). Study staff will follow-up with interested participants and providers by telephone or email. Participants will have the option to opt-out or confirm their attendance at the Hack-a-thon.

Part II, Trial Phase- The trial phase of the study will occur after the design and development of the Pulsewatch system (app and watch algorithms) is complete (Part I). For Aim 2 of Part II, participants will be randomized into either the intervention or control arm of the study. The Aim 2 control participants will wear a gold standard cardiac monitor patch (two patches over the 14-days) but will not be offered use of the Pulsewatch system. Please view visual Diagram 1a for an overview of the 14-day participant process.
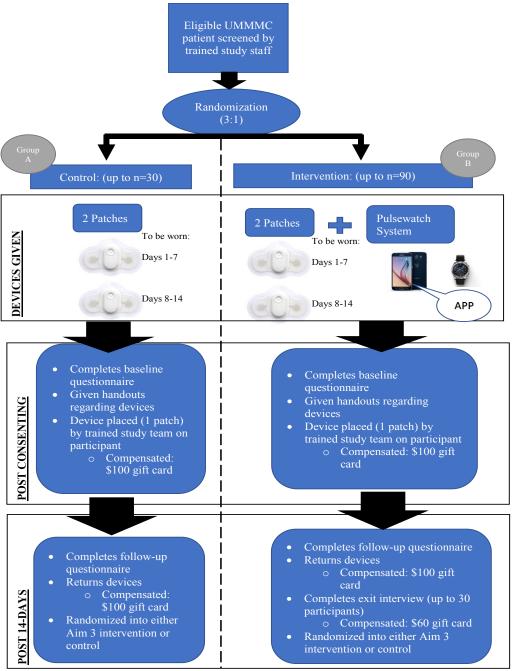
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Diagram 1a. Participant process of trial phase: Group names are corresponding to the Part II Consent V1.2 form submitted in eIRB.

Part II:

At baseline, participants in the Aim 2 control group (up to n=30) will be given two gold-standard Cardiac Insight Cardea Solo patch monitors. Each patch will run for 7-days to automatically monitor for and capture irregular heartbeat data. This patch goes right over a participant's heart on their skin. This patch will allow participants to go home with a continuous AF monitoring method without the hassle of carrying around a bulky Holter device. Our PI has already worked with similar devices in the past and has built a relationship with the study team to ensure proper care and transmission of the data. Trained study staff will place the patch on the participant at
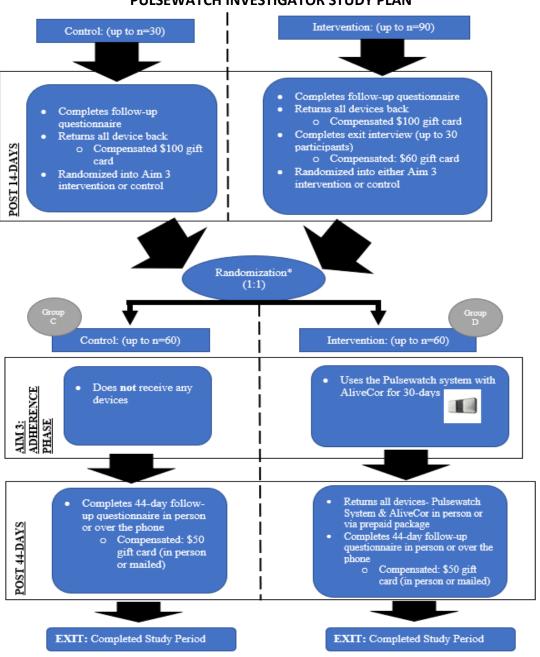
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the baseline visit. There is little risk to the participant from this device, which is widely used technology. The major risk with this device is participant discomfort or skin irritation. Participants will be given a number to contact in the event they have discomfort in the 14 days of using the device. Participants will be given a handout with instructions and care tips for the patch (see Device Handout in eIRB). Only certain sections of this handout will be given to participants depending on which arm of the trial they are assigned to. Aim 2 control participants will be asked to remove the first patch at the end of day 7 and replace it with the second provided patch and wear it for the next 7 days. They will be asked to return both patches at their follow-up visit (approximately 14 days). At their study visit, the participants will be asked to complete an exam and questionnaire that includes standardized scales. Aim 2 control participants will be compensated for their time and effort, as outlined above. The device will be read by a study physician blinded to intervention/control status. Abnormal findings on the monitoring patch, in either the intervention or control groups, will result in notification to the participant's treating physician.

All participants will be given a Device Handout regarding instruction for the appropriate devices they are given. In addition, the study team will review with each participant all instructions regarding how the Cardiac Insight patch functions and the participant's responsibility. The participant will also go home with information regarding the patches (see in eIRB, Cardea Solo Quick start guide- this will be added the Device handout). The study team, specifically the PI, may need to contact participants directly about their results. This will be disclosed in the informed consent form that participants sign.

The Aim 2 intervention participants (up to n=90) will be asked to use the same gold-standard Cardiac Insight patch monitor device for 14 days as the control group described above. Aim 2 intervention participants will also be given a Samsung smartwatch and a Galaxy smartphone. The Samsung smartwatch and Galaxy smartphone are standard devices that are sold commercially and will be labeled, nonetheless, as research devices. If the participant has a smartphone that is compatible to our Pulsewatch app, then we will download the app onto the participant's smartphone.

The Aim 2 intervention group (up to n=90) will be asked to self-monitor using the Pulsewatch system for at least 9 hours daily for 14 days. The intervention system is designed to be minimally intrusive. Participants will be asked to return all study devices (2 Cardiac Insight patches, Samsung smartwatch, and Galaxy smartphone) at the end of their 14 days of use at the follow-up study visit. Participants will be asked to complete a questionnaire at this follow-up study visit and will be compensated.

At enrollment in Part II, all study participants will be informed of the possibility that they may be randomly selected at the completion of their 14-day monitoring period to use the Pulsewatch system for up to 30 days. We chose to assign a larger proportion of participants to the Aim 2 intervention group because the primary analyses for Aims 2 and 3 are focused on Pulsewatch users.

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Control: (up to n=30)

Intervention: (up to n=90)

POST 14-DAYS
- Completes follow-up questionnaire
- Returns all device back
  - Compensated $100 gift card
- Randomized into Aim 3 intervention or control

- Completes follow-up questionnaire
- Returns all devices back
  - Compensated $100 gift card
- Completes exit interview (up to 30 participants)
  - Compensated: $60 gift card
- Randomized into either Aim 3 intervention or control

Randomization*
(1:1)

Group C

Group D

Control: (up to n=60)

Intervention: (up to n=60)

AIM 3: ADHERENCE PHASE
- Does **not** receive any devices

- Uses the Pulsewatch system with AliveCor for 30-days

POST 44-DAYS
- Completes 44-day follow-up questionnaire in person or over the phone
  - Compensated: $50 gift card (in person or mailed)

- Returns all devices- Pulsewatch System & AliveCor in person or via prepaid package
- Completes 44-day follow-up questionnaire in person or over the phone
  - Compensated: $50 gift card (in person or mailed)

EXIT: Completed Study Period

EXIT: Completed Study Period

Diagram 1b. Participant process of Part II, trial phase. This diagram outlines what the participant process is after 14 days and after 44 days. Group names are corresponding to the Part II Consent V1.2 form submitted in eIRB. Please note: for this "Randomization*" we would like to ask permission from the IRB for an adaptive plan; refer to section 13 Data Analysis and Management, sub section AF Detection Analysis for this plan. We have provided further details about this process below.

To accomplish Aim 2, we will examine the performance of Pulsewatch monitoring compared to conventional cardiac monitoring for pAF detection (accuracy of detection). We will also explore the participant factors (e.g., hearing or cognitive impairment) associated with app performance.
   By enrolling patients from both inpatient and outpatient clinical settings, we will be able to recruit patients who have stroke/TIA and/or who are at risk for stroke (deemed to have a

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CHA_2DS_2-VASc score $\geq$3). At the end at 14 days, if less than 5% of participants have AF based on the gold-standard Cardiac Insight patch, then we would like to ask participants to extend the use of their monitors for further monitoring. (See Section 13, Data Analysis and Management, AF Detection Analysis.)

To accomplish Aim 3, we will randomly select 60 participants from both the intervention group and the control group of Aim 2 at the end of the 14 days and ask them to continue using, or begin using, the Pulsewatch system to upload their pulse recordings. We will also provide participants randomized to the Aim 3 intervention group with a gold standard AliveCor Kardia mobile ECG device to use if they wish to verify their pulse reading from the smartwatch. We will also examine factors (e.g., vision) participants report related to their adherence to using the Pulsewatch system. The 60 participants randomly selected to the Aim 3 control group will not use any devices during this time.

Part II Exit interviews: We will use exit interviews for Part II Aim 2 intervention trial participants to identify 'what worked' and 'what didn't work'. The exit interviews will be in addition to the questionnaire and will take place at the same study visit depending on the participants schedule. We will also solicit feedback on the Interactivity Manager and Annotation Panels, features that will be developed too late in Aim 1 to be fully explored by Aim 1 focus groups. We will invite up to 30 Aim 2 intervention participants to complete an exit interview. Exit interviews will happen after the participant's 14-day study visit. These exit interviews will be important for usability data collection and overall feedback from the participants. Each exit interview will last for approximately 30 minutes. Semi-structured tentative and open-ended agendas have been written and submitted to the IRB as part of our packet (see in eIRB, Exit Interview Usability Script V1.0). Discussions will be audio-recorded and transcribed, protecting confidentiality by replacing participants' names with study IDs. Consent for interviews and taping will be part of the study consent.

Questionnaire-
Part II (only):
At enrollment and at their 14-day follow-up study visits, all Part 2 participants will complete a questionnaire that includes standardized scales to assess quality of life (QoL), depression, anxiety, and self-activation. Questionnaires will take approximately 45 minutes to complete. If a participant does not return for a follow-up study visit or is unable to complete an in-person questionnaire assessment, then a phone call will be made to the participant to see if they are willing to complete the questionnaire via a phone assessment. These participants will still need to return their devices to receive compensation. We will permit phone calls and assist with return by mail on a case-by-case basis.

We will compare changes from baseline to the 14-day follow-up in these measures between the Aim 2 intervention (n=90) and Aim 2 control (n=30) groups.

At the end of each participant's 44-day enrollment, they will complete a questionnaire either over the phone or in person, whichever is easier for the participant, to assess QoL, anxiety, and self-activation. This questionnaire will take approximately 20 minutes to complete. Participants who were not randomly chosen to use the Pulsewatch system for 30 days (Aim 3 control group) will receive compensation upon completion of the 44-day follow-up questionnaire. Participants who were randomly chosen to use the Pulsewatch system for 30 days (Aim 3 intervention group) will receive compensation upon completion of the 44-day follow-up questionnaire and return of their devices.

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We will compare changes from the 14-day follow-up to the 44-day follow-up in these measures between the Aim 3 intervention (n=60) and Aim 3 control (n=60) groups.

We will create a short-form questionnaire assessment in the event that a participant is unable to complete the full questionnaire. The only difference between the full assessment and short form is that the short form will contain only outcome measurements for the questionnaire.
Here is an overview of the variables our questionnaires will be collecting. We have uploaded all of our questionnaires to eIRB.

Measurement	Questionnaire Tool	Outcome or Stratifier	Baseline Assessment (All Part II)	14-Days Follow-up Assessment (Control)	14-Days Follow-up Assessment (Intervention)	44-Days Follow-up Assessment (All Part II)
Physical assessments						
Vision	Questionnaire (4 items)	Stratifier	✓			
Hearing	Questionnaire (3 items)	Stratifier	✓			
Psychosocial measures						
Cognitive impairment	MoCA (30- items)	Stratifier	✓			
Social support	Social Support Scale (5 items)	Stratifier	✓			
	Lubben Social Network Scale (6 items)	Stratifier	✓			
Depressive symptoms	PHQ-9	Stratifier	✓			
Anxious symptoms	GAD-7	Outcome	✓	✓	✓	✓
Quality of life measures						
Physical and mental health	Health survey SF-12 (12 items)	Outcome	✓	✓	✓	✓
Patient activation	CHAI (10-items)	Outcome	✓	✓	✓	✓
Disease management self-efficacy	Stanford Chronic Disease Management Self-Efficacy Scales: Manage Disease in General Scale (5 items)	Outcome	✓	✓	✓	
	Stanford Chronic Disease Management Self-Efficacy Scales: Manage Symptoms Scale (5 items)	Outcome	✓	✓	✓	
Medications						
Medication adherence	Adherence to Refills and Medication Scale (ARMS) (12-items)	Outcome	✓	✓	✓	
Health Related Behavior						
Social history	Smoking and alcohol use	Stratifier	✓			
Other						
Interaction with provider	Perceived Efficacy in Patient – Physician interactions (PEPPI)	Stratifier	✓			
Technology use	Device ownership/internet access	Stratifier	✓			

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Usability Assessment	System usability scale, Investigator generated questions	Outcome			✓	
App usability assessment	Mobile Application Rating Scale (MARS) App Classification (11-items)	Outcome			✓	
Demographics	Social economic status, employment, race and ethnicity questions	Stratifier	✓			

Aims 2-3: Questionnaire will include the following domains-

Anxiety: Anxiety will be assessed using the Generalized Anxiety Disorder-7 scale (GAD-7),[86] a revised version of the anxiety module from the Patient Health Questionnaire, which consists of DSM-IV criteria for generalized anxiety disorder over the past 2 weeks.[87] The GAD-7 score ranges from 0-27 with scores of 5, 10 and 15 representing validated cut-points for mild, moderate and severe levels of anxiety symptoms, with a score ≥10 having high sensitivity (0.89) and specificity (0.82) for psychiatrist diagnosed anxiety disorder and correlates significantly with health-related QoL. [86][OBJ]

Physical and mental health: The SF-12 is a short form health survey to assess health related quality of life, this validated instrument domains include general health questions and mental health related questions.[116] Scores range from 0 to 100, where higher scores indicate higher level of health.

Patient Activation: Patient activation refers to a patient's ability and willingness to manage their health Consumer health activation index (CHAI) is a 10-item scale. Scores range from 10 to 60 the higher the score the higher the activation the patient has for self-management of their condition. This is a validated questionnaire instrument.

Cognitive function: The Montreal Cognitive Assessment Battery (MoCA)[94] is a 10-minute, 30-item screening tool designed to assist physicians in detecting mild cognitive impairment. MoCA correlates well (.89) with the widely used Mini Mental State Exam,[95] but outperforms it in the detection of mild cognitive impairment (CI).[94,96] The MoCA score can be used to examine a magnitude of change over time and offers validated, education-adjusted cut-points for mild CI and dementia..

Social Support: We will use a 5-item modified Social Support Scale and the 6-item Luben Social Network Scale.[99,100] Together these measures assess breadth (e.g., help with activities) and depth (e.g., network size) of the participant's social support.

Depressive Symptoms: We will use the 9-item version of the Patient Health Questionnaire (PHQ-9),[101] the depression module from the Patient Health Questionnaire,[87] which can yield both a provisional diagnosis of depression and a severity score that are associated with functional status, disability days and healthcare utilization.[102] The PHQ-9 consists of the 9 criteria upon which DSM-IV depressive disorders are based. Using a cut-point of ≥10 (range = 0-27), the PHQ-9 has high sensitivity (.88) and specificity (.88) for detecting major depression among patients with CVD.[88,104] Study staff will follow UMass Extreme Emotional Distress protocol approved by the IRB in the event that a patient indicates suicidal thoughts.

Vision: We will test vision using a Snellen eye chart. Participants will also be asked the question, 'How much does your vision interfere with your activities?' based on a 4-point Likert scale from 'not at all' to 'a lot'.

Hearing: We will use the Whisper test where participants are asked to repeat back numbers whispered into their ear.[105,106] Impairment is defined as hearing ≤6 of 12 numbers. We will complement objective hearing assessments with subjective self-reported responses to the question: 'How much does your hearing interfere with your activities?'

Disease Management Self-Efficacy: Self-efficacy for disease management is associated with engagement in health behaviors and with improved medication adherence[107,108]The General Disease Management scale is a 5-item scale assessing confidence in disease self-management (scores 0-50, higher scores = greater confidence). The Symptom Management scale is a 5-item scale assessing confidence in managing chronic disease symptoms (items tailored to sample).

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Medication Adherence: Medication adherence will be measured using the 12-item Adherence to Refills and Medications Scale (ARMS), a well-validated measure of patient-reported adherence.[110] ARMS scores range from 1-4 (higher scores=poorer adherence).

Social history: Social and behavioral factors such as smoking and alcohol use are related to strokes and cardiovascular conditions. Given that the goal of this study is to prevent recurring strokes in this patient population, we believe it is necessary to obtain this information from participants.

App usability: Mobile Application Rating Scale (MARS) App Classification (11-items) these questions will help us capture the participants experience with the application.

Deployment of devices/app-

Part I: Participants will use the Pulsewatch System prototype version of the app (AFExam), a smartphone, and a smartwatch during focus groups or a Hack-a-thon to provide feedback for further development of the app, and to enhance the deployment of the system in Part II of the study.

Part II: We will provide up to 120 randomly selected participants with an Android smartphone if they do not own a compatible phone. The smartphone will be active – meaning we will pay for a standard cellular data/voice/text plan for the duration of the study period. The smartphone will be preloaded with a Samsung application to enable communication with the smartwatch, the study software application, the AliveCor Kardia application (used in Aim 3), the participant, and the study team. Participants who are selected for the intervention arm of Aim 3 will be given the AliveCor Kardia application, which is an FDA-approved, commercially available, single-lead ECG recording device that communicates with the smartphone. Participants will also be provided with a smartwatch and a handout outlining how to use the devices (see in eIRB, Device Handout). We will ask participants to wear the smartwatch day and night for 14 days, removing it only to charge each morning or during a shower. The Pulsewatch app interface will allow participants to enter into the app symptoms they may feeling.

We have selected the Galaxy Android smartphone because it can interface seamlessly with the Samsung smartwatch. If participants have compatible phones they want to use for the study, we will download the Pulsewatch and AliveCor apps onto their phones, and we will pair their phones with the Samsung study watch. We will also provide compensation to participants when they return the smartphone and watch to study staff after completing the study. Participants will be encouraged to call study staff with any problems encountered when using Pulsewatch during the 14-day monitoring period.

Participants will also have a cardiac patch placed on their chest at enrollment. This monitor will serve as a gold-standard comparator in our study and is a diagnostic-grade, FDA-approved, and fully regulated medical device manufactured by Cardiac Insight. The gold-standard cardiac patch will be placed onto participants by trained study staff at enrollment. Participants will be instructed to call the study team if they have any problems with the monitor.

Research staff (RA or study coordinator) will provide enrolled participants with detailed instructions about the operations and proper usage of the Pulsewatch smartwatch, smartphone

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apps (including the Pulsewatch app and AliveCor app), ECG, and 14-day monitor. A checklist and a YouTube video may be made available to participants to remind them of how to charge, wear, and perform ECG self-checks using the smartwatch and phone app. Participants (including all control and intervention participants) will return smartphones and watches and/or 14-day monitors after their study visit at 14 days. For Aim 2 intervention participants, pulse and ECG data from the smartwatch and annotations/adherence data from smartphones will be uploaded by study staff after the 14-day visit to the secure cloud server. Aim 2 control participants will be provided instructions on the gold-standard Cardiac Insight patches. Study staff will be available via telephone to answer any questions participants have with using the smartwatch and smartphone, charging the battery, and uploading data throughout the 14-day trial period as needed. The 60 randomly selected participants, who were consented at baseline to participate in this aim will receive additional training at their 14-day study visit, taught on how to use the AliveCor Kardia mobile device and will use the Pulsewatch smartwatch and smartphone for an additional 30 days. Participants in Aim 3's intervention group will be asked to upload pulse and ECG data from AliveCor if they would like to do a self-check after receiving the watch notification. The secure server architecture used by Samsung minimizes the potential for loss of health information and is similar to one used in our prior work.

<u>COVID-19 Modified Study Procedures:</u>
During COVID-19 restrictions, we will enroll participants over the phone. To do this, we will mail patients a COVID-19 specific patient invitation letter and the COVID-19 specific informed consent form 7-14 days prior to their scheduled clinic appointment. If the patient has not called and opted out of the study, we will call the patient the day before their scheduled appointment to assess interest. If the patient is interested in participating in the study, we will review the COVID-19 specific informed consent form, which includes a HIPAA authorization, in which we replace the wet signature that was originally obtained with an acknowledgement of the study details, risks, benefits, and the acknowledgement to disclose protected health information through the process of agreeing to participate in the study.

Once the participant has agreed to participate, we will then randomize the participant into either the intervention or control group for Aim 2. After the participant has been randomized, and we know what combination of devices they will be receiving, we will then mail the participant their specific devices with the correct device handouts that we would normally give in-person.

Upon receiving the package, a phone call will be conducted with a study team member in order to complete the baseline questionnaire and train the participant on their respective devices. Each participant will be walked through how to place their Cardiac Insight patch. If the participant so wishes, we can also conduct this study visit over a teleconferencing system, like Zoom. Before completion of the study visit, the study team member will arrange the date and time for the participant's 14-day follow-up visit, which will happen virtually. Our normal study protocol remains the same for the participant during this Aim 2 period. After this baseline visit is complete, we will mail the participant their $100 gift card.

On the day of the participant's scheduled 14-day follow-up visit, a study team member will call the participant and complete the 14-day follow-up questionnaire. Upon completion of the questionnaire, the participant will be randomized into an Aim 3 arm. If the participant is randomized into the control arm for Aim 3, we will ask the participant to mail back all of their Pulsewatch devices via a prepaid package. We will then mail the participant their $100 gift card. Our normal study protocol will be followed for the rest of these participants study period, which includes conducting a questionnaire over the phone 30 days later and mailing their $50 gift card.

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For participants randomized into the Aim 3 intervention arm, we will ask them to mail back their Cardiac Insight patches via a prepaid package. If the participant was in Aim 2 control and is now in Aim 3 intervention, we will mail them the Pulsewatch System and the AliveCor Kardia Mobile device. We will also mail them their $100 gift card. If the participant was in Aim 2 intervention and is now in Aim 3 intervention, we will mail them the AliveCor Kardia Mobile device and their $100 gift card. Upon receiving their devices, a study team member will conduct a phone call, or a Zoom call, with the participant to train them on their new devices. Our normal study protocol will be followed for the rest of these participants study period, which includes conducting a questionnaire over the phone 30 days later, mailing devices back via a prepaid box, and mailing the participant their $50 gift card.

For participants who have agreed to complete an exit interview, the interview will take place over the phone upon completion of the participant's 14-day follow-up study visit. The fact sheet for this exit interview will be explained to the participant prior to completing the exit interview. We will include this fact sheet in the package we send to participants before completing their baseline interview, so the participant can have it to reference. If the participant misplaces the fact sheet, we will mail it to them again.

12. Data and Specimen Banking*

Any data collected by this study may be used for future research. The PI or another approved member of the study team will determine who is allowed to access this data. It may include collaborators or entities external to UMMS.

ECG and pulse data from all smartphones and watches will be sent to a secure server managed by UConn's information technology services. The data will not be transmitted with participant name, DOB, or MRN. The Pulsewatch system will upload data when prompted by participants during Aim 3 or by a trained study staff member during the 14-day study visit. This data management system is encrypted. Data storage capacity on the Pulsewatch is nearly 14 days at the above noted sampling rates for PPG. Thus, pulse data will be safely stored and will be retrieved when the Pulsewatch is returned for Aim 2 after 14 days. All ECG and pulse data will be password protected and encrypted so that only research personnel can access stored data. Once smartwatches are returned, we will have the study coordinator "push" pulse and ECG data from the smartwatch and adherence/annotation data from the smartphone. If the smartphone is lost, however, we will extract the latest adherence and annotation data and then remotely delete the File Store. This protocol protects participants' confidentiality in addition to the data encryption and password protection. We have the programming expertise necessary to carry out these operations.

The AliveCor Kardia platform used to store ECG data from the AliveCor ECG system is a HIPAA-compliant, HL7 compliant service used by the Cleveland Clinic, UMMMC, and other services for clinical grade ECG storage and analysis. This protocol protects participants' confidentiality in addition to the robust means of data encryption and password protection. We will upload only ECGs linked to participant IDs. ECGs will be reviewed within 3 days of uploading by study staff. The platform will be checked daily on normal business days to observe any tracking completed by participants.

The Cardiac Insight patch data will be transferred to the PI via a summary report for review. This will be reviewed and stored in a locked, secure space. The data from the Cardiac Insight

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patches will be de-identified, containing only a participant study ID #. The raw data and digital summary reports will be stored on secure UMMS HIPPAA-compliant servers. Similar to the watch pulse and ECG data, the Cardiac Insight ECG data will also be uploaded to the same secure server managed by UConn's information technology services. The data will not be transmitted with participant name, DOB, or MRN.

Focus group and exit interview recordings, Hack-a-thon materials, and questionnaires (baseline and follow-up) will be stored in a digital format (using the nVivo system for audio recordings and the RedCAP system for questionnaire data) as well as on paper. All digital data will be password protected and encrypted so that only research personnel can access stored data using the RedCAP system. All paper questionnaires, consents, etc., will be stored in a locked, secure UMMS space.

Screening documents to identify patients to approach for the study will be stored in the Redcap File Repository and deleted when we have finished enrolling participants. We will destroy the master file of the identifiers of the enrolled participants 5 years after all data analysis is completed. De-identified data coded with the Subject ID of participants will be retained indefinitely to be reviewed for future publication use. Any paper or physical copies will be stored in locked spaces. Audio recordings will be deleted after a research staff member has completed the transcription process and quality check process. Transcription will be de-identified, protecting confidentiality by replacing participants' names with study IDs. The master file that links the participant to the identifiable information will be in a secure database (RedCAP) and only limited research personnel will have access to this information to help protect participants' personal information. Please see our HIPAA Waiver, which is in eIRB.

13. Data analysis and Management*

Overall Data Management:

Each participant enrolled in this study will receive a participant ID to ensure that limited personal information of our participants is not accessed unnecessarily. Our study team, including the study PI, will meet with an independent monitor quarterly to ensure adequacy of human subject's protections, including participant privacy.

For all patient participants, sociodemographic, clinical, laboratory, and medical care information will be abstracted from records into a web-based centralized data repository, which was developed and is being used in SAGE-AF. As in our prior studies,[73] we will abstract data on history of TIA/stroke, stroke severity, and clinical variables necessary to derive the CHA_2DS_2VASc (stroke) risk scores.[74] We will abstract use of medications (e.g., beta-blockers) known to influence vulnerability to AF.[74] Data from health records will be imported to our data repository as in the SAGE-AF study.[73]

Data streams will be merged into the Pulsewatch master database that will include audio and digital information from focus groups, exit interviews, and questionnaires. AF rhythm status will be determined based on ECG data, and summary reports will be stored in the Pulsewatch master database utilizing our data system architecture similar to that used in SAGE-AF. Data acquisition and quality control processes will be the same. Unique, password-protected, registry websites assure consistent staff identification at entry. A data collection manual with coding

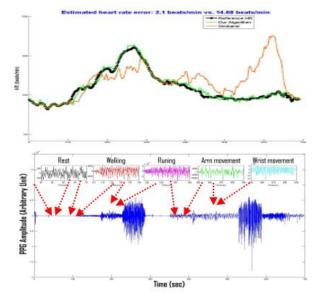**PULSEWATCH INVESTIGATOR STUDY PLAN**

instructions for each data item in SAGE-AF has been developed and will be updated for Pulsewatch.

Questionnaires will be available in a digital format on password protected iPads (using the REDCap system) as well as on paper copies. All laptops, desktops, and iPads that we use in this study will meet the UMMS encryption policy. All digital data will be password protected and encrypted so that only research personnel can access stored data using the REDCap system. All paper questionnaires, consents, etc., will be stored in a locked secure UMMS space. ECGs will be sent to the AliveCor Kardia Pro platform, a secure provider ECG management system. The AliveCor Kardia Pro platform is a HIPAA-compliant, HL7 compliant service used by the Cleveland Clinic and other services for clinical grade ECG storage and analysis. This protocol protects participants' confidentiality in addition to the robust means of data encryption and password protection.

Cardiac Insight patches have a module chip inside the sensor that stores the data being collected over the 14-days. Participants will be asked to bring back both patches at the end of the 14-day monitoring period to collect those modules for data collection. A trained study staff will remove the modules and place them into the Cardiac insight smart cable to be uploaded to a UMass Medical School server. The module will be labeled with the participants ID # and stored in a locked cabinet. The report will be read by a blinded Cardiologist for review. Details about the Cardiac Insight system can be found in the FDA approved Letter in eIRB (K162503 Cardiac Insight FDA) for the IRB to review. Similar to the watch pulse and ECG data, the Cardiac Insight ECG data will be uploaded to the same secure server managed by UConn's information technology services. The data will not be transmitted with participant name, DOB, or MRN.

Smartwatch Data:

We will reduce the potential for false positive AF detection from corrupted (MNA) or low amplitude (poor contact) PPG data using two methods. First, the Pulsewatch app will send a message to participants to remain still and perform a 30-sec ECG self-check (wrist electrode, high accuracy) should they have an AF episode detected. The second approach involves the cancellation of cyclical frequencies, seen in accelerometer data, from the PPG signal. This approach was recently developed in our lab and should allow us to use segments such as shown.[23,24] We demonstrate this MN correction performance via a representative result from offline analysis of raw Samsung watch data.(Looking at the figure above, the top panel of shows the comparison of our MN correction algorithm (green line) on raw data vs. Samsung's own embedded motion artifact correction algorithm (brown line). The black line is the reference heart rate from a 5-lead ECG. The bottom panel shows the raw PPG data recorded from the Samsung watch, and note MN artifacts starting at 100 seconds. The data were recorded during treadmill exercise (first 300 seconds), followed by 30 seconds of cool down, as well as with arm movements (up and down and shaking) on the side of the smartwatch. Despite the severity of the MN artifact, the estimated heart rates calculated by our algorithm closely follow the reference (black line) heart

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rates. Thus, these 2 approaches can be effectively used to recover some data segments contaminated by MNA or by poor signal quality and correctly identify the presence or absence of AF. Once MN artifacts have been corrected, we will look at patterns to analyze pulse waveforms for AF detection, including discrimination of PVCs and PACs. The MNA and AF algorithms will be embedded using Samsung's Vobio API. Based on our pilot, we estimate 50% usable data during active periods and 90% during rest. The majority of the user's day will be at rest (sitting or sleeping), as older stroke patients typically perform limited exercise.

To fine tune and maximize the accuracy of our MNA algorithm, we will use data collected on AF subjects (Aims 2 and 3) using the Pulsewatch system. We will compare the performance of our MNA algorithm using the Pulsewatch signal to the simultaneous gold-standard Cardiac Insight patch. The data analysis and statistical evaluations will be similar to our recently published article on our MNA detection/reconstruction algorithm,[25,77] but will also involve calculation of absolute error of the estimated heart rate via our algorithm to the reference Holter ECG-derived heart rate. Moreover, we will calculate sensitivity, specificity and accuracy of AF detection using our algorithm when compared to Cardiac Insight patch data.

AF Detection Analysis:

Analysis for the study focus on the performance of daily wear of the Pulsewatch system for 9 hours compared to standard Cardiac Insight patch monitoring over the course of 14 days. We will examine the system's accuracy for pAF identification as well as estimation of AF burden. A participant will be classified as having pAF or not at the end of the 14-day monitoring period based on the gold standard monitor. Data from the Pulsewatch is divided into 30-second segments for analysis and a positive reading will be defined as AF being detected in at least 7 out of 10 continuous data windows (5 minutes). The total number of positive readings collected over 14 days from Pulsewatch will be used as the independent variable in a logistic regression to predict the binary outcome of pAF (yes vs. no). The area under the receiver operating characteristic (ROC) curve (AUC) will be calculated based on the results from the logistic regression to evaluate Pulsewatch performance for pAF screening. From the ROC curve, we can identify the cutoff point of total number of positive readings that produces the highest sensitivity and specificity combination.

    Preliminary data suggest that Pulsewatch will have sensitivity, specificity and AUC of at least .9 to detect pAF. Assuming [115].

    Similar analysis will be conducted using the % of positive readings among all readings collected from each participant as the independent variable. The 95% confidence intervals (CI) of the AUC will be calculated using formula given by Hanley and McNeil. We will then conduct exploratory analyses to examine whether characteristics affect watch performance over 14 days. For example, we will compare the area under 2 independent ROC curves of female vs. male participants (or vision impaired vs. not) using a chi-square test. At the end of 14-days we will review the data of 45 participants in Aim 2 intervention and see what % of participants have AF. If we see less than 5% of all participants using the devices have AF, we will have an adaptive protocol for analysis. We would ask participants to extend their use of the devices for an additional 14-days and continue to monitor the participants for potential AF cases. Their follow up assessment for participants in Aim 2 of Part II would be at the end of the 28 days if we take this approach.

Usability Analysis:

We also aim to examine whether participant characteristics (e.g., demographics, level of technology use, cognitive impairment, etc.) affect usability and adherence of the Pulsewatch system. Usability will be examined by semi-structured interviews, investigator generated

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questions regarding user experience, and the System Usability Scale (SUS), a validated instrument for perceived system usability. Investigator generated questions will have responses in a 5-point Likert-like scale, and ordinal regression will be used to evaluate participant characteristics that may be associated with more favorable responses regarding usability of the Pulsewatch system. The SUS score ranges between 10 and 100, and linear regression will be used to examine the participant level factors that are associated with higher SUS scores. Logistic regression will also be used to examine whether certain participant factors are associated with having a SUS score of over 68, the acceptable cut off being deemed as a highly usable system.

Adherence Analysis:

In Aim 3 of Part II of the study, adherence will be operationalized to determine whether pulse recordings were present on each day over the 30-day period. We will examine whether participant characteristics, e.g., sex, cognitive impairment, or stroke-related quality of life, affect the likelihood of adherence over the 1-month study period. We will use a mixed effects logistic regression model, including the participant as the random effect to capture the correlation among repeated measures from the same participant, using participant characteristics as the fixed effects, and a binary indicator of daily adherence as the dependent variable. We will also examine the adherence time-trend by including time (day) as a fixed effect in the model and participant as a random effect to estimate the slope of adherence over time. To examine whether the time trend varies by participant characteristics, we will include the interaction between characteristics and time in the model so that the slope of adherence over time can be estimated for each category of participant characteristic variables and be compared among the categories (e.g., pAF diagnosed vs. no pAF). Secondary analyses will examine rates of adherence to Pulsewatch ECG prompts and will compare Pulsewatch users to the usual care group with respect to stroke-related quality of life, anxiety, and self-activation. We will calculate the change score between baseline and 1 month as a dependent variable. First, a t-test will be used to compare 2 study groups on the change score. We will use a linear regression model, which will include group indicator (Pulsewatch users vs. usual care) as the independent variable and possible confounders (e.g., medication adherence and participant demographics) as covariates, to estimate adjusted group differences on the change scores.

14. Provisions to Monitor the Data to Ensure the Safety of Subject*

Please review the Data Safety Monitoring Plan (DSMP) in the eIRB for a detailed description regarding human subject's protection.

This plan recognizes the nature of Part II of this study as a clinical trial and this Part involves more intensive data safety monitoring, including involvement of an independent monitor, Dr. Steven Lubitz. The plan has been reviewed and approved by the Director of the Quantitative Methods Core, Dr. Bruce Barton, who has extensive expertise in the design and conduct of clinical trials.

As outlined in the DSMP, we will employ an adverse event reporting system (see DSMP Report template in eIRB) that will be reviewed by the PI and the independent data study monitor to ensure safety of all enrolled participants. However, we have provided an overview of our analysis and management plan herein. For any incidental findings, the PI will review the recording of the pulse/ECG data and make a clinical decision; if necessary, the PI then will

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contact the participant's treating physician to report the findings and recommend follow-up plans.   In the unlikely event of incidental findings during Part I, the PI will be contacted if he is not present.

All recruitment and training will be conducted by trained personnel who are certified according to our study protocols, which include training in procedures for recruitment in the clinical environment. Modeled on the PI's ongoing studies, medical record review protocol uses "gold standard" medical records and requires that each abstractor satisfactorily complete 10 practice cases before certification. We will have ongoing data quality control checks via audited interviews and medical records abstracted in duplicate for 5% random samples. If error rates are too high, we will retrain staff and increase quality control sampling until the rates decline to acceptable levels. We will continue our ongoing quality control measures with dynamic range and consistency checks, missing data surveillance, and error tracking.

All study participant Pulsewatch ECG recordings (both from the 14-day monitor and individual AliveCor ECGs) will be manually reviewed by trained study staff under the direction of the PI. Two readers, blinded to the determination of the automated rhythm analysis, will review ECG data and code sinus rhythm, AF, or other arrhythmias (e.g., premature atrial beats) using standard criteria.[6] In cases where there is disagreement with respect to rhythm, the PI will review the tracing to obtain consensus. ECG data will be reviewed within 3 days by a study cardiologist. If cases of AF are detected on manual review or if a participant calls the study hotline to report a new health concern, the research coordinator will notify the participant's primary healthcare provider, cardiologist or neurologist and assist in arranging a follow-up. Providers will be given the PI's contact information to arrange care or to speak with a cardiologist familiar with the Pulsewatch protocol.

All of the Cardiac Insight patch monitoring data will be de-identified using alpha-numeric study IDs. The ECG data from the cardiac monitor will be uploaded to a secure server (UMMS) and downloaded for interpretation. The ECG data from the cardiac monitor will also be uploaded to the secure UConn server and downloaded in order for UConn to compare their PPG data from the smartwatch to the ECG data from the cardiac monitor. Only Dr. Fitzgibbons and the UMass research staff will have access to the code linking the subjects to study IDs. The study cardiologists will review any arrhythmias on the cardiac monitoring device for accuracy. If any arrhythmias are detected, then Dr. Fitzgibbons will notify the participant's treating clinician.

We will report any issues to the UMMS IRB in accordance with the Investigator Manual and Prompt Reporting Requirements.

We will have independent data safety personnel who will evaluate the process of ECG review and reporting as well as any adverse events related or unrelated to study participation. Please see resource available section.

The PHQ-9 and GAD-7 in the questionnaire are the only instruments that require monitoring and a UMMMC Protocol plan has been submitted with this IRB application. Per our protocol, if study staff detect high PHQ-9 and/or GAD-7 scores, they will suggest that participants discuss their symptoms of depression and/or anxiety with their doctors and/or the trained personnel at the UMMMC Emergency Mental Health hotline (508-334-3562). Study staff will be fully trained to note that the checkbox on the cover page of each questionnaire will remind them to follow the extreme emotional distress protocol when warranted.

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15. Withdrawal of Subjects without their consent

Participants, including patients, caregivers and providers, will be able to withdraw from the study at any time. Participants will be withdrawn from the proposed study if they are unable or unwilling to wear the smartwatch and are found to meet exclusion criteria. At that point, they will be informed of why they are being removed from the study and given an opportunity to ask questions.

16. Risks to Subjects

No more than minimal physical risks will be involved with this study. First, use of a smartphone or smartwatch does not pose any significant health concerns. Use of a single-lead, FDA-approved, commercially available ECG device (AliveCor) does not require placing of electrodes on the human body and does not pose any physical risk. The Cardiac Insight monitor poses no more than minimal risk, but the monitor may cause skin irritation at the site of application. Prior to approaching patients, we will be screening to ensure that the patient does not have any contraindication to be using the Cardiac Insight patch as listed under exclusion criteria (see section 6). This poses no significant risk to participants since this is the standard device used in clinical practice.

Another potential but minimal risk to participants is feeling psychologically uncomfortable disclosing sensitive information (e.g., depressive symptoms) or performing geriatric assessments (e.g., assessments of cognitive function) while answering questions during the interview process at baseline/follow up visits. Depressive symptoms will be collected as part of the interview and there is the possibility that emotional distress or depression will be identified. There is no risk of extreme stress as a result of participants answering these questions. All study staff interacting with participants will be trained to detect when a participant is feeling uncomfortable and will re-iterate that the participant can stop an interview at any time and can refuse to answer any question for any reason.

Another risk to participants will be the possibility of a breach in confidentiality. However, we will try our best to protect participants' confidentiality to minimize the risk (see data safety plan). All participant data will be held behind secured firewalls at UMMS. As noted in Section 12, ECG and pulse data from all smartphones and watches, as well as ECG data from the Cardiac Insight cardiac monitors, will be sent to a secure server managed by UConn's information technology services. The data will not be transmitted with participant name, DOB, or MRN.

Access to databases will be restricted to only authorized personnel. We will utilize all electronic data capture procedures and, therefore, no paper records will be kept long-term. Any paper records (such as medical record information) that are needed for the study will be destroyed immediately following entry into electronic databases. All consent and other forms that are required to be kept will be kept in a locked file cabinet in locked study offices.

17. Potential direct benefit to subjects

There are no direct benefits to the subjects.

18. Vulnerable populations

We will not be targeting vulnerable populations; all participant must have capacity to be able to consent. Please see the protocol for determination process of capacity to consent.

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Providers may be seen as a vulnerable population and we will have a protocol in place for recruiting them to minimize the potential for undue influence. Please, refer to section 24. Local Recruitment Methods to review this protocol.

19. Multi-site research
NA. Not a multi-site study

20. COMMUNITY-BASED PARTICIPATORY RESEARCH*
NA. This study is not a community-based research.

21. SHARING OF RESEARCH RESULTS WITH SUBJECTS*
Study results will not be directly shared with participants unless a rhythm abnormality is diagnosed based on their AliveCor ECG or Cardiac Insight patch monitor results. See section 11. Procedures involved (Part II, specifically) for the protocol involving the PI having to contact a participant or participant's clinician about an abnormal rhythm when detected.

22. SETTING
Research assistants will enroll participants with a history of stroke and/or TIA from among those presenting for a clinic visit or to the inpatient service or who have a CHA_2DS_2-VASc score $\geq$ 3. Embedding this project in the UMMMC neurology and cardiology inpatient and ambulatory clinics will facilitate recruitment.[78] In the stroke clinic alone, four neurologists see over 500 patients with cryptogenic stroke/TIA yearly. Dr. Majaz Moonis (Co-I) has had high success conducting research within this clinic.

We will also enroll up to 10 UMMMC providers (half cardiologists or neurologists, half nurses/nurse practitioners) with experience treating patients with cryptogenic stroke who need AF monitoring.

We will be holding focus groups in a comfortable conference room at UMMS. Any questionnaires, exams, interviews or study appointments will be completed in a private, comfortable room in the UMMS Clinical Trials Center located in the ACC Building. If this center is not available, we will have another private and comfortable area for participants to complete all study protocols here at the UMMS University campus.

During COVID-19 restrictions, questionnaires and study appointments will be completed via a phone call or a secure teleconferencing system, like Zoom, whichever is more convenient for the participant.

23. RESOURCES AVAILABLE
The study will be led by investigators with extensive experience working with stroke and AF patients. All neurologists/cardiologists, and research coordinators/staff will ensure that regulatory paperwork, such as consent forms and patient confidentiality, are used appropriately.

All recruitment and training will be conducted by trained personnel who are certified according to our study protocols, which include procedures for recruiting study participants in the clinical environment. Modeled on the PI's ongoing studies, our medical records review protocol uses "gold standard" medical records review methods, and requires each abstractor to satisfactorily complete 10 practice cases before certification. We will have ongoing data quality control checks via audited interviews and medical records abstracted in duplicate for 5% random

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samples. If error rates are too high, we will retrain staff and increase quality control sampling until errors decline to an acceptable level. We will continue our ongoing quality control measures with dynamic range and consistency checks, missing data surveillance, and error tracking.

Rhythm diagnoses will be determined based on self-initiated or auto-triggered ECG tracings from the gold-standard Cardiac Insight patch monitor. Two readers, blinded to the determination of the automated rhythm analysis, will review all time-stamped monitor recordings and code sinus rhythm, AF, or other arrhythmias using standard criteria. In cases where there is disagreement between the 2 primary interpreting cardiologists with respect to rhythm, a 3rd physician will review the tracing to obtain consensus.

Personnel Resources are as follows:

- **The PI:** Will be responsible for the direct efforts of the research project and meeting with research coordinators/mangers weekly during the study period. In addition, the PI will adjudicate ECG recordings and, if arrhythmias are detected, will notify the participants' treating clinicians.

- **Co-I's:** Will provide study management, quality assurance, staff oversight, study progress, diagnostic adjudication, data presentation, and preparation of quarterly and annual progress reports. The Co-Is will be available after hours to support research coordinators.

- **Project Manager:** This individual will not be primarily responsible for study enrollment, but will instead take an administrative role and have prior experience managing research staff and overseeing day to day operations and enrollment activities of this research project. She will supervise study progress (enrollment, chart reviews, etc.), maintain records of such progress, and communicate any concerns with the Co-PI's. She will arrange regular meetings with the Co-PI's and the research staff.

- **Research Coordinators:** These individuals will be required to have at least an associate's degree and 6 months of either clinical research or patient care experience as they will be responsible for direct participant enrollment/consent and assisting with chart reviews. They will have completed their CITI certification. They will be trained by the PI's and/or project manager to learn the medical terminology, chart review methodologies, enrollment protocols, and how to interact with clinical staff. In addition, they will also be trained to enter clinical data into a custom REDCap database. The coordinators will be responsible for contacting any potential provider participants and recruiting them.

- **Biostatistician:** There is a budgeted position for a statistician to work on this project. This individual will be responsible for reviewing the study's data calculations and power calculations that are needed to achieve the goal of this study.

- **Research Staff/Research Assistants (RA):** We will develop a manual of operations (MOO) for this study and require that all staff are familiar with this study. We will train all staff on enrollment procedures and will observe 3 enrollments prior to having them work independently to approach patients. The RAs will also be responsible for assuring the proper protocol is followed for the audio recordings obtained in any focus group/interview.

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- **Educating Clinical staff:** The study protocol will be vetted with attending neurology/cardiology physicians and staff (residents, nurses, and MD faculty) in several ways. As part of our monthly faculty meetings, the PI will present the study to faculty and provide study updates and opportunities to ask questions.

- **Independent Data Monitor:** This person will be responsible for reviewing smartwatch adherence data. The monitor will be an independent party who is not from UMMS, who is classified as non-investigator personnel, and who is familiar with the data safety monitoring plan.

- **Engineers and app programmers:** Will be present at the Hack-a-thon event to work with patients and providers on implementing real time edits to the app as suggestions are mentioned throughout the event. The UConn team has ceded to UMass IRB in order to be able to participate in research activities with UMMMC patient participants.

If study staff who have primary affiliations outside of UMMS will interact with subjects or access private identifiable information about them, they will either obtain their own IRB approval or we will work with the UMMS IRB to establish a reliance agreement for UMMS to serve as the Reviewing IRB. Collaborators from UConn and Northeastern University have already completed this paperwork.

24. Local Recruitment Methods

Part I: Trained research assistants (RAs) will screen the UMMMC neurology and cardiology rosters for patients, then will send introductory letters to eligible patients who meet inclusion criteria and are free of any exclusion criteria. Letters of introduction to the study (Patient FG Invitation in eIRB submission) will be sent to eligible patients 5-7 days before their scheduled clinic visits with an opt-out phone number for patients who do not wish to be approached for study participation. Dr. Keaney, Chief, Cardiovascular Medicine, will sign this letter. RAs will approach patients in the UMMMC out-patient clinics. If patients are interested and deemed capable (using the capacity assessment), then they may be enrolled in the study by signing the IRB-approved informed consent form. Caregivers who accompany a loved one to clinic will also be approached for consent to participate in focus groups. Before approaching patients and their caregivers, RAs and study personnel will be trained on how to explain all of the study's components to potential participants.

We will give the Hack-a-thon Fact Sheet (see Fact Sheet: Patient and Provider Hack-a-thon in eIRB submission) to all focus group participants. We will also ask participants at the focus groups to fill out a form to indicate if they would like to be contacted about participating in the Hack-a-thon (see Hack-a-thon Contact Info sheet in our eIRB submission). A study staff member will call participants who indicate they are interested in participating in the Hack-a-thon, and to disclose that participants have the right to opt-out of this event.

Ten providers will be identified from the UMMMC neurology and cardiology groups for focus group or interview participation. We will approach physicians and advanced care nurses via email or telephone (see Provider email and telephone invitation script with this IRB submission). Providers will be given an IRB-approved Fact Sheet (in eIRB submission). The study coordinator, not the PI or Co-Is, will recruit providers affiliated with UMMMC to minimize the

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potential for undue influence. The study coordinator will explain to providers that their decision to participate or to not participate in the study will not affect their employment status at UMMMC.

Part II: We will use a rolling enrollment and randomization design with a goal of 90 participants completing the Aim 2 intervention and 30 participants completing the Aim 2 control group procedures (up to n=120 in the trial). To enroll patients who are admitted to UMMMC, RAs with access to the UMMMC neurology inpatient roster and cardiology/neurology ambulatory clinic schedules will screen the rosters daily to identify potentially eligible patients. We will screen any patient admitted with stroke or TIA to the neurology service (identified from the inpatient neurology roster admitting diagnosis) or presenting with a complaint potentially related to stroke (e.g., facial droop) and evaluated by the stroke service. For potentially eligible participants in whom the diagnosis of stroke/TIA is suspected (e.g., focal weakness), but not yet listed as a diagnosis, a neurology consultation note or history and physical examination documenting stroke/TIA will be needed to confirm eligibility. We will also screen cardiology patient rosters for any ambulatory patients who could have a $CHA_2DS_2\text{-}VASc$ score ≥ 3 by looking at their medical problem list or provider notes.

Patients who are admitted to the neurology/cardiology units at UMMMC will be considered eligible to participate if they meet all of our inclusion criteria and are free of exclusion criteria. They will be approached by the study staff before they are discharged from their inpatient stay. The study staff will approach the patient's clinical team prior to entering the patient's hospital room for approval to approach the patient for this study. Study staff will present information to the patient about the study, including the randomization process, and will perform an assessment of the patient's capacity for informed consent. Study staff will demonstrate the features of the Cardiac Insight monitor, smartwatch, and smartphone/app and then allow the patient to ask questions about the devices. We will involve family who are present in the patient's room to answer their questions about the study. Patients will be given the opportunity to consider participating in the study until their day of discharge from the hospital. If the patient consents to participate, study staff will administer the baseline questionnaire. Study staff will also place the cardiac monitor on the participant's chest by following the Cardea Solo Quick Start Guide (submitted to eIRB). We are not altering usual care, and the devices should not be uncomfortable to wear. The participant will be given guidance on how to use the devices and the process for baseline compensation. We anticipate the explanation of the study and consent procedure in the inpatient cohort will take ≤ 30 minutes.

Research assistants will also screen ambulatory patients with a history of stroke or TIA in their problem list or medical history. For ambulatory patients, letters of introduction to the study will be sent to eligible patients 5-7 days before their scheduled clinic visit with an opt-out phone number for patients who do not wish to be approached for study participation. We have successfully used a similar approach in other studies. This invitation letter is enclosed in our application packet.

The consent will include permission for follow-up contacts and medical record review, and will also request access to identified proxies, who would be able to help us contact patients in the event they change practices and do not follow up at UMMMC. We will offer modest incentives for recruitment and retention in Pulsewatch: T-shirts and/or bags and/or pens with Pulsewatch logos offered at recruitment and mailed during follow-up.

All participants will be brought back for a study visit approximately 14 days after enrollment. This visit will take place in a research area that is private and comfortable. There, participants will

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return both of their patch monitors, smartwatch, and smartphone, and will complete a questionnaire. From the 120 participants in both the Aim 2 intervention and control groups, we will randomly select up to 60 participants to be offered an opportunity to self-monitor at home using the Pulsewatch smartwatch/smartphone for 30 days, as well as the AliveCor ECG recording device. The 60 participants who are randomized into the control arm of Aim 3 will not be offered the opportunity to self-monitor with any device. At the completion of the 30 days, participants in Aim 3's intervention group can either return for a follow-up visit to return all equipment and complete the 44-day follow-up questionnaire, or can return their devices through a prepaid package and complete the 44-day follow-up questionnaire over the phone. Participants in Aim 3's control group will have a choice to complete their 44-day follow-up questionnaire either in person or over the phone. All participants coming back for an exit interview in Part II of the study will be sent a Fact Sheet reviewing all the details of the process (Fact Sheet: Part II Exit Interviews in eIRB submission). Upon receipt of the study equipment and/or the 44-day questionnaire, the study team will compensate the participants.

Compensation will be given as an incentive. All patients and caregivers who participate will be compensated for their time and efforts in the study as shown in the table below. Providers will not be compensated for participating.

Participant Sub-groups	Compensation Amount	Time Earned
Part I: Focus Group	$60.00 gift card	After completing the focus group
Care-givers	$60.00 gift card	After completing the focus group
Part I: Hack-a-thon	$15/hour gift card	After completing the Hack-a-thon event
Aim 2: Control group	$100.00 gift card	After completing the baseline interview
	$100.00 gift card	After completing the 14-day follow-up visit
Aim 2: Intervention group	$100.00 gift card	After completing the baseline interview
	$100.00 gift card	After completing the 14-day follow-up visit
	$60.00 gift card	Participants who complete exit interviews in Part II
Aim 3: Control group	$50.00 gift card	After completing the 44-day follow-up questionnaire
Aim 3: Intervention group	$50.00 gift card	After returning the study devices and completing the 44-day follow-up questionnaire

Before the focus groups or the Hack-a-thon are held, we will inform all participants that they will receive parking passes if they park in the Visitor Parking Lot to attend these events. Valet parking uses a different voucher that our study is not purchasing at this time.

To help with participant retention, the study team may contact participants by phone or mail to remind them of upcoming visits or to check in and see how participants are doing, particularly in Part II. The study team may also contact participants by phone or mail if it implements the adaptive design (due to low rates of AF) in which participants are asked to extend wearing the devices for longer than the initial 14-days. Any letters will be submitted to the IRB as a Modification for review and approval prior to use.

COVID-19 Modified Local Recruitment Methods
During COVID-19 restrictions, we will screen both the cardiology and neurology ambulatory care clinics to identify eligible patients. When eligible patients are identified, they will be sent our

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COVID-19 modified patient invitation letter 7-14 days prior to their scheduled appointment. As with our normal, IRB-approved patient invitation letter, there will be a number listed for the patient to opt-out of being contacted for the study. A day prior to their scheduled appointment, a study team member will contact the potential participant to assess interest in the study. If the potential participant agrees to participate, we will follow the consent and enrollment procedures outlined in Section 11: Procedures Involved.

25. LOCAL NUMBER OF SUBJECTS

There will be a total of up to 170 participants in this study.
Part I: Up to 40 out-patient stroke participants or caregivers and 10 providers.
Part II: Up to 120 participants, including 30 in the Aim 2 control group and 90 in the Aim 2 intervention group. Of the 120 participants in both the Aim 2 intervention and control groups, 60 will be invited to participate in the intervention arm of Aim 3 and use the devices for 30 days. At the 14-day follow-up visit, the other 60 participants randomized into the control arm of Aim 3 will be invited to complete a questionnaire in person or over the phone at the end of 30 days.

In order to obtain 170 participants who complete the research, we may over enroll or replace participants who drop out.

Adaptive enrollment design (Part 2): If we struggle to identify sufficient numbers of eligible participants from the inpatient stroke service or clinics over the first 6 months of enrollment (<50% targeted enrollment), we will employ an adaptive design and approach patients presenting to UMMMC out-patient and in-patient cardiology and/or neurology clinics who have high risk for atrial fibrillation and stroke on the basis of a CHADSVASC score >=2. Furthermore, If we struggle to enroll a sufficient number of participants from the UMMS University campus, we will recruit at the stroke treatment centers at UMass Memorial - Health Alliance Hospital in Leominster, MA, and at UMass Memorial - Marlborough Hospital in Marlborough, MA. The PI has actively sought approval from these sites to approach patients from these locations in order to meet study enrollment goals.

26. CONFIDENTIALITY
Trained RAs will use Subject IDs for all the data collected from participants to limit the use of the participants' personal information. Information will be collected via the UMass EHR system for screening and basic demographic information. The data collected at the focus groups/exit interviews will be recorded but then transcribed later and the recording will be deleted. Please refer to section 13 for more details regarding confidentiality of data and management.
The audio recordings of the focus groups/exit interviews will be deleted after the recording has been transcribed and checked for quality. The transcription will be kept in the secure database of REDCap.

27. PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS
All PIs and research assistants/coordinators will complete CITI training to understand the necessary measures to protect personal identifiers and reinforce the importance of sound ethics in conducting this research study. The study team will also search for the best and most private setting in the UMMMC environment to help participants feel at ease with the study and explain that their information will be protected. Participants will also be told they have the right to refuse

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to answer any questions they feel uncomfortable answering or/and the right to refuse to be in this study.

    a. PI - Will have ongoing access to REDCap clinical data for data integrity and Q/A checks.

    b. RAs/Research coordinators will have access only to EHR data, and study data they are entering into REDCap.

    c. We will request a waiver of HIPAA authorization in order to do preliminary EHR and clinical record searches to determine if patients are eligible for study enrollment based on our inclusion and exclusion criteria. A signed HIPAA form will be obtained once a patient is enrolled and able to sign the form.

    d. A biostatistician/database manager will be given access to clinical data that does not readily identify subjects by name for data analysis.

    e. Independent monitor will review deidentified safety, adverse events, and study reports (see DSMP)

28. COMPENSATION FOR RESEARCH-RELATED INJURY

This study involves research procedures that are considered minimal risk; no funds have been set aside.

29. ECONOMIC BURDEN TO SUBJECTS

There is no economic burden to subjects because of participating in this research. Study funds will be providing all of the devices at no cost to participants.

30. CONSENT PROCESS

Prior to enrolling participants, the study team will have a training session. This training session will focus on all study aspects but particularly to ensure that all study staff are familiar with and will follow HRP-802 INVESTIGATOR GUIDANCE: Informed consent. We will be obtaining IRB-approved informed consent and HIPAA authorizations from all patients who are participants in Part I and Part II of this study. Participants who are caregivers and providers will receive a fact sheet instead of signing an informed consent form - this recommendation for the IRB is because the study team does not need any health record information from these participants to take part in our study procedures.

It is important to obtain HIPAA authorization from the patients who become participants in order for the study team to have access to certain aspects of their EHR. Information such as demographics (age and sex), related medical information like family history, current and past medications or therapies, and information from physical examinations will help the team understand the type of population in this study. For example, medical notes on physical exams can describe how much patients may be able to move their arms; this will help us assess if we should approach patients who have very limited arm movement since our study asks participants to wear a watch. In addition, this information will help us capture the severity of our participants' physical and medical limitations. We will also need this information for patient participants in the focus groups because we would like to be able to compare these participants to the Part II participants who will be using the Pulsewatch System.

After RAs identify a potential participant and explain the study, RAs will ask the potential patient participant to read, sign, and date the consent form. If a caregiver is present, then a fact sheet may be given to them regarding more information about participating in the focus groups. If patients or caregivers want more time to decide whether to participate in the study, RAs will

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provide them with the study phone number (774-455-3799) on which they can call us. Part I and Part II of the study will have a separate consent form because each part requires different types of participation. In part I, we will have a consent form for eligible patients to participate in the focus groups.

The research coordinator will be responsible for contacting providers who have expressed interest in this study. The coordinator will inform all potential provider participants that this study is completely voluntary and will not affect their status as employees of UMMMC or UMMS. If providers wish to opt-out, they may directly contact that study team and/or coordinator.

In Part II, we will have one consent form that outlines the randomization trial method and what patients will be required to do to participate in the study.
We will only use IRB-approved stamped consent forms.

During COVID-19 restrictions, since we will not be meeting the patients in person to obtain their informed consent form and HIPAA authorization signature, we will instead send them a COVID-19 specific informed consent form. This form will be extensively reviewed with the patient over the phone to obtain their informed consent, and their acknowledgement to disclose protected health information.

31. PROCESS TO DOCUMENT CONSENT IN WRITING
Written informed consent will be given to participants who are patients (not caregivers or providers, who will receive a Fact Sheet). All study staff members who a part of this study will be trained properly and have a complete understanding of all study related documentation in order to help answer any questions participants may have. The approaching staff member will assess the capacity of the patients to consent; we have submitted to the IRB a "Capacity for Informed Consent" form that can be used. We anticipate that due to the study selection criteria (older patients), some patients will not be able to provide informed consent. Thus, all patients will be assessed for their understanding of the study, the risks and benefits associated with the study, the voluntary nature of participation, and the confidential nature of all study data. If patients answer 3 or more questions out of 8 incorrectly, they will be deemed unable to provide informed consent and excluded. Safeguards will be put into place to protect the rights of cognitively impaired participants.
For caregivers and providers, we will obtain informed consent via an unsigned fact sheet given to them prior to study visits.
All participants who sign the consent form will be given a copy to keep for their own records. The study team will keep the original copy of the signed consent forms in a locked cabinet in a locked room. The study team will also make another copy and send it to UMMMC Medical records to be kept on file for each patient who participates in the research.

Please see Section #30: Consent Process for information regarding consenting patients during COVID-19 restrictions.

To minimize patient burden during this time, we are requesting a waiver of documentation of written consent for subjects. We attest that all of the following are true:
- The research involves no more than minimal risk to the subjects.
- The research involves no procedures for which written consent is normally required outside of the research context, and all study activities are conducted over the telephone or Zoom.

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- Subjects will be provided a written statement including the elements of consent (described on the COVID Informed Consent Form).

32. DRUGS OR DEVICES

This study will use only commercially available devices (Samsung gear, Android smartphones) or FDA approved devices (AliveCor Kardia Mobile device and app). Part II participants will use the AliveCor Kardia Mobile devices and smartphones that will only run the AliveCor app (FDA approved for single-lead ECG recording) and the Pulsewatch app. A gold-standard, commercially available (Cardiac Insight Cardea Solo) monitoring technology will be deployed and used by all Part II participants. We have enclosed a copy of the FDA approval letter for both AliveCor and Cardiac Insight into this submission. In addition, we have also enclosed a copy of detailed information regarding these devices for any review.

The mobile device application (Pulsewatch App) that will be developed in this study at the end of Part I is not commercially available nor FDA approved. This application (Abbreviated IDE) is only to be used with participants of this study. For this reason, we would like to document the following:

i. The device is not a banned device;
ii. The device is not intended as an implant that presents a potential for serious risk to the health, safety, or welfare of a subject;
iii. The device is not purported or represented to be for a use in supporting or sustaining human life that presents a potential for serious risk to the health, safety, or welfare of a subject;
iv. The device is not for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health that presents a potential for serious risk to the health, safety, or welfare of a subject; and
v. The device does not otherwise present a potential for serious risk to the health, safety, or welfare of a subject.
vi. The device will be labeled in accordance with 21 CFR 812.5.
vii. The PI as sponsor will
　　1. Comply with the requirements of 21 CFR 812.46 with respect to monitoring investigations
　　2. Maintain the records required under 21 CFR 812.140(b) (4) and (5) and make the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10)
　　3. Ensure that participating investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 21 CFR 812.150(a) (1), (2), (5), and (7)
　　4. Comply with the prohibitions in 21 CFR 812.7 against promotion and other practices

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