PRINCIPAL/OVERALL INVESTIGATOR
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PROTOCOL TITLE
A smartphone-based application post-myocardial infarction to manage cardiovascular disease risk

FUNDING
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I. SPECIFIC AIMS

Specific Aim 1: To recruit and onboard 100 patients sustaining a myocardial infarction and 50 patients with symptomatic coronary artery disease without myocardial infarction who have undergone PCI with the Wellframe patient engagement platform. Patients will be recruited during index cardiac hospitalization in the inpatient setting.

Specific Aim 2: To determine feasibility of inpatient onboarding of the Wellframe patient engagement platform in the setting of acute myocardial infarction. We will evaluate process outcomes, including proportion of eligible participants agreeing to participate, survey completion rates, content engagement, patient application engagement, and patient satisfaction scores.

Specific Aim 3: To assess the clinical efficacy of the Wellframe patient engagement platform post-myocardial infarction compared to matched historical controls. We will also evaluate outpatient clinic follow-up rates after hospitalization as well as cardiac rehabilitation enrollment rates (primary outcome) for all participants. We will evaluate 90-day and 30-day readmission and ED visit rates for post-myocardial infarction participants.

We hypothesize that the patient engagement platform will be an efficient method for cardiology staff to engage, follow-up, and educate patients peri-percutaneous coronary intervention (PCI) in the setting of acute myocardial infarction.

II. BACKGROUND AND SIGNIFICANCE

Public Health Significance

Myocardial infarction is a leading cause of morbidity and mortality in the United States and worldwide.[1,2] Acute management of myocardial infarction involves pharmacological and revascularization strategies to reduce recurrent ischemic events, including cardiovascular death.[3,4] Secondary prevention measures include adherence to guideline-based pharmacologic strategies, management of cardiovascular risk factors, diet and lifestyle counseling, and participation in cardiac rehabilitation. Both patient- and treatment-specific factors are associated with short-term adverse events.

Prevention of recurrent atherosclerotic cardiovascular disease (ASCVD) events after a myocardial infarction requires implementation of acute care, coordinated follow-up care, adherence to multiple new medications in the outpatient setting, patient education, dietary and structured exercise therapies through outpatient cardiac rehabilitation.

Description of Wellframe Platform

Through this novel mobile platform developed specifically for this clinical scenario, patients will receive education about their specific procedure PCI, AMI, and coronary artery disease as well as facilitate outpatient care and adherence for approximately 90 days after the PCI. They also have the option of receiving condition-specific and lifestyle education programs including: hyperlipidemia, hypertension, diabetes, weight loss, physical activity, smoking cessation, and stress management. We will customize condition-specific and lifestyle programs as necessary using the Wellframe dashboard based on individual health needs. Thus this intervention is designed to optimize secondary prevention of ischemic heart across the continuum of care in the critical period post intervention through to outpatient continuinity appointments and comprehensive outpatient cardiac rehabilitation.

Patient Mobile App Purpose & Function

The Mobile Health platform is developed by Wellframe, a Boston, Massachusetts-based health care technology company. Wellframe aims to improve patient engagement in their health, and enable convenient, effective support by allowing for messaging between study staff and patients based on a patient's progress with their care plan. The Mobile Health platform consists of a patient held mobile app, a clinician dashboard and a suite of clinical programs with configurable rules. The patient mobile app features a personalized adaptive daily health checklist that includes reminders to patients to engage in health behaviors and a series of personalized, interactive surveys, articles, and encouragement. The app connects to the mobile device's movement sensors to facilitate a structured clinical program with physical activity monitoring. In addition, there is a patient education library with both written and video content specific to their health condition or procedure. The written patient education content is curated from evidence-based guidelines. The video content delivers standardized teaching. The App was developed using user-experience and design principles to ensure a user-friendly design for all users. The registration process is streamlined so that it only takes a few minutes to set up. In addition to requiring a password-secured account for the Mobile App, patients are encouraged through an educational article to add a passcode to their mobile device for additional security.

Wellframe Content Development

All content is derived from the government sources, or from professional society publications that have been licensed for commercial reuse or for reference and citation within documents intended for commercial use. See below for a select list of sources; all referenced sources are cited in the references section of each article that appears in the patient mobile app. Referenced sources include:

- American Heart Association
- Centers of Disease Control and Prevention

- Harvard Medical School
- MedlinePlus, U.S. National Library of Medicine
- National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health
- National Heart, Lung and Blood Institute, National Institutes of Health
- NIH Senior Health, National Institutes of Health

Once authored by Wellframe's medical writers, who have expertise in health literacy and health communications, clinical content undergoes structured clinical review by Wellframe clinical leadership. Clinical content has also been reviewed by clinical leadership from Boston Scientific.

Clinical Team Dashboard Purpose & Function

The Clinical Dashboard is also developed by Wellframe to work in conjunction with the Wellframe Mobile App for patients. Wellframe aims to amplify existing clinical resources and reduce the burden and time spent on patient preparation and follow-ups by surfacing real-time insights to clinical teams, and providing the tools to support patients easily and efficiently. The Dashboard features secure, 2-way messaging to individuals and groups of patients, enabling efficient follow-up to answer patients' questions and outreach to encourage engagement with the care program. Clinicians can also reach out to patients through multi-channel communication methods, including email, text message, and phone calls, to promote engagement and responses to surveys. The clinical team is alerted based on patients' survey responses and engagement patterns, allowing them to identify risks, intervene early through supportive messaging, and avoid recovery complications. In addition, the clinical team can customize the experience for each patient by using features such as secondary programs, instructions, and reminders. In summary, Wellframe's real-time insights about patients' health status, combined with secure messaging with patients, enables an efficient, effective workflow for clinical teams to support patients through preparation and recovery.

A Health Advocate, a non-clinical coach, will also work with patients through the dashboard to promote adherence to care plans and provide support and encouragement throughout preparation and recovery. This Health Advocate would partner with research site staff to ensure a seamless support system for patients. The Health Advocate is a Wellframe employee who is a trained health coach. This individual is sub-clinical – not a trained clinician. The Health Advocate is trained in patient support, engagement, and encouragement.

The Health Advocate builds a supportive, coaching relationship with the patient and provides non-clinical support, encouragement, and accountability to maximize engagement. The Health Advocate sends encouraging messages and addresses patients' non-clinical needs, facilitates patient adherence to care programs, promotes patient program retention and engagement through multiple communication channels, and monitors the patients' Mobile App behaviors. As a part of these activities, the Health

Advocate directly encourages patients to complete the tasks in their Wellframe care program, including reading their health education and completing their surveys.

The Health Advocate co-manages patients with the clinical team via the Wellframe dashboard. The Health Advocate facilitates triage of clinical needs to clinical staff. As a non-clinician, the Health Advocate operates under the supervision of Wellframe's team of licensed clinicians (physicians and nurse practitioners), and all patient communication adheres to structured protocols and guidelines set forth by Wellframe clinical leadership.

III. RESEARCH DESIGN AND METHODS

Sample size: 150 post-PCI at Massachusetts General Hospital (MGH) and Brigham & Women's Hospital (BWH): 100 with myocardial infarction, 50 with symptomatic coronary artery disease without myocardial infarction

Inclusion/Exclusion Criteria

- Acute myocardial infarction – defined by typical symptoms, characteristic kinetics of cardiac biomarkers or characteristic EKG changes

  Or

  Symptomatic coronary artery disease without myocardial infarction – defined by typical symptoms (i.e. angina) and signs (i.e. abnormal non-invasive cardiovascular testing: stress testing or coronary CTA)

Inclusion Criteria
- Age 21-85
- English-speaking
- PCI: balloon angioplasty, bare-metal stent, or drug-eluting stent at MGH
- Smartphone or Tablet (iOS or Android)
- Long term provider in Massachusetts (or records available through Care Everywhere)

Exclusion Criteria
- Recent (within 1mo) illicit substance use or alcohol abuse
- In-hospital AMI
- Known pregnancy
- Dementia or cognitive disability
- Incarceration

Study Outcomes

Clinical and Utilization Outcomes

Clinical outcomes will be ascertained from electronic medical records. Patients will also be called at 90 days to determine potential readmission, representation, and cardiac rehabilitation enrollment at other hospitals or clinics during the follow-up period. The following outcomes will be assessed:

- Utilization and Attendance
    - 4 Week Follow-up Appointment: % of patients who attend cardiology follow-up appointments after PCI
- **Readmission Rates**
    - **30 Days- Primary Outcome**
    - 60 Days
    - **90 Days – Secondary Outcome**
- Representation Rates (ED presentation with hospitalization)
    - 30 Days
    - 60 Days
    - 90 Days
- **Enrollment in clinic-based cardiac rehab**
    - **% of patients discharged after intervention who attend at least one session of clinic-based cardiac rehab -Secondary Outcome**
- Cost Effectiveness

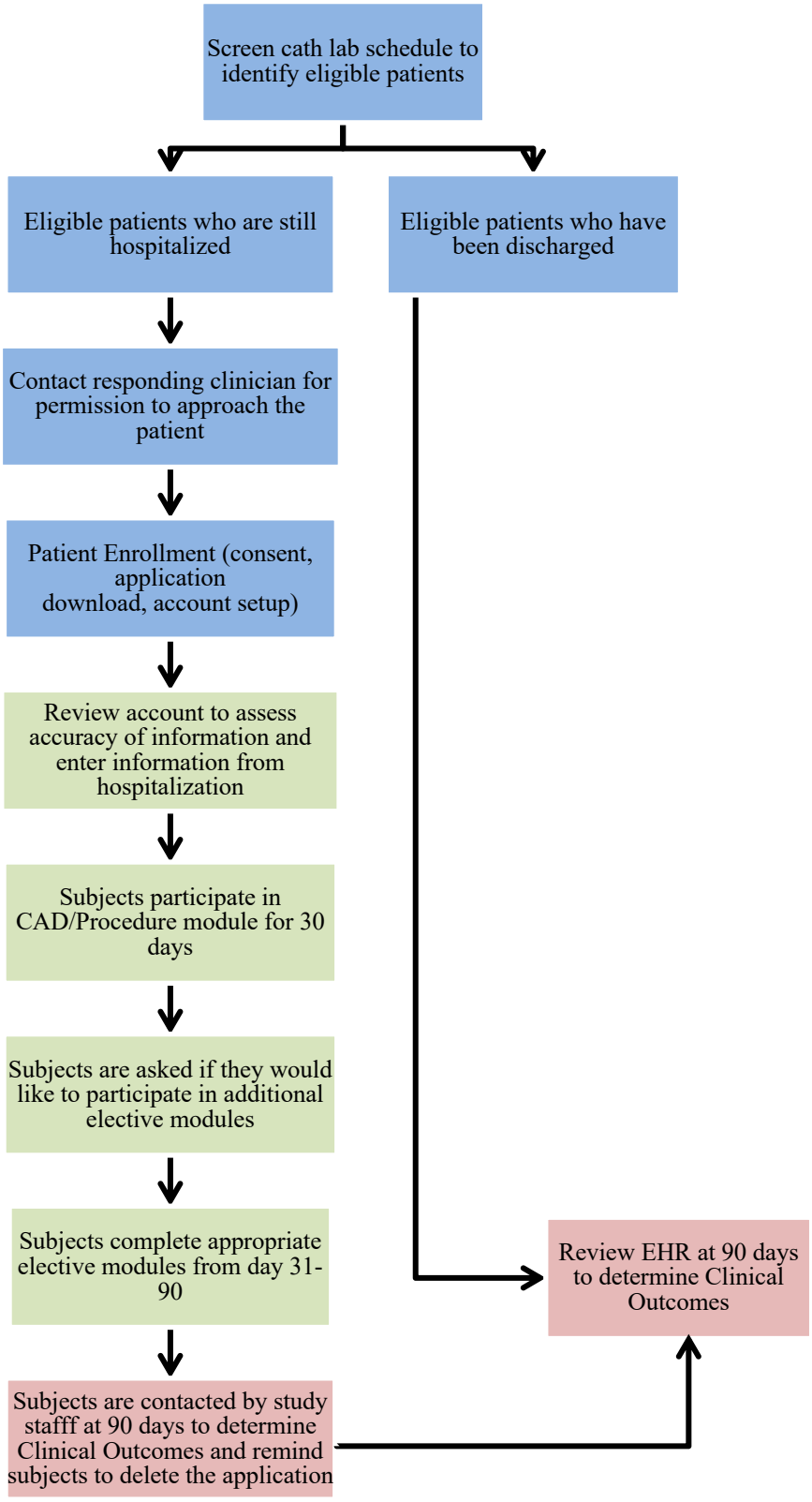
Process Outcomes

These data will be provided by Wellframe to the PI. "Conversion rate" will be the primary outcome as this will indicate patient acceptability of initiating the platform and the remainder listed below will be secondary outcomes. The proportion of individuals with cardiovascular disease who accept a smartphone application upon discharge is largely an outstanding question. We hypothesize that >50% of eligible and recruited patients will enroll in the Wellframe app. Data from Wellframe will be used to assess:

- Conversion Rate: Number of patients who enroll in Wellframe app out of the number of patients eligible for participation
- Medication Adherence: % of medication reminder tasks that were completed
- Content Completion: % of content tasks that were completed
- Survey Completion: % of survey tasks that were completed
- Patient Engagement:
    - % Weekly engagement (percent of days in which patient had engaged at least once over the previous 7 days)
    - % Daily engagement (percent of days in which patient had engaged)
- Patient Messaging:
    - Number of messages sent
    - Percent of messages sent to patients that were opened at any point
    - Percent of messages sent to patients that had at least one message from the patient afterwards
- Patient Satisfaction: average response to patient satisfaction questions asked through app's survey functionality
- Patient Physical Activity
- Clinical Messaging:
    - Total number of messages sent
    - Percent of patients who received at least one message

Primary and secondary outcomes are labeled and in bold, all other outcomes are exploratory outcomes.

Schema



Subject Enrollment

Study Procedures

Study Closeout and Post Study Follow-up

Subject Enrollment

Overview
Approximately 150 patients will be enrolled in the study. Patients undergoing PCI at MGH and BWH will be screened by study staff for inclusion/exclusion criteria. Study staff will obtain approval to approach eligible patients by the inpatient treating physicians. On the day following PCI, prior to discharge, suitable patients will be consented and onboarded with study staff, with the technical help of Wellframe.

Procedure for obtaining informed consent

We will use Partners electronic resources identify and screen patients for the eligibility criteria listed above.

We will focus on patients undergoing PCIs in the cardiac catheterization lab on Blake 9, and who are then admitted to Ellison 10 or 11 (inpatient cardiac telemetry floors). We will screen for both elective PCIs and those for after an MI. We will create a database of potentially eligible subjects and obtain permission to approach them. We will only approach patients that have given permission to be approached. We will contact either the patient's nurse or other care team member so this person can ask permission of the patient before the research coordinator talks to the patient.

We will also send an email explaining the study to the subjects' outpatient cardiologist. We will mail to cardiologists who are not in the Partners network.

We will also use the attached study flyer to advertise the study to patients on inpatient floors and in the cath lab, with nurse manager approval for the respective floors.

Eligible patients will be approached by the study coordinator on the day of their discharge. The study coordinator will then review the consent form and study procedure and obtain written consent from the patient. Study coordinators will use an iPad to go over the consent form with the patient. The subject and the study coordinator will sign electronic copies of the consent form using Adobe Sign. Subjects will be sent a copy of the consent form via email using the Partners send secure system. Subjects with any cognitive disability that prevents them from consenting for themselves will also prevent them from using the Wellframe application. Therefore, subjects who cannot consent for themselves will be excluded from the study. We will make it clear that participation in the study is voluntary and the subject can choose to withdraw from the study at any time.

The demographics (Age, Sex, Race/Ethnicity) of those screened for our study will be collected for recruitment analyses. Subjects who are not approached for participation will be reviewed for outcomes. For anyone who declines to participate in our study, we will not review their charts for outcomes.

It will not be possible to obtain consent from all of these patients as some of them will have already left the hospital. Not obtaining consent from these patients will not be a risk to the patients as no active intervention will be made and all information obtained from the records will be deidentified and stored in a secure database.

Patients who leave the hospital on the day of their procedure or before a coordinator can approach them will be recruited via flyer and then a phone call. Patients will be approached in the cath lab before or after their procedure and given a flyer. Coordinators will explain the study to the patient and that their eligibility will be confirmed after their procedure if it has not occurred yet. We will call these patients at

least a day after their procedure and conduct informed consent over the phone. Those who did not receive a flyer or do not want to be contacted will not be called.

Informed consent will take place over the phone and the subject will sign the consent form electronically using Adobe Sign. This study involves minimal risk. We cannot mail to patients or ask their physician to speak with them first, because patients must begin the study at maximum a few days after their procedure. Patients can also refuse the study when talking to the research coordinator. Patients can simply stop using the app whenever they want with no risk associated with stopping. We will attempt to contact patients twice using contact information provided in Epic.

If a patient agrees to participate over the phone, after signing the consent form, we will send instructions on how to download the app (a PDF version of the brochure) via email. Patients can then download and begin using the app.

We think it is feasible to recruit some patients remotely for the intervention arm, but for those that do not answer their phone or do not download the application, we do not believe it is necessary or possible to contact them solely to obtain consent to review their records for the non-intervention group.

Onboarding with Wellframe

STEP 1: Download Wellframe

- On the a smartphone or tablet, patients go to http://guide.wellframe.com/ and click "Install Now" *OR* open the App Store (iOS) or Play Store (Android) and search for **Wellframe**.
- Install the Wellframe app on their smartphone or tablet.

STEP 2: Sign Up

- Open Wellframe and tap Create New Account.
- Type in this access code to sign up for an account: **[ACCESS CODE]**
- Patient enters demographic information (first name, last name, date of birth, gender, and telephone number), then an email and password to complete registration.
- The patients will be prompted to set up reminders for any medications they take. Enter the medication name and choose the time(s) of day they'd like to be notified to take their medications.
- They'll be prompted to accept push notifications from Wellframe. Patients say "Yes/Accept/OK" to allow notifications for medication reminders, messages from the clinical team, and updates to instructions. These notifications will appear on the lock/home screen of the mobile device. They will never contain personal health information; they will simply prompt patients to open Wellframe for a new task, message, or instruction, e.g. "You have a task to complete (9:00 AM)" for a medication reminder.

- Lastly, when patients tap on the Physical Activity task, they'll be prompted to allow Wellframe to access motion & fitness tracking data from Apple Health Kit (iOS devices) or Google Fit (Android devices). Accepting this permission will allow Wellframe to track the patients' steps throughout the day. Wellframe cannot see patients' location; Wellframe calculates steps based on the movement of the device when the patients carry their smartphone or tablet in their hand, pocket, or bag.

Study Procedures

Study Staff and Health Advocate Role

During the study, subjects will be encouraged to complete daily tasks by the Health Advocate as described above in the Clinical Team Dashboard Purpose & Function section.

Study staff will monitor the subjects' Wellframe applications. Study staff will explain to subjects that for this study, the clinician messaging function will be used for study communications only (i.e. reminding them to enter their medications), and health advocate messaging will be for non-clinical communications about health behaviors; any clinical questions should be directed to their healthcare providers.

Should the study staff or health advocate receive clinical questions from subjects, these questions will be directed to the study doctors. For questions that are not appropriate for the study doctors to answer, the study doctors will facilitate contact with one of the subject's healthcare providers.

Study staff will use the electronic medical records to determine the following, and post this information to the subject's Wellframe application:

- What type of stent they have (also used to determine care program outlined below)
- Location of stent: which artery
- Catheter insertion site: wrist or leg
- Discharge Instructions

Study staff will be alerted by Wellframe on the Clinician Dashboard when:

- Subject has not entered medications 3 days after onboarding with Wellframe:
    - Study Staff will send a message encouraging the patient to enter their medications using the clinician messaging system.
- Subject has entered their medications:
    - Study staff will then reconcile the patient reported medication list with the discharge medication list on the subject's medical record.

If any medications entered into the Wellframe account are incorrect, study staff will encourage the subject to consult their discharge medication list and their healthcare provider to ensure they are taking their medications correctly.

PCI Care Programs

Patients will go through two programs. The content provided to patients will be reviewed by the study cardiologists.

During Program 1 subjects will be enrolled in 1 of 3 modules based on what kind of procedure/stent the subject had (Bare Metal Stent, Drug-Eluting Stent, or Angioplasty); all patients will get the coronary artery disease (CAD) module during Program 1. Program 1 will last for approximately 30 days.

Program 2 will be based on secondary patient specific conditions (Hypertension, Hyperlipidemia, Diabetes, etc). Study staff will message patients at day 30 when Program 1 finishes and ask if they would like to participate in additional modules. Subjects will be prompted with a survey question from Wellframe that asks them what factors of their health they are interested in learning more about. Study staff will then assign a module to the subject from the selection of modules in Program 2 based on the subject's responses to the question and information from their health record, and then subsequent modules as are applicable. Program 2 will start when the subject finishes Program 1, and will end after approximately 90 days (for the longest version of the program).

The educational content for the modules in each program are listed below:

There will be separate clinician dashboards for MGH and BWH managed and monitored by each study site team. Summary data regarding survey responses and engagement will be shared across the study team.

Education content has been reviewed by MGH physicians, and the BWH team will also review.

Program 1

Module	Education content
CAD	• **Pathophysiology**: Heart anatomy, atherosclerosis, causes, complications • **Symptoms**: angina management, cardiac precautions • **Medications**: Nitroglycerin, DAPT, statins, beta blockers, ACE inhibitors • **Lifestyle**: Smoking, diet, exercise, sleep, alcohol • Other: Depression, intimacy, vaccines
Bare Metal Stent	• Warning signs, self-care, follow-up and meds specific to procedure and device
Drug-Eluting Stent	• Warning signs, self-care, follow-up and meds specific to procedure and device
Angioplasty	• Warning signs, self-care, follow-up and meds specific to procedure and device

Program 2

Module	Description of Module	Education content
Hyperlipidemia	*Program on managing high cholesterol based on the Therapeutic Lifestyle Changes (TLC) program*	• **Pathophysiology:** Causes, anatomy, complications • **Symptoms:** CAD • **Medications:** statins, aspirin • **Lifestyle:** Smoking, diet, exercise, sleep, alcohol, meal planning, calories, portion control, reading labels
Hypertension	*Program on managing high blood pressure, including medications, diet, and other lifestyle factors.*	• **Pathophysiology:** Causes, anatomy, complications • **Symptoms:** blood pressure management, cardiac precautions • **Medications:** Beta blockers, ACE inhibitors, diuretics, ARBs, aspirin, statins • **Lifestyle:** Smoking, diet, exercise, sleep, alcohol • **Other:** Depression, intimacy, vaccines
Diabetes	*Program on managing diabetes, including monitoring, medications, and lifestyle factors.*	• **Pathophysiology:** Causes, anatomy, complications • **Symptoms:** hypoglycemia, hyperglycemia, red flag symptoms • **Medications:** Oral, insulin • **Lifestyle:** Smoking, diet, exercise, sleep, alcohol, meal planning, calories, portion control • **Other:** Depression, kidney disease, foot care, eye care, oral health, falls, intimacy, vaccines
Weight Loss	*Structured weight loss plan with a weekly curriculum*	• Calories • Fiber • Portion size • Meal planning • Goal setting • Exercise • Cravings • Alcohol
Beginning Physical Activity	*Structured physical activity plan with weekly goals*	• Guidelines, safety • Making a plan • Injury prevention • Barriers

		• Endurance • Strength training • Balance • Flexibility
Smoking Cessation	*Structured smoking cessation program*	• Quit date • Reasons to quit • Strategies: withdrawal, cravings, meds, nicotine replacement therapy, milestones, rewards, support • Weight gain • Stress, depression
Stress	*Program on recognizing and managing stress*	• Chronic stress • Stress cycle • Triggers • Time management • Attitude, emotions • Getting help • Conflict negotiation • Anxiety, depression

To track patient reported clinical outcomes (cardiac rehabilitation and cardiology appointment attendance) through Wellframe, subjects will be asked the following questions via the survey function in Wellframe:

- At 30d: Have you attended an appointment with a cardiologist?
- At 30d: Have you scheduled an appointment for cardiac rehabilitation?
- At 60d: Have you attended an intake appointment for cardiac rehabilitation?
- At 75d: Have you attended the first exercise session for cardiac rehabilitation?

Throughout the study, Subjects will also be asked to complete surveys on Wellframe to assess process outcomes. The survey questions are listed in the attachment titled "Data".

Study Closeout and Post Study Follow-up

Lastly, after 90 days, subjects who are enrolled in the study will be contacted by a member of the study staff to determine clinical outcomes: potential readmission, representation, and cardiac rehabilitation enrollment at other hospitals or clinics during the follow-up period. We will review the health records of both eligible but discharged and study subjects at 90 days to determine these same clinical outcomes at MGH. Subjects will be reminded during the 90 day phone call that they should delete the Wellframe application.

IV. RISKS TO SUBJECTS

Since the study involves adding a mobile health component to a treatment plan, risks posed to subjects are similar to those involved with following a post-PCI care plan. Subjects will be encouraged to contact their physician with medical questions.

Loss of privacy is a risk of this study that will be minimized by keeping patient health information in a secure database. Only study personnel who have undergone the proper human research training and signed standard confidentiality agreements will have access to this data.

Wellframe also has access to the data on patients' applications. The Wellframe platform, comprised of web-based and mobile solutions, is architected to protect the security of patient information. All data for the platform is stored on cloud servers and only pulled into the platform when accessed by clinician (web-based dashboard) or patient (mobile app). The Wellframe system encrypts patient data at rest and in transmission, and adheres to network security, server security and access control parameters in accordance with HIPAA privacy and security rules.

Clinician Dashboard: By encrypting data in-transit between the browser and services, Wellframe ensures that only authenticated users have access, requires complex passwords, and enforces automatic timeout user sessions.

Patient Mobile App: Wellframe stores as little data as possible on the device, data is stored through secured modalities, and Wellframe encrypts all traffic between the phone and Wellframe servers. Patients are required to create a password for the Wellframe account. Wellframe strongly encourages patients to use a passcode on their smartphone/tablet and patients receive instructions for setting a passcode upon enrolling on the app. Additionally, if patient accept permissions for Wellframe to send notifications to their smartphone/tablet, the notifications will never contain PHI (examples: "You have a new task in Wellframe" or "You have a new message in Wellframe"). For the physical activity monitoring, Wellframe cannot see patients' location; Wellframe calculates steps based on the movement of the device when the patients carry their smartphone or tablet in their hand, pocket, or bag.

V. PRIVACY AND CONFIDENTIALITY

Study data will be kept in a password protected database, subject records will be linked to unique subject IDs. Only study personnel who have undergone the proper human research training and signed standard confidentiality agreements will have access to these data. No data will be sent to collaborators outside Partners. Wellframe will collect the data for "Process Outcomes" as described in the study procedures above. This data will be linked to the subject via their unique access code. When the subject enrolls in the Wellframe study their access code will be recorded. This access code will be used to link the data collected by Wellframe to the specific subject, and allow the study group to receive deidentified data from Wellframe, and later link it to specific subjects, and keep this linked data in a secure database.

VI. EXPECTED BENEFITS

We hope that this study will help us better understand and improve prevention of recurrent atherosclerotic cardiovascular disease (ASCVD) events after a myocardial infarction, through patient specific factors. During the time between when a patient leaves the hospital and attends their follow-up appointments it is critical for patients to comply with the diet and exercise advice given to them, and take their medications as prescribed. This study will help us better understand patient compliance with these activities when they leave the hospital, and guide future studies on patient mobile health application usage. We hope this study will also lead to development of better strategies to coordinate care between the time of discharge and the next follow up appointment. Potential benefits to subjects from this study would include increased medication adherence, and better adherence to health behaviors associated with decreased cardiovascular disease risk.

VII. POWER ANALYSIS

We plan to compare 30 day readmission rates amongst study participants to historical controls. We will match subjects to controls based on age +/- 5 years, sex, and insurer (commercial, non-commercial). Controls will be gathered through RPDR. Identified data sets may be used to conduct chart review of controls.

We have at least 80 percent power with 150 enrolled participants, 600 matched historical controls, with alpha equal to 0.05, to detect an effect of at least 2.5-fold for the primary clinical outcome, likelihood of readmission to the hospital during the 30 day study period with 5% readmission rates.

VIII. REFERENCES

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