Myocardial Infarction, COmbined-device, Recovery Enhancement Study

NCT03760796

April 22, 2020

Myocardial Infarction, COmbined device, Recovery Enhancement (MICORE) Study

JHM IRB - eForm A – Protocol

- **Use the section headings to write the JHM IRB eForm A, inserting the appropriate material in each. If a section is not applicable, leave heading in and insert N/A.**
- **When submitting JHM IRB eForm A (new or revised), enter the date submitted to the field at the top of JHM IRB eForm A.**

****

1. **Abstract (**Provide no more than a one page research abstract briefly stating the problem, the research hypothesis, and the importance of the research.)

Our mobile application is reinventing the cardiology discharge process to assist the heart attack patient in navigating from the hospital to home. These patients may have had a stent placed or bypass surgery to help open blocked vessels in the heart, and they will have had critical medications prescribed to help prevent further blockage. At present, the discharge process for cardiology patients is antiquated, involving last minute paper-based instructions often delivered by the least experienced health care providers. In this context, non-adherence to evidence-based therapies and readmission rates remain unacceptably high, and our app is designed to ultimately change this. There are now emerging scientific and clinical data strongly indicating that post-discharge-related complications including medication adherence and readmissions can be significantly reduced through interventions initiated prior to discharge, and our app will maximize inpatient time, engaging patients from hospital day 1. This study has shown feasibility and usability of our mobile application for hospital discharge and now primarily aims to assess 30-day readmissions. We are also collecting prospective data on ED visits, medication adherence, patient satisfaction scores, app usability, and patient activation/engagement. Our research team collaborates with inpatient care teams to assist patients with downloading the app which provides functionality allowing patients to develop medication self-management skills, coordinate follow-up appointments, learn about heart health, and connect with health resources.

2. **Objectives** (include all primary and secondary objectives)

Primary objective: To assess time to first readmission within 30 days post-discharge from the hospital in patients recovering from acute myocardial infarction who use the mobile application as compared to a historical standard of care comparison group.

Secondary objectives: To assess medication adherence, patient satisfaction scores, app usability, patient activation, user engagement, user knowledge, and cost-effectiveness in patients recovering from acute myocardial infarction who use the mobile application. To assess recurrent myocardial infarction, ED visits, observation visits, and mortality in both groups.

3. **Background** (briefly describe pre-clinical and clinical data, current experience with procedures, drug or device, and any other relevant information to justify the research)

Nearly 20 percent of the 39 million patients discharged from the hospital in the US yearly are subsequently readmitted within 30 days with cardiac patients among the leading subset of patients with early readmissions. Current evidence raises major patient safety concerns with the discharge process and rate of avoidable morbidity and mortality. Furthermore, the cost to healthcare system is $17.4 billion annually and accounted for 17 percent of total hospital payments from Medicare. Improving hospital discharge will likely reduce the rate of early hospital readmission which has been identified as a high priority for the US healthcare system to improve patient safety and reduce avoidable healthcare expenditures.

Dr. Seth S. Martin, MD, MHS, PI, has an extensive clinical research experience and experience in clinically testing mobile health technology, including a blinded, randomized mHealth Activity Trial (mActive), and evaluation of the Instant Blood Pressure mobile application. Dr. Martin leads the Cardiology mHealth Interest Group at Johns Hopkins which brings together multiple disciplines from

through the University. Francoise Marvel, MD also completed a HEXCITE Fellowship with Johns Hopkins Medicine and Technology Innovation Center focused on developing skills in designing, testing, and implementing mobile health projects with patients.

4. Study Procedures

Study design	A 1-month observational study, with a historical comparison group, involving Johns Hopkins Hospital and Johns Hopkins Bayview, as well as Massachusetts General Hospital, Reading Hospital, Franklin Square Hospital, and Union Memorial Hospital
Study duration	Each participant in the Corrie Digital Health group will join the study for the entirety of their hospitalization following enrollment and the study duration of participation is up to a year. The historical comparison group consists of English-speaking AMI patients admitted from October 1, 2015 to October 1, 2016, prior to the availability of Corrie.
Routine care	Participants in the Corrie Digital Health group will receive all routine care. Participants in the historical comparison group would also have received the standard of care at the time of admission and during follow up. We are not assuming clinical responsibility with the App as this is an informative health coaching and coordination of care app. Although we will instruct participants not to direct their clinical questions to our study team, our study team is configured to respond to queries within 24 hours during working hours and help participants connect with their care team. An email and phone number will be provided and it will be made clear that this is for technical questions related to App use. For medical questions, we will instruct patients to reach out to their primary care provider or cardiologist. The participant will be able to reach their care providers by clicking the call feature in the app. If they feel they have an emergency after hours, then they will be instructed to call 911.
Treatment failure or participant removal criteria	None
Participants receiving therapy when study ends or if a participant's participation in the study ends prematurely	Participants in the Corrie group will continue to have access to the App on their personal smartphone after discontinuation of the study or if their participation in the study ends prematurely, but will need to return the Apple Watch after the study period. If an iPhone is loaned to a participant, then he or she will need to return it after the study period.
Procedural steps	Procedural steps for the Corrie Digital Health group: a. Patients presenting with acute myocardial infarction as the primary diagnosis for admission to a participating site, and meeting other eligibility criteria, will be recruited b. Participants must be approved to participate in this research study by his/her primary care team - As resources allow, to make participation possible for participants who are not iPhone owners, we will offer an "iShare" device share program wherein we loan an iPhone along with the Apple Watch during the study period - We will also introduce a family and friends program wherein we offer the app (but not Apple Watch) to family and friends who have an iPhone and would like to use the app for the purpose of supporting the participant (participant must agree and designate the family/friend, including email and phone number, in the app) c. If the participant passes screening questions for study inclusion (i.e., owns a

	smartphone and not limited from normal smartphone usage due to conditions such as visual, motor, auditory impairment), the participant will proceed to e-Consent d. e-Consent will be done through ResearchKit on a study iPad e. The study team member will be present to guide the participant and give the participant an opportunity to ask questions before having the participant sign the consent form. If consent is provided, a Corrie sign will be placed on the door or in the room to indicate study participation to clinical staff or an Epic research flag will be placed. f. Next, the study team member will guide the participant through download of the app, and setup of the app including inputting medications and profile information. Participants will also be given a StartKit (See Supplemental Study Documents) which will include information on how to use the app to reference following discharge. g. Consenting participants will be given an Apple Watch, Silicone Healthband, and iHealth blood pressure monitor (FDA approved), and will be instructed to wear the Apple Watch/Silicone Healthband on their non-dominant wrist. The Apple Watch and iHealth blood pressure monitor will be paired with the iPhone. h. To promote privacy of health information a login will be required for access to app (created upon e-consent) and the iPhone will be set to password protected mode / touch ID activated i. At the time of enrollment, app permissions will be given. In order for an application to access any information on an iOS/Android smartphone, the application must ask the user for permission and only if that permission is granted, can the application access that information. This is inherently enforced on all applications by the operating system. In our case we only will ask for permissions to access: - relevant digital-health data from HealthKit, in particular physical activity and heart rate - photos to store an insurance card or other card like a stent card; even if the access-permission is granted, it is limited to the images specified by the user - display notifications, such as an alert to take medications - a send email function to allow users to send a PDF of their consent form or a PDF of relevant health info (e.g., medication list) to care providers; no application is allowed to read any data from the mail app j. Participants will be advised that they will need to return the Apple Watch (and iPhone, if loaned) after 30 days. They will be advised that the app can be used freely after the study's conclusion. k. Participants will receive $10 (cash, check, or gift card) after successful completion of all follow-up surveys (see below). l. At enrollment participants will fill out the mHealth literacy scale and knowledge survey. Participants will also be asked whether they own a home weight scale and blood pressure cuff and their perceived value of Corrie. m. All participants will be emailed a usability-feasibility survey, satisfaction survey, and patient activation measure 3 days after the hospital discharge. The standard email greeting is included as a Supplemental Study Document. Survey responses will be recorded electronically via REDCap. n. Participants will be given the option to take a photo in which they are identifiable using the app and can specify authorization for internal or external use on the standard media consent form. o. The study team will also assess the level of adherence based on data collected on usage and self-reported medication and therapeutic adherence collected through the app functionality as well as through The Adherence to

	Refills and Medication Adherence sub scale (ARMS). The ARMS will be emailed to participants 30 days following discharge. User engagement, patient activation, and knowledge will also be assessed 30 days following discharge through the User Engagement Scale, the Patient Activation Measure and knowledge survey. Usability and satisfaction scales will be sent at 30 days also. A question will also be asked to assess whether patients have been readmitted to the hospital or had an ED visit within the past 30 days. If a patient is readmitted to a Hopkins affiliated hospital their record will be search for confirmation and cause of readmission. If the person is readmitted to an outside hospital we will email them an Authorization for Release of Health Information form asking for permission to obtain their records of readmission. p. At 6 months following discharge, a knowledge survey will be sent to the participants again to assess their retention of knowledge. q. A survey question will be asked to assess whether patients have been readmitted to the hospital or had an ED visit within the past year. If a patient is readmitted to a Hopkins affiliated hospital their record will be search for confirmation and cause of readmission. If the person is readmitted to an outside hospital we will email them an Authorization for Release of Health Information form asking for permission to obtain their records of readmission. r. The inpatient phase of study participation will last approximately 1-5 days depending on length of inpatient admission and time of enrollment. The objective of the study team is to enroll the participant as early as possible in their hospitalization. s. All participants will continue receiving routine care. t. When the study ends or a participant's participation ends prematurely, those participants may keep their app (in which case their use will continue to be tracked), Healthband, and iHealth blood pressure monitor, but will be asked to return the Apple Watch. u. After study completion, participants will be sent the previously mentioned surveys (see Supplemental Study Documents) 3 and 30 days following discharge. If at both of these time points, participants don't respond to the online surveys within 7 days a member of the study team will attempt to obtain their responses to the surveys via a phone interview. v. After study completion, participants will participate in a phone interview, if they agree, to gather more information about their experience, using a standardized set of questions (see Supplemental Study Documents). w. Participants may be given the option to participate in future research studies. Data collection for the Corrie Digital Health group and the historical standard of care comparison group to assess the primary outcome: a. Following study completion, we will submit requests to Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center, Massachusetts General Hospital Partners group, and Reading Hospital administrative data managers to obtain the following data on both groups: age, sex, race, language, body mass index, marital status, smoking status, diagnosis of STEMI versus NSTEMI, insurance status (payor index), admission date, discharge date, type of intervention received in hospital (PCI or CABG), a discrete count of AHRQ identified Elixhauser comorbidities based on ICD-9-CM and ICD-10 diagnosis codes, discharge disposition, readmission, days to readmission, reason for readmission, ED visits, observation visits, and mortality. b. These variables will be obtained for both groups via the administrative databases to ensure standardization of variables and collection. c. For the historical control group we will query data for patients admitted to each hospital from October 1, 2015 to October 1, 2016 for a STEMI or NSTEMI. To obtain data for the Corrie Digital Health group, 30 days after the last enrolled participant is discharged from the hospital, we will send a list of

	participant identifiers to the hospital data managers. d. In an ancillary study restricted to both groups of Hopkins participants, we will perform an Epic data extraction focused on measures of 2018 AHA/ACC guideline-directed cholesterol management such as serum lipid values upon admission through 12 months of hospital discharge, whether patients were on lipid lowering therapy at the time of admission, prescription of lipid lowering therapies at the time of discharge including statins and non-statins, whether the statin was a high intensity statin regimen at the time of hospital discharge, if patients were not on statin therapy due to a history of side effects, very high risk vs not very high risk status, and whether additional lipid lowering therapies were prescribed within 12 months of hospital discharge. Data collection for patients who were deemed ineligible/declined to participate in the Corrie Digital Health group to assess selection bias: a. Following study completion, we will submit requests to Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center administrative data managers to obtain the following data on the 541 patient who were deemed ineligible/declined to participate in the Corrie intervention group: age, sex, race, marital status, smoking status, diagnosis of STEMI versus NSTEMI, insurance status (payor index), readmission, days to readmission, and reason for readmission. b. These variables will be obtained via the administrative databases to ensure standardization of variables and collection to those who were enrolled in the Corrie intervention group.

MiCORE Reading Hospital cohort:
Reading Hospital is participating in this study through a grant from the Reading Hospital Foundation. The participation of patients recruited from Reading will be limited to the 30-day (approximate) initial enrollment period. The data collected from this cohort will be used to support the study's primary outcome: 30-day readmission rate.

Study procedures for Reading Hospital	
Study design	Same as for primary cohort
Study duration	Each participant will join the study for the entirety of their hospitalization following enrollment. This inpatient phase will last approximately 1 to 5 days, depending on the length of stay and the enrollment date, with the goal being to enroll the patient participant as early as possible in his/her hospitalization. Then enrollment will continue for 30 days following discharge for an approximate study duration of 30 to 40 days.
Routine care	Same as for primary cohort
Treatment failure or participant removal criteria	None (same as for primary cohort)
Participants receiving therapy when study ends or if a participant's participation in the study ends prematurely	Same as for primary cohort
Procedural steps	Same as for the Corrie Digital Health group in the primary cohort, paragraphs a through n, and r through w. The Reading cohort will not participate in the procedural steps for the 6 and 12-month follow-ups, as described in paragraphs p and q.

	Data collection for the Corrie Digital Health group and the historical standard of care comparison group to assess the primary outcome will be the same.

5. Inclusion/Exclusion Criteria

a) The Corrie Digital Health group

Inclusion Criteria	Exclusion Criteria
-Patient admitted for acute myocardial infarction; MI present at the time of admission and Type I NSTEMI or STEMI -18 years or older - smartphone ownership	-Non-English speaking -Visual, hearing, or motor impairment which precludes use of the intervention -Persons not able to participate on due to severity of illness (e.g., intubated and on sedation in the setting of cardiogenic shock)

b) The Historical Comparison group

Inclusion Criteria	Exclusion Criteria
-Patient admitted for acute myocardial infarction; MI present at the time of admission and NSTEMI or STEMI -18 years or older	-Non-English speaking

6. Drugs/ Substances/ Devices

a. The rationale for choosing the drug and dose or for choosing the device to be used.
b. Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed.
c. Justification and safety information if non-FDA approved drugs without an IND will be administered.

Devices: Smartphone + Apple Watch + Silicone HealthBand + iHealth BP monitor +/- Apple TV
-Corrie is available for iPhone and will be available for Android. -The Apple Watch is only available for iPhone users. -The Silicone HealthBand is an optional component of the program available to all participants. -The iHealth BP monitor is available to all participants through a layered app. -As the Corrie app includes Hopkins-approved Emmi educational videos for AMI patients, and there may be an enhanced experience by participants (possibly along with friends and family) watching these videos on the television monitor in their hospital room, we will pilot installation of Apple TVs to allow the participant to AirPlay the video to the television monitor. -In discussion with an FDA-consultant, because the functionality of the application is as an organizational and navigational tool for patients, it does not require pre-approval from FDA before use with patients. It falls within the category of mobile applications for which the FDA is exercising enforcement discretion. - Patients meeting the eligibility criteria with an iPhone will receive the App, and the Apple Watch/Silicone Healthband. Those without an iPhone may be enrolled in the Device Share Program or the Android program when available. - The study team will deploy a light-weight silicone HealthBand with the team's Corrie logo. It is a one-size fits all band with no native technology functionality at this time. Participants will be asked if they have a silicone allergy prior to offering the HealthBand. The band is optional. The purpose of the Healthband is to serve as an inpatient reminder to nurses and the treatment team that individual is part of study and as a "pledge" by the participant to improve health and engage with the app.

7. Study Statistics

a. Primary outcome variable.
b. Secondary outcome variables.
c. Statistical plan including sample size justification and interim data analysis.
d. Early stopping rules.

Study Statistics	
Primary outcome:	Time to first readmission within 30 days post discharge
Secondary outcome:	ED visits, observation visits, recurrent AMI, mortality, medication adherence, patient satisfaction scores, app usability, patient activation, user engagement, 12-month readmission, and cost-effectiveness
Statistical plan including sample size justification and interim data analysis.	Allowing for 10% of drop-outs during 30-day follow-up, the aim was to recruit N=200 in the intervention group and N=1,000 patients in the comparison group to provide around 90% power at the 2-sided 5% level of significance to detect a hazard ratio of 0.5 (ie, 50% reduction in a hazard of the intervention group), assuming 85% of patients in the comparison group survive or are not readmitted by the end of study (Stata stpower). The incident readmission rate of patients in our historical comparison group admitted to JHH and JHBMC was 16 cases per 100 person-months. We aim to detect a 50% risk reduction in readmission rates because our solution is comprehensive in nature and it is estimated that 76% of 30-day readmissions are potentially preventable using proven standards of care. Our statistics will be primarily descriptive. We will examine characteristics of participants who join the study including demographics (e.g., age, sex, race/ethnicity, level of education, mHealth literacy, body mass index, marital status, occupation, annual income, insurance coverage) and clinical characteristics (e.g., severity of MI by TIMI/GRACE score, Killip Class, severity of cardiovascular disease by ejection fraction, medications, cardiac risk factor profile including dyslipidemia and lipid management characteristics as above), hypertension, diabetes, smoking, prior history of MI, and other comorbidities such as COPD, anxiety, and depression. We will examine primary and secondary outcomes as frequencies (percentage) for categorical variables and mean (SD) for continuous variables according to site of enrollment (JHH or JHBV) and type of mobile device (iPhone or Android). We will compare baseline characteristics of study participants using χ^2 and *t*-tests for categorical and continuous variables, as appropriate. In assessing readmissions and cost-effectiveness, concurrent and historical controls will be matched to enrolled patients based on sociodemographic/clinical variables, and risk stratification using APR DRG / severity of illness scores (which are shown in the literature to be predictive for readmissions). We will conduct a Cox survival analysis to compare time to first readmission between the Corrie digital health group and the historical comparison group. We will build a Markov model of cost-effectiveness with the perspective of a hospital adopting Corrie technology, taking into account the lifelong outcome and cost of the Corrie discharge process versus the standard

	Johns Hopkins cardiology discharge process.
Early Stopping Rules	N/A

8. Risks

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.
b. Steps taken to minimize the risks.
c. Plan for reporting unanticipated problems or study deviations.
d. Legal risks such as the risks that would be associated with breach of confidentiality.
e. Financial risks to the participants.

Intervention Feature	Risks	Steps to Minimize risk
HIPAA Compliance	-Participant medical information is on their personal phone	-We are using a high level of personal security password protection and encryption to meet privacy standards
Unanticipated problems or study deviations, legal risk	-Breach of confidentiality	-Study team will disclose to participant and IRB if a breach of confidentiality occurs
Financial Risks	-None	-None

9. Benefits (Description of the probable benefits for the participant and for society.)

Overall, the participants will be given access to a mobile application that can help them manage medications as well as follow-up appointments with their primary care provider, cardiologists, and cardiac rehab. In addition, they may benefit from greater knowledge about their health from information in the app. Moreover, the data that they contribute as a research participant could help others in the future.

Probable benefits, as they relate to intervention features, are as follows:

Intervention Feature	Benefit
Medication Management	-Organize and track medications -Increase medication engagement, understanding, and adherence -Stay up-to-date with refills, so as not to run out of medications
Follow-up & Cardiac Rehab	-Schedule appointments before they leave the hospital – Primary Care Provider, Cardiologist, Cardiac Rehab
E-Learning Modules for Lifestyle Modification	-Improve lifestyle modification through education and access to resources – Tobacco Cessation, Heart Healthy Diet, Exercise
Timing with Hospital Day 1 Deployment	-Able to use time inpatient to improve self-management skills and ask questions
Apple Watch / Silicone Healthband	-Apple Watch is expected to engage participants more effectively by: i) sending notifications to the Watch regarding the medication and follow-up reminders, and ii) engaging and monitoring participants' exercise activities and goals. -Silicone Healthband will serve as a reminder.
Companion App	-Connect participants with family so they understand the therapeutic and medication plan as well as what the participant has experienced.

10. Payment and Remuneration (Detail compensation for participants including possible total compensation, proposed bonus, and any proposed reductions or penalties for not completing the protocol)

- The Corrie App, iPhone, iHealth blood pressure monitor, and the Watch/Healthband will be provided at no cost to the participant. - Participants will receive $10 (cash, check, or gift card) after successful completion of follow-up surveys delivered 3 and 30 days following discharge.

11. Costs (Detail costs of study procedure(s) or drug (s) or substance(s) to participants and identify who will pay for them.)

- Development costs associated with application development have been be paid through the Louis B. Thalheimer Fund ($44,000) and Wallace H. Coulter Translational Research Partnership ($25,000). Developers are Johns Hopkins students paid through student human resources based on standard rates.