**PARTNERS HUMAN RESEARCH COMMITTEE**
**PROTOCOL SUMMARY**

**Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.**

**PRINCIPAL/OVERALL INVESTIGATOR**

David K Ahern, Ph.D

**PROTOCOL TITLE**

Dashboards for Clinician Monitoring of Patients through a Mobile Sensing Platform

**FUNDING**

Cogito Corporation

**VERSION DATE**

12/01/2016

**SPECIFIC AIMS**

Concisely state the objectives of the study and the hypothesis being tested.

The primary objective of this project is to evaluate and validate the use of Cogito's mobile sensing platform in an advanced Patient-Centered Medical Home (PCMH) with co-located behavioral health services. The Cogito mobile platform is innovative in providing mobile-enabled, scalable, noninvasive tools for detecting and monitoring behavioral health problems across populations. The platform and associated mobile application allow mobile phones to passively and securely gather behavioral data that relates to mental health clinical assessment criteria, run these data through computational models validated against standardized mental health assessments, and provide transparent feedback in both a patient-facing mobile dashboard and a clinician-facing clinical/population health dashboard. The platform enriches the types of behavioral health data that can be collected by patients and the dashboard component allows for flexible, privacy-preserving utilization.

We propose to validate the efficacy of the mobile sensing platform through a 2-arm, randomized controlled study comparing the intervention with a control group. We hypothesize that the two groups will differ across six outcome domains. Cogito plans to evaluate specifically and objectively how the platform can (1) enhance provider workflows, (2) improve patient treatment outcomes, (3) raise patient engagement, (4) increase patient self-help behavior, (5) improve population health management and research, and (6) moderate the upward trend in the total cost of care. We will use quantified metrics of each of these outcomes, measured at the beginning and end of the study, in order to compare differences between the intervention and control group.

## BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

Behavioral health programs are highly effective for patients who receive care consistently (Katon et al, 2010). However, currently, the state of the art care cannot provide clinicians with any objective information on patient health status in between clinical visits. Clinicians can not strategize, plan, or triage patients based on what happens outside of the clinic. The only means that clinicians have to gather information on patients who are not in the clinic is via arduous phone calls or mailed survey responses. When clinicians need to reach patients who are not in the clinic, these patient self ratings have been widely favored as a way of tracking one's mood in daily life. The underlying rationale is that early detection of emerging symptoms can lead to pre-emptive action (Selby et al, 2008). For example, if worsening of depressive symptoms is detected early, patient and provider can initiate steps to prevent relapse (Valderas et al, 2008). However, unfortunately, in daily life, patients use active mood monitoring at best inconsistently, or not at all. Patient self-ratings often do not match a clinician's assessment of the patient, thus providing the clinician with potentially biased point in time information upon which to make critical clinical decisions (Takayanagi et al, 2014). Therefore, as a means for detecting the deterioration of mental and behavioral health early in the service of early intervention, self-reported mood ratings are suboptimal.

Due to this urgent need, Cogito has developed a mobile sensing platform and partnered with the South Huntington Clinic, Brigham and Women's Primary Care Associates of Brookline and the BWH Department of Psychiatry. Mobile health interventions have been shown to be effective (Donker et al, 2013; Harrison et al, 2011). The Cogito mobile sensing platform is unique in providing mobile-enabled, scalable, noninvasive tools for detecting and monitoring behavioral health problems in many populations. From the rich data streams provided by the platform, Cogito delivers a system of passive behavioral monitoring, including a phone application that gathers data, stores and transfers the data securely, and provides feedback on a patient mobile dashboard. In addition, the platform includes a clinical dashboard that displays both individual and aggregate level patient information. This efficacy study will determine the value, for clinicians, patients, and researchers, of using the Cogito system in an integrated PCMH.

Cogito has previously completed an IRB approved field trial of this technology, as part of a Department of Defense (DOD) Defense Advanced Research Program Agency (DARPA) contract, to build tools to objectively identify the early stage warning signs of major mental health issues. This three-month 100-participant trial validated both the technical infrastructure and the data security protocol, and provided valuable feedback on how to correctly design mobile phone technology intervention protocols that provide the least amount of risk and greatest benefit to the participants. Participants rated the application as emotionally supportive and the process of leaving audio diaries as helpful, even though no feedback was given. Participants were comfortable with the security and privacy aspects of the technology (Place et al, 2013).

## RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

This project is designed to research the effect of a novel technology on a sample of behavioral health patients. The study design is a two-arm clinical trial with 1:1 randomization. It is a single site study. The clinics are within the Partners network. Given results from previous behavioral research involving technology interventions (Quinn et al 2011; Titov 2011), and our own unpublished data using the Mobile Sensing Platform in DARPA clinical trials, we expect effect sizes (cohen's d) of outcome changes in the .35-.80 range. We will measure change both within-subjects over the course of the trial, and between-subjects in the control and treatment group. Using conservative estimates, a minimum cohen's d = .35 and a needed power of .75, with a two-tailed independent group t-test, we estimate sample sizes per group to be 115 to achieve an alpha of .05. We will recruit 150 participants per group (300 total) to account for retention and potential data validity issues.

One arm, the experimental group, will receive the technology intervention in addition to standard treatment, while the other arm, the control group, will receive standard treatment only. Potential study participants will be assigned to the experimental or control group by coin-flip randomization.

The study will be open to patients with varying mental health and physical diagnoses and treatment programs. Patients with either an iPhone or Android smartphone will be eligible to participate in the research study. Patients with an Android smartphone randomized to the experimental group will receive a patient mobile phone application that gathers data passively from the participants' phones. The mobile application is installed and activated on the participants' phones by study staff. Patients with an iPhone smartphone randomized to the experimental group will receive a patient mobile phone application that does not gather data passively from the participants' phone. Participants with an iPhone will receive a version of the app that collects data and provides feedback on mood. Patients with iPhone and Android smartphone will not be separated out by phone type when determining randomization to experimental or control group. Patients with iPhone or Android will be equally likely to be randomized to the experimental or control group. During the study period, participants in the experimental group will receive feedback on their mobile device, while their corresponding clinicians will receive comparable feedback via the clinical dashboard. The metrics presented as feedback are calculated by analyzing the sensor data that is built into current generation mobile phones. Patients receive daily feedback, which falls under four categories: mood, sleep, social activity, and physical activity. Patients with an iPhone will receive feedback on mood only. Clinicians receive the same information for a panel of patients they treat. Users of the system can view feedback both historically and in real time. More details on the feedback system are provided in Section 3.3.

Patients in the control group will receive no mobile phone application. Neither iPhone nor Android smartphone users randomized to the control group will receive the mobile phone application. The treating clinicians for these patients will not receive any feedback on their behaviors in the clinical dashboard.

For all patients, the study period lasts 6 months per participant. At the end of the study period the mobile application will be removed from the participant's phone. For all participants in both groups, outcome metrics will be gathered at the conclusion of the study. These outcomes measures will be analyzed for differences between the control and experimental group.

All patients will continue to receive behavioral health programming, irrespective to participation in this study. Treatment at the high standard of Partners Healthcare will be provided to all participants. There will be no designated changes made to that treatment as part of this protocol. No systems will be integrated in any way into existing behavioral health or medical record technology. Treatment is not contingent on participation.

## 3.1 Inclusion Criteria:

1) Must be a patient at the South Huntington or Brookline Clinics (See Before Study Enrollment Section).

2) Must be between ages 18-75.

3) Must be receiving direct care or care management within Behavioral Health.

4) Must have a smartphone with voice and data plan as their primary phone.

5) The smartphone must meet study requirements. Current requirement is Android OS Version 4.0.0 or newer or iOS version 9.0.0 or newer.

6) Must speak and read conversational English or Spanish.

7) Must report that he/she is the primary user of the phone, meaning he/she is the sole user 90% of time the phone is in use.

## 3.2 Exclusion Criteria:

1) Active primary psychotic disorder.

2) Cognitive impairment that would impede adherence to study procedures, or ability to provide informed consent.

3) Acute suicide or homicide risk as defined by best practice clinical judgement.

4) Terminal illness as diagnosed by physician, with prognosis of survival of less than 12 months.

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

**Before Study Enrollment:**

The two clinics for the study are the Brigham and Women's Advanced Primary Care Associates, South Huntington Clinic and Brigham and Women's Primary Care Associates of Brookline. Patients, both existing and new to the behavioral health program will be referred to the study by their clinical social worker. Only patients that have been cleared by social workers for safety risk will be allowed to enroll in the study. To clear a patient, social workers will use clinical judgement to determine if the patient poses an imminent safety risk. If the clinician does not have enough information to make an informed decision about safety, he or she will reach out to the patient in order to better assess current risk. No patient will be contacted by study staff until a Social Worker has cleared the patient as not an imminent safety risk. Once a patient has been cleared, they will be asked to answer a brief series of screening questions.

These questions will be limited to the compatibility of the patient's phone and service plan, as listed in the inclusion criteria above, and will not be clinical in nature. All patients will be provided with printed information about the study and time to ask the recruiting staff any questions that may arise about any aspect of the study. A recruitment brochure and study description are attached to this application. Informed consent and administration of self-report measures can occur in one of two ways. First, a member of the research team can take informed consent face-to-face on site. Consent could happen immediately or could be scheduled for a later date; the consenting period will not be restricted to 12 hours or less from time of recruitment.

Second, research staff can take informed consent by phone. After a potential participant has received clinician approval and expressed interest in the study, s/he may be given a copy of our current IRB-approved brochures about the study and/or a brief in-person overview (5 minutes) with the research assistant. The patient will have the chance to ask the research assistant any questions. If s/he remains interested, s/he can take the Consent Form home for review and schedule a 5-10 minute phone call with research staff within the next week.

In this call, research staff can answer any questions on the Consent Form or about the study. If the patient agrees to participate, s/he can sign the form and return the signature sheet to study staff either as a hard copy or as a scanned copy through email. Research staff will then sign the copy and send the participant a final copy of the Consent Form with both signatures. The participant may decide not to participate at any time after taking the Consent Form home or at any time during the study.

A second phone call or an in-person visit will be scheduled with research staff after a signed copy of the participants consent form is received, to administer the self-report measures to the patient and instruct them on usage of the mobile application. If the participant scores positively on the last item on the Patient Health Questionnaire, research staff will page the patient's social worker. The Social Worker and patient will talk privately in a separate room or call. Once the Social Worker has cleared the patient, s/he will call research staff to notify them. Research staff will then call the patient back and commence the enrollment process.

The control group has completed their enrollment at this time. For the experimental group, research staff will help to install the mobile application on the participant's phone. Research staff will also train participants in usage of the mobile application. This can be done in person or by phone.

All participants will receive a document that includes study contact information. This document will allow participants to reach out with any questions during the course of the study. All participants will remain in the study for 6 months but can withdraw from the study at any time. Withdrawal will have no effect on behavioral health treatment. At the end of the study, outcome data will be obtained from records. Participants will continue with behavioral health programming irrespective of participation in the study.

All patients receiving behavioral health care or care management at the South Huntington Clinic are assigned to one of three provider teams. Each provider team is composed of at least one social worker, referred to as clinicians. The Brookline Clinic has one full-time social worker for all patients receiving behavioral health care or care management.

**During Study Enrollment:**

During the course of the study, participants in the experimental group will have the research application installed on their mobile phone. For participants with an Android smartphone, the application on the participants' phones will be recording data about their behavior. These data will include:

1. The application will use a combination of GPS, WIFI, and cell tower data to record the participant's approximate location.
2. The application will record when the participant makes and receives phone calls, and the length of those calls. It will create anonymous numbers to represent the phone numbers of the people the participant calls. These anonymous numbers will be the same for each phone number, such that the system can tell if the participant communicates with the same number repeatedly, but it cannot tell what the actual phone number is. This application will not record the actual phone numbers or what is said in any calls.

3. The application will record when the participant sends and gets SMS/MMS (texts). It will create anonymous numbers to represent the phone numbers of the people the participant texts with. These anonymous numbers will be the same for each phone number, such that the system can tell if if the participant communicates with the same number repeatedly, but it cannot tell what the actual phone number is. The application will not record the actual phone numbers or what any SMS/MMS says.
4. The application will record how a participant uses the mobile application including how frequently it is used and which features of the application the participant chooses to view or click. These usage logs will have no impact on the participant's standard of care or compensation.

The application will never record participants' names, the names of people in their contact list, any phone numbers, what is said in phone calls, what is said in SMS/MMS, or any details on any other applications that are used on their phone, including but not limited to email, web browsing, Facebook, financial management applications, or any medical or mental health applications. The mobile application is standalone. It does not interact with EHR in any way. It does not send data to EHR. It does not receive data from EHR.

The application will also ask the participants to leave audio check-ins. This will be the only feature currently available on the iPhone version. These audio recordings are free form single channel audio recordings about how the participant's day is going. They are stored on the phone and do not use the participant's cell phone plan minutes. Leaving audio check-ins is optional and voluntary but will be encouraged as part of the research. Any prompt for audio check-ins can be skipped. Participants are asked to complete audio check-ins weekly. Participants will be made aware that no member of the research or care team will hear what is said in these audio check-ins until after the study is complete.

Patients receive mobile feedback on their own behaviors. These behaviors are calculated via passive mobile sensing. Patients with an iPhone in the experimental group will only leave audio recordings and receive feedback on mood. While serving as a contractor to the Defense Advanced Research Program Agency (DARPA), Cogito gathered an extensive dataset of individual trauma survivors' mobile data. With the goal of developing mobile phone behavioral health monitoring for military personnel, the Cogito team ran a 3-month study of 100 participants. The participants, both veteran and civilian, were enrolled for 12 weeks during which time they each carried a mobile phone equipped with a research application. The research application passively monitored, on an intermittent fixed schedule, probe readings from sensors hardwired into the current generation mobile phone. These sensors included call logs, sms logs, locational pattern changes, acceleration, and battery levels. During the study, participants also filled out weekly self-report metrics around mood disorder symptomatology, left weekly "audio check-in" recordings of themselves speaking, and met with a clinician for a Structured Clinical Interview DSM-IV-TR (SCID) at both intake and exit dates of the study. This interview included the Mood Disorders module of the SCID testing paradigm and the

PTSD section of the Anxiety Disorders module, providing scored results of symptom presence and severity for PTSD and depression.

Cogito used structured machine learning to create models, which took in as inputs these raw data streams and predicted the clinical level assessment of symptomatology. Each model outputs a score from 0 -100, indicating the probability of presence of the behavioral component of mental health. The model uses a week of data to create a score, and updates on a daily basis.

As a part of the Phase I proof of concept efforts for the current project, Cogito researchers met with clinical staff, medical directors, and psychiatrists at the South Huntington Clinic to assess the most useful and actionable means of presenting feedback to patients.

When a patient first opens the mobile application, smiling faces represent the current health of the user. Each component will have a face indicating the score in the prior week. These values update automatically on a daily basis so that a patient can, at a glance, view the state of his or her own well-being. For any category, patients can choose to explore further for more details. By clicking on the applicable component face patients will be taken to a new screen with both current and historical information on their own behaviors.

On each component page, the patient will see their current state at the top of the screen. The patient can look below to see in the last week how their patterns have changed.

Clinicians will provide care and/or care management for both experimental and control participants.

Clinicians have access to a dashboard which tracks and reports patient behavioral metrics. The clinician dashboard is a composite of the individual dashboards viewable to each patient, presenting information for a panel of patients. The application is standalone. It does not interact with EHR in any way. It does not send data to EHR. It does not receive data from EHR. The application is only accessible from secure workstations within the clinic.

Clinicians can use the dashboard to track continuous changes over time for a group of patients and view significant changes in behavior since last appointment. This display would allow clinicians to have insight into the behaviors of their patient population between appointments, sorted by risk group, treatment, or change in behavior.

The data presented in the clinical dashboard are organized into the same components as the mobile display --mood, sleep, social isolation, and physical isolation.

Score indicates the probability of a clinically significant presence of the component. A higher score indicates a higher probability of presence of the behavior.

+/- indicates change, and directionality of change, in score from the previous appointment.

Trend presents a line graph of the score over the previous month. This line graph can be used to easily understand a continuous pattern of change, including time outside of the clinic.

Clinicians may reference changes in patient's mood, sleep, and social and physical activity within the progress notes of the patient's medical record.

**Completing Study Enrollment:**

After 6 months of monitoring, participation in the study is complete. Research staff will schedule all participants for a final appointment. A second phone call or an in-person visit will be scheduled to administer survey measures to the patient. Clinical staff will be made aware of which participants are scheduled to complete the study. In this final appointment, patients will complete the same self report packet that they did at study enrollment, and will be provided with a debrief form with information about the study. Experimental patients will receive an additional exit survey asking about their experience using the mobile research application. Participants who have previously completed the study may be later sent a copy of this exit survey.

If the patient chooses to complete the study visit by a phone call, research staff will administer all survey measures over the phone. If the patient scores positively on the last item on the Patient Health Questionnaire, research staff will page the patient's Social Worker during the call. The Social Worker and patient will talk privately in a separate call. Once the Social Worker has cleared the patient, s/he will call research staff to notify them. Research staff will then call the patient back and commence the study completion.

During this final appointment, the mobile research application will be removed from the participants' phones, and all the data stored by the application will be deleted from the participants' phones. **No data recording or tracking as a part of this research will continue from this point on.** Participants will be compensated for their participation in the study, as described in Section 4.5 of the detailed protocol. Once all patient-participants have completed the study, the dashboard will be uninstalled from clinical workstations.

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

This study will not interfere with any existing treatments or procedures that are available for the participant's condition. Nor will any aspect of the study provide a diagnosis. The participant will continue to receive standard behavioral health treatment at South Huntington or Brookline Clinics, not limited to the duration of the study. Participants in the control group will experience no changes to their daily lives or to their quality of care. The participants in the experimental group will receive access to the behavioral feedback component. The mobile application does not provide advice, treatment, programming, or diagnosis. The only novel information provided to patients and

clinicians are automated markers of behavioral activities (mood, sleep, social activity, physical activity).

In the event a South Huntington clinician should leave the study, leave the practice, or be otherwise unable to perform the duties outlined in the study's protocol for any reason, such as illness or vacation, a coverage plan will be enacted. Current clinic practice designates the social work team to oversee a coverage plan between the pool of available South Huntington Clinicians. In the event of a staff change or absence, Social Workers work together to develop a coverage schedule in which the pool of clinicians collaboratively assumes all responsibilities of the absent clinician. During the course of the study, these responsibilities will include those outlined in the protocol, such as responding to alerts should they be issued. Study staff will be made aware of clinicians' absences daily and will be provided with the contact information for the covering clinician so that any alerts generated by our system will reach a clinician that is able to respond, as necessary. Patients will not experience any disruption in care; they will not be reassigned to other care teams or providers, but will rather be followed by a covering clinician. In addition, the South Huntington clinicians have designed this mitigation plan so that each clinician will not be burdened by additional responsibility even in the unlikely event of a clinician leaving the study. This is the current working protocol in place. Furthermore, during the study, each clinician will not be assigned more than approximately one third of the research participants. Out of this one third, only half (one sixth of the total population) will be in the experimental group and require anything more than the standard of care at any time.

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.
This study poses minimal risks to the participants. Only patients enrolled in behavioral health care at the South Huntington or Brookline Clinics are eligible to participate. All information provided to participants of this study via the mobile application is purely supplemental to the behavioral health care received at the South Huntington or Brookline Clinics.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.
Currently, patients in behavioral health are monitored closely for suicidal thoughts, plans, and behaviors by gold standard safety protocol. In this protocol, participants who develop active suicidal ideation, represented by a positive score on question 9 of the PHQ-9 or positive answers on suicidal ideation questions within the Behavioral Health Assessment and by best practice clinical judgement, will be further assessed by

clinicians, and if need be, referred for urgent or emergent clinical assessment. Clinicians will only approve patients for study participation who are not at imminent risk.

Clinicians, with the support of Jane Erb, M.D., Director of Clinical and Educational Initiatives and Outpatient Services, will review the urgent or emergent safety assessment and determine if the participant can continue in the study. Any participant who requires a level of care exceeding customary outpatient services (i.e., psychiatric hospitalization or participation in a partial hospital program), or who otherwise report or manifest thoughts or behaviors suggesting possible safety concern due to participation in the study, will be removed from the study.

In addition to the safety monitoring that takes place as part of standard care, study staff will provide clinicians with notifications about patients of potential concern through a daily email. This email will be sent through the secure Brigham email system. This email will be sent each morning (Monday - Friday). Patients will be told that the notification system is active only during the business week and expectations for emergency situations will be clearly set. Social Workers will receive this email if a patient experiences a dramatic change in feedback scores in either the positive or negative direction, or if a patient has sustained a high score for an extended period of time. The email will include the number of cases a social worker must review, but no patient names. Once an email is received, clinicians will review both the clinical dashboard and the patients' medical record. At this point, the clinician will make a decision about next steps.

**FORESEEABLE RISKS AND DISCOMFORTS**

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

**Possible problems or worries of the study:** Answering questions about current psychological and personal life problems may be uncomfortable or unpleasant for some people. However, very few additional questions will be asked as part of study participation.

All participants are Brigham and Women's patients and have full access to the standard of care and clinician availability.

Patients may also feel uncomfortable about the knowledge that their behavior is being recorded by the research application. Patients are free to withdraw from the study and have the application removed at any time. Previous data suggests that this withdrawal will be minimal (less than 1% of participants in a prior Cogito mobile monitoring trial).

**Possible risks of study:** It is possible that patients in the experimental group could experience increased distress as a result of thinking of past experiences and current life issues. Additionally, consistently negative feedback from the research application could be upsetting to the participant. If a participant feels uncomfortable at any time during the

study, he or she can speak with their existing care provider at clinics where the study takes place or can choose to withdraw from the study at any time. Finally, as part of this study, there is no change to medication, treatment, care, or access to clinicians, thus there are minimal risks for enrollment in this study.

**EXPECTED BENEFITS**

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

For the control group, there are no known benefits other than the satisfaction in participating in a research study that will benefit others like them.

The hypotheses for this research program are that participants in the experimental group will have reduced treatment times, improved treatment outcomes, better engagement, and be better able to self manage health issues. Due to the novel nature of the technology platform, it is difficult to estimate the effect size of outcomes. Cogito's previous DARPA-funded field trial of the mobile sensing platform suggested that participants found great cathartic and personal value in recording audio diaries. Participants reported the associated benefits of journal keeping. Through allowing patients in behavioral health access to actionable real-time data on their own behavior, and through sharing that information with clinicians, Cogito expects that patients will experience benefits along engagement, self-management, and treatment outcomes.

For future patients, if the results support the hypotheses that the technology can improve clinician workflow and generate new research opportunities, then there is enormous clinical benefit for patients within and outside the Partners network.

Additionally, if the hypotheses are supported, provider networks may experience reduction in treatment length and emergency room visits, resulting in the potential for cost saving benefits.

Additionally, clinicians are expected to be able to more efficiently triage and attend to patient needs with the novel information provided via the Cogito sensing platform.

Finally, the dataset generated as part of this research study will be able to provide opportunity for novel population behavioral health research, providing additional downstream benefit to both researchers and patients.

**EQUITABLE SELECTION OF SUBJECTS**

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or

ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

This study is designed to test the efficacy of technology developed for an integrated behavioral health program in a Patient Centered Medical Home for adult behavioral health patients. All participants will be sampled from this population.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

Given the nature of the population of the clinic, and given the nature of the technology and the use of the smartphone application, only those who can understand, speak, and read conversational English or Spanish will be eligible to participate. The vast majority of patients in the South Huntington Clinic are fluent in at least one of these languages. The South Huntington team has clinicians who are fluent in both English and Spanish.

For guidance, refer to the following Partners policy:

Obtaining and Documenting Informed Consent of Subjects who do not Speak English
**http://healthcare.partners.org/phsirb/nonengco.htm**

**RECRUITMENT PROCEDURES**

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

All participants will be recruited from the South Huntington and Brookline Clinics, under the supervision of the clinic's staff. Patients that are existing patients of the clinic as well as patients that are new to the clinic will be recruited.

Existing patients will be reviewed by the clinical team on a weekly basis. Only established patients within the South Huntington or Brookline Clinics and who have had a visit within the last twelve months will be considered for the study.

Once a patient has been identified as a potential participant he or she will be contacted in a four step process. First, he or she will be sent a recruitment letter providing basic information about the study and detailing whom to contact for further information. This letter will also include opt-out information and a prepaid postcard providing patients with the opportunity to express interest or decline participation in the study. If the patient does not opt-out within two weeks of receiving the recruitment letter, study staff will

attempt to contact the patient by phone or email. The clinician may also reach out to the patient about the study.

If a patient has been identified as a potential participant (review and approval by Social Worker), the Social Worker may also ask the patient at their appointment if they are interested in participating in the study. If the patient is interested, the Social Worker will contact study staff after the appointment and study staff will invite the patient to complete a screening in the clinic. Alternatively, if the patient is interested in participating, he or she can tell the front desk, which will page study staff. Study staff will then invite the patient to complete a screening in the clinic. If the patient does not have time after their appointment, study staff will follow up with a phone call.

We have drafted a short one-page addition to the Behavioral Health packet for patients to complete if they are interested in learning more about our research study. They will be asked about the type of phone they use, as well as their contact information and preferences; if they are eligible, we will follow up with the preferred contact method.

We also propose posting about the study on HOPE, a Partners platform connected to Patient Gateway. Patients can log onto HOPE to learn more about the study and contact study staff if they are interested in participating. The platform features studies in the health areas of arthritis, cardiovascular disease, depression, and diabetes; our study will be included in the depression category.

Individuals that are new to the South Huntington or Brookline Clinics will undergo normal intake processing until it is determined that they are appropriate candidates for behavioral health treatment at the South Huntington or Brookline Clinics. During the initial assessment appointment with a new patient, clinicians will provide eligible patients with a recruitment letter and study description. Both documents will be available in English and Spanish. Patients will have the option to speak with study staff in a private area, leave, or schedule an appointment with study staff for a future appointment. Spanish translation service will be available.

In addition, we will have four advertisements on the available television monitors in the clinic waiting room. The advertisements will each include one or two sentences describing the study and invite interested patients to notify the front desk or call study staff at 617-525-6018.

This study does not target any minority groups, and no specific recruitment methods will be used to enhance the recruitment of women and minorities.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital,

parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

Participants will be compensated for participation in the study. Compensation is not dependent on study group assignment. As suggested by the Partner's Remuneration Policy, participants will be compensated at a reverse pro rate. Participation in each month of the study will be compensated at $20. If participants complete all 6 months of the study, they will be compensated with a bonus of $30. Thus, the total possible compensation for a participant will be $150. Participants will be paid by check.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects
**http://healthcare.partners.org/phsirb/recruit.htm**

Guidelines for Advertisements for Recruiting Subjects
**http://healthcare.partners.org/phsirb/advert.htm**

Remuneration for Research Subjects
**http://healthcare.partners.org/phsirb/remun.htm**

**CONSENT PROCEDURES**

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

Informed consent and administration of self-report measures can occur in one of two ways. First, a member of the research team can take informed consent face-to-face on site. Consent could happen immediately or could be scheduled for a later date; the consenting period will not be restricted to 12 hours or less from time of recruitment.

Second, research staff can take informed consent by phone. After a potential participant has received clinician approval and expressed interest in the study, s/he can may be given a copy of our current IRB-approved brochures about the study and/or a brief in-person overview (5 minutes) with the research assistant. The patient will have the chance to ask the research staff any questions. If s/he remains interested, s/he can take the Consent Form home for review and schedule a 5-10 minute phone call with research staff within the next week to review the consent form.

In this call, research staff can answer any questions on the Consent Form or about the study. If the patient agrees to participate, s/he can sign the form and return the signature sheet to study staff either as a hard copy or as a scanned copy through email. Research staff will then sign the copy and send the participant a final copy of the Consent Form with both signatures. The participant may decide not to participate at any time after taking the Consent Form home or at any time during the study.

Face-to-face informed consent will be obtained on location at the clinic by study staff after successful recruitment. It will take place in a private space. Consent could happen immediately or could be scheduled for a later date; the consenting period will not be restricted to 12 hours or less from time of recruitment. Patients will not be recruited or consented who are exclusively and only patients of investigators. Only shared patients of the medical center who are within the behavioral health program will be recruited. Printed study descriptions will be provided to reduce recruiter coercion.

Details about the study, including objectives, procedures, and potential risks and discomforts will be given in both oral and written form to the participant by the principal investigator or study staff. Participants will be given the opportunity to ask any questions and will be given ample time to consider whether they wish to participate. In the event that any clinical questions arise, patients will be provided with the opportunity to speak with a social worker co-investigator. They will be informed that refusal to participate will not interfere with their subsequent medical care.

All records of consent will be housed in a locked file cabinet within the office of the Brigham site lead, Dr. David K. Ahern, located at 1249 Boylston Street, 3rd Floor, Boston MA 02215.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
**http://healthcare.partners.org/phsirb/newapp.htm#Newapp**

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects
**http://healthcare.partners.org/phsirb/infcons.htm**

**DATA AND SAFETY MONITORING**

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

1. Safety and Efficacy Review:

All participants are patients within the Partners network, and benefit from all standard of care, including adverse event reporting and protocol.

In addition to the safety monitoring that takes place as part of standard care, staff will provide clinicians with daily notification about patients of potential concern through an email. These notifications will be based on the novel signals gathered through the research mobile application. These signals have not been validated to risk categories. Notifications are a security provision. In addition, all patients will continue to receive active best practice risk assessment by BWH clinicians. For this notification process, clinicians will receive this secure email if a patient experiences a dramatic change in feedback scores in either the positive or negative direction, or if a patient has sustained a high score for an extended period of time. Clinicians are responsible for reviewing the dashboard and patient notes, then making a decision on next steps.

1. Planned frequency and responsibility of review:

The secure email will be sent daily during the business week. Patients will be made aware that the notification system is only active during the business week and in the case of an emergency to follow standard protocol. Clinicians will review its contents each morning. If there is a notification, clinicians will follow a standard protocol including risk assessment. This protocol was developed in conjunction with the clinical staff at South Huntington.

The Principal Investigator, David Ahern, PhD, and the co-investigator, Skyler Place, PhD will meet bi-weekly during enrollment to review participant status with respect to any safety concerns or risks that emerge during the trial.

1. Determining if the research should be altered or stopped:

In general terms, a participant will be discontinued from the study for the following reasons: (1) The participant has experienced an adverse event that, in the opinion of the principal investigator, requires early termination, (2) The participant becomes a safety risk due to participation in the study at any time during the trial, (3) The participant withdraws consent, (4) The participant loses or damages their phone or loses their service plan to the extent that they are no longer able to adhere to study procedures.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

The participants are required to inform the clinical staff or study staff of any side effects or changes in medical or mental status due to participation in the study. Study staff must report to the principal investigator any adverse events from this study. All adverse events will be reviewed and immediately reported to the Partners Human Research Committee in accordance with ICH guidelines.

## MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

The principal and site investigators will be responsible for insuring the accuracy and completeness of the consent forms and case report forms.

Cogito Corporation will be responsible for monitoring and maintaining the quality of all data obtained via the research application. The data streams that are gathered from the participants' phones are passed through several levels of monitoring and quality assurance. Cogito possesses the capability for automated system deployment and quality assurance. All of Cogito's system components possess scripted automated QA tests run at regular intervals. Systems can be recreated using predefined profiles and tests can be run against the latest versions to ensure quality. Cogito uses a continuous integration system, Jenkins, which checks out source code nightly and compiles, build, and runs automated tests. If any code does not pass a test, developers are notified within a day. Cogito uses Foreman and Puppet systems for automated creation of system and configuration enforcement. Individual Cogito developers can leverage the automation capability to deliver software features more quickly and efficiently, ensuring that they meet acceptable quality.

All servers and centralized hardware are locked down both physically and electronically.

Centralized secure file servers hold the software code base as well as documentation and technical reports. Servers are primarily rack mounted in a dedicated storage room. Virtualization is used to ensure employees have resources they need while maximizing server capabilities. Networking infrastructure is done through a series of access-controlled devices, which restrict access of outside presences and protect inside resources.

Datasets are stored on encrypted volumes or under systems with full disk encryption, as appropriate. Data that are sensitive are locally replicated. Otherwise, data are encrypted and backed-up externally. Data access is granted under least privilege.

Cogito is fully equipped with an internal system for project management and documentation of non-PII (personally identifiable information) research materials. This system is fully backed-up and accessible by all employees, both on and off-site. Project leads maintain its organization to ensure that it is easily readable, providing up to date information on all existing projects. This wiki system facilitates cross team communication and planning.

Capacity is monitored on a regular basis and infrastructure is designed in such a way that bringing new capacities is automated within existing system architecture. Cogito supports off site work locations via shipping of Cogito controlled resources.

Cogito offices include a laboratory dedicated to mobile software design, testing, and validation. They store mobile development phones, development tablets, charging accessories, and batteries in a locked cabinet accessible only to the appropriate researchers and engineers. Mobile development phones have been rooted for control over testing. Laboratory computers are enabled with mobile testing software to download files containing raw measurements across each mobile dataset. Computers are equipped to download these data both in real-time and historically, ensuring that testing can be done both instantaneously and in the field.

The computing infrastructure has automated monitoring capacities to alert Cogito engineering for downtime, data anomalies, security risks, and directed attacks. End point data will be validated and confirmed by members of the research team.

Cogito has secured Federal wide Assurance (FWA) for the Protection of Human Subjects.

For guidance, refer to the following Partners policies:

Data and Safety Monitoring Plans and Quality Assurance
**http://healthcare.partners.org/phsirb/guidance.htm#13**

Reporting Unanticipated Problems (including Adverse Events)
**http://healthcare.partners.org/phsirb/guidance.htm#7**

## PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data;

use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

The Cogito mobile phone application will gather data on the cell phone. There will be several layers of security to protect the data. All data on the phone will be stored in encrypted format within the application directory. Data stored within this directory is only accessible by the application. Users of the phone and other phone applications will not be able to access the data stored in this secured directory. In addition, in order to open the mobile application itself, the user will have a unique username and password.

The mobile data itself is inherently identifiable (due to location information and voice prints), however every effort is made to reduce the amount of personally identifiable information included. Names will not be used, and phone numbers will be hashed to create unique identifiers. All participant data will be labeled only by their unique identifier (UID), assigned to the phone by the research staff at the start of the study. No patient medical data or name will be stored on the mobile device.

All data gathered on the phone, including passive sensor data and audio diaries, will be automatically and securely transferred in encrypted format. Once the data is successfully transferred, it will be deleted off of the phone automatically.

The data will be transferred to Cogito controlled servers, either in the cloud or at Cogito headquarters. All servers utilize full disk encryption, to allow for maximum data security. Data access will be limited to Cogito and BWH study personnel who are listed on this protocol. All research efforts will take place within the Cogito computing environment or within Partners; identifiable participant data will not be shared or taken off of Cogito servers. Access will be limited by secure virtual private network (VPN) connections and secure shell (SSH) logins to the computing environment. This ensures that when an authorized member of the study staff accesses the computing environment all traffic between the client and the server is encrypted.

While all data are de-identified using the aforementioned UIDs, patients names must be displayed on the clinician facing dashboard for efficient and accurate workflow. In order to ensure the privacy and safety of participants' data, the information needed to link UIDs to patient's names is only stored within the Cogito platform on the secured Cogito server. This means that although the clinician dashboard lists the participant's names, it does not have the information required to link these names to any UID or PII. Cogito's platform will automatically link and present only the minimum amount of data required for the clinician dashboard to function.

Study staff will create a master list that links participants' names and phone numbers to UIDs. This list is stored within the database system saved on an encrypted server, hosted at Cogito. The research staff responsible for recruitment will securely log into the Cogito platform and enter linking info at time of patient enrollment.

Only team members who need the information to perform a specific job will be granted access to names and phone numbers by the primary investigator as they need it to complete specific tasks. The list linking UIDs to personal identifiers will be destroyed at the completion of data collection and transcription.

Both the patient facing mobile application and the clinician facing dashboard have the added benefit of not storing any data from the Cogito servers. Both sides of the software are merely 'viewers' of the feedback data on Cogito servers and do not permanently store these data.

The paper self-report measures gathered at intake and outtake will be labeled only by UID. They will not be linked to participant name.

All measures will be kept indefinitely after the study is closed. The study staff as well as the overseeing IRB and specific governmental overseeing bodies may access study records. Beyond these bodies, access to identifiable data will not be granted to any other entity.

De-identified data, such as summary statistics, prediction model outputs, and averaged measures of mental health and behavior may be shared with other researchers, companies and government organizations. These data will meet the HIPAA standard for de-identification before being shared with any individuals or organizations that are not listed as study staff on this protocol.

**SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS**

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

The relevant de-identified data outlined above (versions of paper self-report measures and outcomes from medical records and scheduling systems) will be saved in Partners secure file store. All paper records of consent will be housed in a locked file cabinet within the office of the Brigham PI, Dr. David K. Ahern, located at 1249 Boylston Street, 3rd Floor, Boston MA 02215. Digitized versions will be sent directly from the South Huntington or Brookline Clinics to Cogito Corporation (7 Water Street, Boston, MA 02109) for specialized data analysis. Data will be delivered to Cogito using an encrypted USB drive or the Send Secure feature. If shared via USB, the key necessary to decrypt this information will be sent to Cogito using Partner's 'Send Secure' encrypted email feature, meaning the information required to decrypt the USB drive will not be stored on the drive itself.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw

their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

Research records will be kept indefinitely after the study is closed. Approved study staff may use research records for future studies.

The results of the study may be published for scientific purposes, but participant identity will never be revealed unless required by law.

Data may be shared with other research organizations or government agencies for scientific purposes, but participant identity will never be revealed unless required by law.

Research records and the information within them will not be used for any purpose other than that which is described in the protocol.

**RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS**

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

All data gathered on the phone, including passive sensor data, audio diaries and usage logs will be securely transferred to Cogito in an encrypted format. Once the data is successfully transferred, it will be deleted automatically off of the phone. Both the transfer and deletion of data occur automatically without the need for any user intervention.

The data will be transferred to Cogito controlled servers, either in the cloud or at Cogito HQ. All servers utilize full disk encryption, to allow for maximum data security. Data access will be limited to Cogito and BWH study personnel who are listed on this protocol. All research efforts will take place within the Cogito computing environment or within Partners; identifiable participant data will not be shared or taken off of Cogito servers.

From this point, these low level data will be fed into Cogito's machine learning algorithms and transformed into behavioral data. These data will be displayed to clinicians at the South Huntington and Brookline Clinics via the "Clinician Dashboard". Access to this dashboard is restricted to the clinical staff at the South Huntington and Brookline Clinics. Each staff member will have a unique username and password to allow for auditing of logins and usage. Participants in the study will also be able to see feedback based on their behavioral data over time via the Cogito mobile app. Both the patient facing mobile application and the clinician facing dashboard have the added benefit of not storing any data from the Cogito servers. Both sides of the software are

merely ‘viewers’ of the feedback data on Cogito servers and do not permanently store these data. This feedback does not provide advice and is not an intervention. This information is purely supplemental to the care participants receive from their behavioral healthcare provider.