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
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PROTOCOL TITLE
Virtual Reality for Pain Management in Orthopaedic Patients: A Prospective Randomized Control Study

FUNDING
Orthopedic Trauma Association

VERSION DATE
8/13/20

SPECIFIC AIMS

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

1. We will determine the feasibility of a virtual reality pain control program (VR-PCP) as a non-pharmacologic adjunct for pain management while in the hospital (i.e. patient ability and willingness to use the system measured by average time spent on the device).
2. We will evaluate if there is a difference between the average daily use of opioid medications taken by patients who received usual care pain management versus patients using a VR-PCP.
3. We will assess for differences in short-term postoperative patient-reported pain intensity (PROMIS Patient Intensity v1.0) for patients who received usual care pain management versus those who also have access to a VR-PCP.

Null Hypothesis: The use of a virtual reality pain control program does not decrease opioid pain medication consumption by patients during hospitalization after fracture fixation compared to patients who do not use VR.

BACKGROUND AND SIGNIFICANCE

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

Orthopedic surgeons rank third amongst physician prescribers of opioids to adults in the United States[4]. The deleterious effects of the opioid epidemic have been well studied at both the individual and population level.[2] [3] Orthopaedic trauma patients in particular have high rates of psychological stress and disability related to protracted narcotic usage [5]. However, opioid medications may not need to be the mainstay of pharmacologic pain

management for patients with orthopaedic injuries. For example, one recent study from the Netherlands showed that 82% of patients with ankle fractures treated in the United States were prescribed opioids at discharge, whereas only 6% of Dutch patients were given narcotics. [6]

Non-pharmacologic interventions for pain management in the acute orthopaedic injury setting deserve full investigation. Virtual reality for pain management has been used in burn patients, pediatric patients, for procedures under local anesthesia and in the chronic pain setting. Results of these investigations are promising and demonstrate reduced narcotic usage and improved pain scores.[7] [8] [9] Currently, there are no published reports on the use of virtual reality for pain management in the orthopaedic literature. By investigating VR as a non-pharmacologic intervention for pain, orthopaedic trauma patients may be able to avoid the known risks of narcotic medication while still controlling their pain and regaining function after their injury. Our study will lay groundwork for longer-term studies to evaluate the impact of virtual reality on functional outcomes, opioid usage after hospital discharge and patient satisfaction scores. VR can also be investigated for post-operative pain control across other orthopedic subspecialties.

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."

In this prospective randomized control study, all patients presenting to MGH for orthopaedic trauma surgery will be eligible for inclusion. Subjects will be identified by reviewing the list of patients admitted to the hospital or presenting to the outpatient Orthopedic Trauma clinics. Patients will be recruited from the inpatient floors, or during an outpatient clinic visit. A research team member will explain the study and its objectives to the subject. The subject will be provided a fact sheet, which outlines the study goals, data points collected, and what will happen to subject PHI. Cognitive screenings are standard of care for any patient 65 and older and are performed by a doctor on the treating team. If there is any suspicion of cognitive impairment in a patient under the age of 65, a doctor on the team will perform a cognitive screening.

Once consent has been obtained, patients will be randomized to either 1) usual care pain management or 2) usual care plus the use of a virtual reality pain control program (VR-PCP). The primary outcome of the study will be opioid usage during the postoperative hospitalization. This will be measured in average daily morphine milligram equivalents (MME). Secondary

outcomes will include length of stay and patient-reported pain scores, which will be measured using the PROMIS Pain Intensity Scale.

Inclusion criteria
-18 and older
-Patients who sustained factures treated with open reduction internal fixation. Polytrauma patients whose fractures are definitively fixed in one discrete operating room visit will be included. Presence of CAM/Mini-Cog assessments for patients over 65.

Exclusion criteria
-Cognitive impairment
-Injuries requiring staged surgical fixation (i.e. ex-fix to ORIF)
-Seizure disorder or other contraindication to VR usage
-Significant medical complications during hospitalization precluding use of a VR headset
-Significant surgical complication during hospitalization requiring unanticipated return to the operating room during index admission.

Data variables to collect
Data gathered encompasses three broad categories: Demographic data, hospitalization data, PROMIS data. Basic demographic data: MRN, DOB, DOS, age at surgery (calculated), sex, height, weight, BMI (calculated), ASA classification (anesthesia note) and race. Hospitalization data includes: AO fracture classification, narcotic type, dose, total MME (morphine milligram equivalents) and hospital LOS. PROMIS pain (v 1.0 short form 3a) questionnaires will be collected daily.
Assuming patients take an average of 45mg of morphine equivalents daily, a robust RCT would be powered at 90% to detect a 10% decrease in opioid use amongst the experimental arm. The goal of the study will be to enroll 200 patients.

Computer-generated randomization through REDCap will be utilized. Assuming a normal data distribution, mean daily opioid consumption will be analyzed using independent samples t-test. The change in PROMIS pain scores between the immediate post-op period and discharge will be compared between groups using a repeated measures ANOVA test.

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.

If patients consent to the study, they will be randomized to either 1) usual care pain management or 2) usual care plus the use of a virtual reality pain

control program (VR-PCP). Patients may be randomized before or after their surgical treatment.

The intervention arm will receive standard analgesia plus access to the use of a VR-PCP as designed by VRHealth™. After a brief orientation, the device will be left with the patient for the duration of their post-operative hospital stay. While many of our patients may have an easy time understanding and using the product, some patients may find it more challenging to use the device. We will spend the necessary time with all patients to ensure safe and appropriate use of the VR system. If at any time there is question of safe usage of the VR system, we will terminate that patients' study participation immediately.

The VRHealth™ software records time spent using the device. Please see the attached brochure for specific details about the product.

Data collection will take place in two phases. Phase one will be at the time of enrollment where basic demographic data, fracture characteristics and AO classification will be recorded in a database. The enrollment questionnaire will also include questions about recent narcotic use. Patients will fill out a baseline PROMIS pain intensity questionnaire at time of enrollment and will be given a packet of pain intensity questionnaires to be filled out daily during the hospitalization. Phase two will be after discharge where data will tallied from the PROMIS questionnaires and also be collected from the electronic medical record.

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.

The usual care for pain management at our institution consists of standing Tylenol, oxycodone PRN and IV Dilaudid PRN for breakthrough pain. Existing MGH nursing protocols evaluate when to give PRN narcotics to patients based on functional pain levels and are aimed at minimizing narcotic use. In elderly patients, the PRN dose of narcotics prescribed is generally half that of their younger counterparts (2.5-5mg q4h PRN versus 5-10mg q4h PRN in younger patients).

Geriatric fracture patients admitted to the orthopaedic trauma service are comanaged with geriatricians who also carefully monitor the effects of these medications. In this manner, the standard of care for orthopaedic trauma patients is a multimodal pain management approach aimed at minimizing narcotic usage, particularly in our geriatric fracture patients. Standard practice is to never give so much opioids, to any patient, that the renders them confused or obtunded.

We have attached the standard MGH nursing protocol for administration of PRN narcotics for your review. This is completely independent of our study and all patients in the hospital are administered PRN narcotics in this manner.

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.

The orthopaedic trauma service at MGH has a very broad range of patients with a variety of lifestyles and baseline levels of health. We recognize that in one room may be a healthy young woman who broke her ankle and in the next may be a geriatric patient with a hip fracture. We also recognize that treating a broad patient population necessitates sensitivity to the needs of different types of patients. In particular, geriatric hip fracture patients can be medically complicated and may have needs beyond their acute hip fracture. It is standard of care on the orthopaedic trauma service at MGH that patients over the age of 65 be comanaged with our geriatrician colleagues. They are an excellent resource and steward most of the post operative care for these patients.

Utilizing virtual reality in geriatric patients is not unprecedented. Here are two examples:

1) Marivian et al. Rehabilitation of the psychomotor consequences of falling in an elderly population: A pilot study to evaluate feasibility and tolerability of Virtual Reality Training. Technol Health Care. 2016 24 (2):169-75;

2)https://www.npr.org/sections/healthshots/2016/06/29/483790504/virtual-reality-aimed-at-the-elderly-finds-new-fans

In our experience, many of our geriatric hip fracture patients are out of bed on post operative day one, working with physical therapy, taking minimal narcotics and doing very well. These are the patients who, we hypothesize, may benefit from use of a virtual reality pain control program.

However, we also recognize that this is not always the case. Geriatric fracture patients are certainly at risk of delirium while in the hospital and can have other medical complications. Please note that any patient, regardless of age, who fails their Mini-Cog or CAM test (administered by a physician, further explained in the recruitment and consent process outlined below and mentioned as part of the exclusion criteria) will <u>not</u> be considered for this study. This means that geriatric patients with baseline dementia will not be considered and patients with delirium will not be enrolled. Furthermore, if enrolled, patients who demonstrate a change in mental status or fluctuating

awareness, be it from narcotic medication or otherwise, will be immediately disenrolled from the study.

The risk to subjects and their privacy is no more than **minimal risk** because subject participation is limited to the safe use of a VR device and completing short questionnaires.

Any protected (identifiable) health information will be de-identified when the study has been completed. PHI will be stored on a password-protected Partners network computer with access limited to study staff. We will be using REDCap to collect survey responses, which is hosted behind the Partners Firewall.

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.

Patients who indicate that they do not wish to participate will not be included in the study.

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.

The one other risk we can foresee is a breach of patient confidentiality. We will take the utmost care to ensure that confidentiality is maintained. Patient specific identifiers will be erased once data analysis is completed.

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.

Some patients may find that he VR pain control program helps with their pain management and reduces their use of narcotic pain medications.

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.

All eligible patients over the age of 18 presenting to MGH will be included without regard to race, ethnicity, or gender.

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.

Individuals who do not speak English will be excluded from this study because the pain control program is only available in English.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf

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.

Research staff familiar with the study inclusion and exclusion criteria will review the day's inpatient list and outpatient clinic schedule to identify potential subjects. Subjects eligible for inclusion will be approached by a member of the patient's care team to first ascertain interest in participating in research. If they indicate interest, research staff will either approach the patient in-person, or, if remote-working procedures are in place, will contact the patient via room phone or cell phone. Research staff will not contact patients who are cognitively-impaired, the designation of which is outlined below.

It is standard of care on the orthopaedic trauma service that preoperative, geriatic patients who demonstrate lack of mental competency are screened with a CAM and Mini-Cog test. If they fail these screens, the health care proxy must sign the consent form for surgery. Any patient who fails a CAM or Mini-Cog test at the time of consent for surgery will not be approached for enrollment.

All subjects eligible for inclusion in the study and who consented themselves for surgery will be approached by a physician to evaluate mental status in person. A CAM and Mini-Cog screen will be performed.

The Confusion Assessment Method (CAM)

A series of 4 questions: (1) Acute onset and fluctuating course: Is there evidence of an acute change in mental status from the patient's baseline? Did this behavior fluctuate during the past day, that is, tend to come and go or increase and decrease in severity? (2) Inattention: Does the patient have difficulty focusing attention for example, being easily distractible or having difficulty keeping track of what was being said? (3) disorganized thinking: is the patient's speech disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas or unpredictable switching from subject to subject? (4) Alerted level of consciousness: overall how would you rate their level of consciousness—alert, vigilant, lethargic, stupor or coma.

The diagnosis of delirium requires a present/abnormal rating for criteria: 1 and 2 AND EITHER 3 or 4.

A positive CAM test will automatically exclude the patient from study participation.

Ref: Inouye SK et al Ann intern Med. 1990; 113:941-8

Mini-Cog

1)Registration: Ask the patient to remember 3 words—apple, table penny—have them repeat it back to you. Then tell the patient that they need to remember these words to repeat them back to you later.
2) Clock draw test: give the patient a pre-drawn circle and as them to place the numbers on the face of the clock and draw the hands to read "ten after eleven".
3) Recall: Ask the patient to recall the three words.

The Mini-Cog test is then scored based on number of words recalled and the ability to draw a normal clock.

If the Mini-Cog test suggests any underlying dementia, the patient will immediately be excluded from study participation.

(Ref: Borson S et al. Int J of geriatr Psychiatr 2000: 15: 2031-1027)

By using these two screening tools, our goal is to enroll patients who will be able to successfully use the VR tool without subjecting them to an unnecessary risk of confusion or delirium. Vigilance in the application of these screening tools will ensure that we safely implement this study.

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

Subjects will receive no remuneration.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf

Remuneration for Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf

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.

All subjects eligible for inclusion in the study and who consented themselves for surgery will be approached by a clinician investigator for consent to study participation. A CAM and Mini-Cog screen will be performed. Any patient who is CAM positive or whose Mini-Cog screen raises concern for underlying dementia will not be enrolled in the study.

Research staff will thoroughly explain the study and its objective and will give the subject time to decide whether to participate. If research staff are working remotely and call the patient on their room phone or cell phone, they will also e-mail an electronic version of the consent form via a RedCap survey for the patient to review. The consent form will also be available to download on this link. Subjects will be given time to weigh the risks and benefits of participation in the study. After any and all questions from the subject have been answered by the research staff or the clinician investigator, written consent will be obtained from the subject. If an experienced research assistant/coordinator is the one obtaining consent, they will offer that a physician investigator will answer any additional questions posed by the patient, if preferred. If research staff are working remotely, they will obtain consent via e-signature on RedCap. This signed e-

consent form will then be sent back to the patient for their records once it has been signed by research staff, either via secure e-mail or paper copy.

Investigators and research staff will reinforce with their own patients that participation is voluntary, that they do not have to participate, and the decision not to participate will not affect their care, now or in the future.

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:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects:
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf

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.

Adverse events will be categorized as follows:

1. Non-medical issue (NMI) –- i.e. device technical problem

2. Adverse Event, not device related (AENDR) – an adverse event that occurs during the hospitalization that is unrelated to the VR headset. For example, this may include a postoperative bleeding event, cardiac complication.

3. Adverse Event, device related (AEDR) — an adverse event thought to be directly related to usage of the VR headset. For example, a patient acutely develops a medical condition secondary to using the headset. These can be subclassified as "serious" and "non-serious", see below.

All adverse events will be recorded immediately in the Redcap database being used for the study.

Management of Adverse Events:

Non-medical Issue (NMI)

These issues may arise while patients are using the VR headset. For example, the device runs out of charge, malfunctions, or freezes. These events will be reported to the study staff and triaged appropriately on an event by event basis. These issues will be addressed at the monthly study group meeting to ensure efficient device usage and study implementation. They will be reported to the device manufacturer.

Adverse Event, not device related (AENDR)

These are the medical and surgical complications that unfortunately occur after orthopaedic surgery. These include postoperative bleeding, cardiac or pulmonary complications or a multitude of other postoperative complications that occur on the orthopaedic trauma service.

When postoperative complications occur in a patient enrolled in the study, the PI will immediately be notified. The PI will be responsible for collecting laboratory data and medical history to ensure that the AE was not device related. The PI will also be ultimately responsible for determining if it is safe to continue using the VR headset in that patient. Patients who are transferred off of the orthopaedic trauma service due to a post op complication will automatically be disenrolled. All AENDRs will be re-reviewed in the weekly research meeting.

Adverse Event, Device Related (AEDR)

These are complications thought to be directly related to the device. They can be subclassified as "serious" and "not serious."

Not serious AEDRs include nausea, motion sickness, eye soreness, claustrophobia. In these cases, the Not Serious AEDR will be immediately reported to the PI. The decision to disenroll the patient from the study will be made in a conversation between the patient and the PI of the study.

Serious AEDRs such as seizure, loss of consciousness, acute change in mental status or delirium will be immediately reported to the PI. Disenrollment from the study and removal of the VR headset will occur immediately. All necessary medical care will be expeditiously provided to the patient. The AEDR will be reported to the VR headset manufacturer. Following a serious AEDR, the PI will convene all members of the research

team, any members of the patients' medical care team and the representative from the device manufacturer for a discussion about any broader implications of the serious AEDR. The event will be reported to the IRB within 24 hours of the event.

Geriatric Patient Safety Monitoring

Finally, our geriatric colleagues will be acutely aware of any geriatric patients enrolled in the study and will be extra vigilant in ensuring the devices are being safely utilized. We recognize that our geriatric patient population are at increased risk of delirium and occasionally have more volatile hospital courses. Pain scores collected daily will give the study team an opportunity to evaluate each patient daily. If at any time, the patient seems to have altered mental status or a significant change in their hospital course, they will be immediately assessed clinically, and an adverse event will be investigated.

This is a non-invasive study which does not require a DSMB. The PI will regularly monitor safety.

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

This is a non-invasive study and there will be no additional risk by participating in the study; however, if adverse events are encountered, they will be reported immediately to the PI, Site PI, and to the IRB in accordance with the IRB adverse event reporting 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 investigator is responsible for adherence to all IRB rules and guidelines. The research staff will be responsible for the accuracy and completeness of all forms, entries, and informed consent.

As an added quality assurance measure, study staff will hold monthly meetings to ensure adherence to protocol is maintained by all of the study staff as well as to monitor the status and quality of the study.

For guidance, refer to the following Partners policies:

Data and Safety Monitoring Plans and Quality Assurance
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP_in_Human_Subjects_Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting_Unanticipated_Problems_including_Adverse_Events.pdf

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.

Care will be taken to preserve the confidentiality of patient information. Information specific to the study (the questionnaires and scores) will be maintained in a private database on a secure network, to which access is limited. All iPads used for administering questionnaires are encrypted and password protected, and REDCap software is behind Partner's Firewall. Only IRB approved staff will have access to these data.

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.

None of the information collected will be sent to research collaborators outside of Partners.

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.

No specimens/data will be stored at sites outside of partners for future use.

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.

No specimens/data will be received from sites outside of partners for future use.