**Project ID: IIR 13-196-1**
**Smart Phone Application for Post-Concussion Symptom Reduction**

**HSR&D**

**Tracy Kretzmer, PhD, Principal Investigator**

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## Abstract

The proposed study will address a very important issue for the VA both currently and in the future -- the high percentage of OIF/OEF/OND Veterans who have been medically diagnosed with a mild traumatic brain injury (mTBI) and experience distressing symptoms. “Smart phone” mobile applications have become a primary source of information and communication among large percentages of Americans, especially those of the OIF/OEF/OND generation. The proposed study is a 4-year randomized control trial investigating the utility of an interactive, self-management smartphone application, “Concussion Coach”, one of a suite of mobile applications developed by the VA. The primary goal of the proposed study is to evaluate the efficacy of Concussion Coach for improving clinical outcomes in those with a history of mTBI and to determine what aspects of Concussion Coach are most useful to Veterans. An overarching goal of this line of research is to improve access among Veterans with mTBI who still have symptoms months to years after injury.

The study will pursue the following objectives:

(1) Evaluate the efficacy of Concussion Coach for improving clinical outcomes among recipients of Concussion Coach.

(2) Determine the aspects of Concussion Coach most associated with positive outcomes.

(3) Obtain qualitative information on factors associated with use of Concussion Coach or with deriving benefit from use of Concussion Coach that can be used to inform future modifications of the application and wide scale implementation.

**Design:**

Patients who meet eligibility criteria and consent to participate in the study are randomly assigned to one of two arms, either the Concussion Coach group, which will receive the Concussion Coach “Explorer” version either downloaded onto their own phone or via an iPod touch® given to them for this purpose, or the no mobile app Control group.

Both groups are assessed in a pre/post intervention design and compensated for their time completing study questionnaires. During the 3 months that they are involved in the study, the intervention group is sent (via Concussion Coach) reminders to engage with the App. At the completion of the study, both groups are encouraged to download the App for their own personal use, with assistance from the study team if needed.

In addition, individual interviews will be conducted with 10% of the Concussion Coach users to evaluate their satisfaction with Concussion Coach in terms of its ease of use, their perception and satisfaction with other TBI-related education received within the VA to date, barriers and facilitators to using Concussion Coach, and behavioral intention to use Concussion Coach in the future.

**Recruitment/data collection/status:**

419 patients (93% of our goal) with a history of mild TBI and current symptom complaints have been recruited and enrolled thus far. Participants have been recruited from both the Tampa VA

(lead site) and the Bay Pines VA, and their respective outpatient clinics (CBOCs). The average age of our participants to date is 41.5; 91% are male and most (93.0%) sustained their mild TBI over one year ago. In addition, 24 participants have completed the recorded interviews. Study recruitment is ongoing.

## List of Abbreviations

| | |
|---|---|
| CBOC | Community Based Outpatient Clinic |
| CPR | Cardiopulmonary Resuscitation |
| DoD | Department of Defense |
| OIF/ OEF/ OND | Operations Iraqi Freedom, Enduring Freedom, New Dawn |
| PCS | Post-Concussion Symptoms |
| PTSD | Post-Traumatic Stress Disorder |
| RCT | Randomized Controlled Trial |
| T1, T2 | Time 1, Time 2 |
| TBI | Traumatic Brain Injury |
| USF | University of South Florida |
| VHA | Veterans Health Administration |

## Contents

# 1.0 Study Personnel

Note: Tampa VA is the primary and coordinating site for this study. Bay Pines is the other site. Minneapolis will be considered a non-engaged site. (One of our co-investigators is located there but the study will not be conducted there).

**Principal Investigator/Study Chair**

Tracy Kretzmer, PhD 813.558-3911

Tampa VA/Univ. of South Florida

**Co-Investigators:**

Gail Powell-Cope, PhD, RN, FAAN (Co- Investigator). Dr. Powell-Cope is the Associate Chief for Research, Nursing Service, at the James A. Haley Veterans Hospital, and Director of the HSR&D COE in rehabilitation outcomes at the Tampa VA.

Sharon Haire, MS (Co-Investigator) is a Speech Therapist for the outpatient Polytrauma Rehabilitation Center Network Site, Tampa VA.

Peter Toyinbo, PhD (Statistician) is a biostatistician at the Tampa HSR&D/RR&D Center of Excellence (COE). He also holds a position of adjunct assistant professor at the Department of Epidemiology and Biostatistics, University of South Florida.

Emily King, PhD (Local Site Investigator, Bay Pines Site PI) is a Clinical Neuropsychologist at the Bay Pines VA.

Zoe Proctor-Weber, PhD (Co-Investigator, Bay Pines Site) is a Clinical Neuropsychologist at the Bay Pines VA.

Tanya Harris, MD (Co-Investigator, Bay Pines Site) - Physical Medicine and Rehabilitation at Bay Pines VA.

Tamara McKenzie-Hartman, PhD. (Research Associate, Tampa VA) is an experienced Research Associate

**Off-site Consultants/Co-Investigators (no access to data):**

Nina Sayer, PhD. (Consultant/Co-Investigator) is a Psychologist and Research Director for the Polytrauma and Blast-Related QUERI.

***NOTE: However, she will not have access to identifiable participant data and there are no study procedures taking place there. Minneapolis will therefore be considered a site that is not engaged in the study.***

**Collaborators:**

Kevin Kip, PhD, (Consultant)

Nitin Patel, MPH, (Consultant)

Susan Horrigan, MA, (Bay Pines VA) is an experienced Recruiter/Study Coordinator.

Barbara McKenzie, MA, (Tampa, VA) is an experienced Project Manager

Padmaja Ramaiah, MSBME, (Tampa VA) is an experienced Research Assistant

Angel Klanchar, MS, (Tampa VA) is an experienced Recruiter

Lee Augello, Transcriptionist (Tampa VA)

Blake Barrett, MSPH, (Tampa VA) is an experienced Data Manager

Jemy Delikat, MOT, OTR/L (Tampa VA) Interviewer

Heather Belanger, PhD. (Consultant)

Sarah Bradley MA, Provisional CPH (Tampa VA) experienced Qualitative Data Manager

# 2.0 Introduction

## Traumatic Brain Injury (TBI)

Unfortunately, TBI is a common injury among returning Veterans from OIF/OEF/OND; the majority of TBI is mild in severity. Through meta-analytic study on mild TBI, we demonstrated that athletes tend to recover cognitively within the first 7 days following injury[4] while most individuals recover completely within 3 months following a mild TBI.[5] However, a significant percentage continues to complain of post-concussion symptoms (PCS). Though there are formal criteria (i.e., DSM, ICD-10) for the PCS syndrome, PCS symptoms are variable over time (i.e., some get better over time and some do not).[6] As such, many argue that PCS is not actually a syndrome.[7] In this document, the term PCS will be used to describe symptoms rather than specific diagnostic criteria.

**Mild TBI is a Common Health and Economic Problem –** Approximately 80 to 90% of TBIs are classified as mild.[8] Mild TBI has been recognized as a major public health concern with an annual worldwide incidence ranging from 100 to 550 per 100,000.[9] The economic impact of mild TBI is substantial, accounting for about 44% of the 56 billion dollar annual cost of TBI in the United States;[10] medical costs are 76% higher on average for individuals with a history of mild TBI than for those without.[11] For those hospitalized following a mild TBI, up to 70% stay home from work for up to 6 months.[12] Even for patients not admitted to the hospital, the economic burden of mild TBI is considerable with many patients not returning to work until 1 to 3 months post-injury and having reduced self-rated productivity for several months thereafter.[12] In the

current military conflicts, the number surviving brain injuries is second only to those surviving orthopedic injuries.[13] When compared to the overall population of service members discharged from the military, those who sustained a mild TBI are more likely to be discharged from the military for behavioral reasons.[14]

**Post-Concussion Symptoms or PCS** – Immediately following a mild TBI, 80 to 100% of individuals will experience some PCS symptoms.[15] In our own research, we found the prevalence of long-term (long after injury) symptoms to be about 18%,[16] while others have reported 20 to 25%.[17 18] PCS symptoms often occur without demonstrable structural changes to the brain[19] or neuropsychological dysfunction.[15 20] As we discuss in our review of the experimental neuroimaging literature,[21] even more sensitive imaging modalities (e.g., fMRI) have yet to explain symptoms associated with mild TBI in a convincing way. PCS symptoms are not unique to mild TBI and are frequently reported in other medical conditions.[22 23] As such, some authors argue that while neurological factors may play a role in the onset of PCS, psychological factors likely play a role in the maintenance of symptoms. These symptoms may be the result of, or exacerbated by, psychological mechanisms such as poor coping style.[24] In a recent study, negative expectancies were predictive of PCS at 6 months.[17] Depression and anxiety (including PTSD) correlate highly with symptoms[25 26] and are predictive of symptoms at 3 months post-injury.[27] Many other risk factors are associated with PCS such as litigation status,[28] older age, less education, lower levels of intellectual functioning, female gender, prior head injury, poor socioeconomic status, alcohol abuse, social difficulties, environmental stress, and multiple traumas. Finally, medical factors (e.g., pain) and sleep problems are significantly associated with PCS.[29 30] Although PCS symptoms are not unique to TBI, they nevertheless have an independent association with mild TBI.[31 32] Regardless of the cause, PCS symptoms are associated with poorer quality of life[33] and have the potential to be costly to the military and VHA, both in terms of continued symptom complaints and healthcare utilization, as well as premature discharge from the military. Finally, PCS can interfere with work and family life even a year or more post-injury.[16 34]

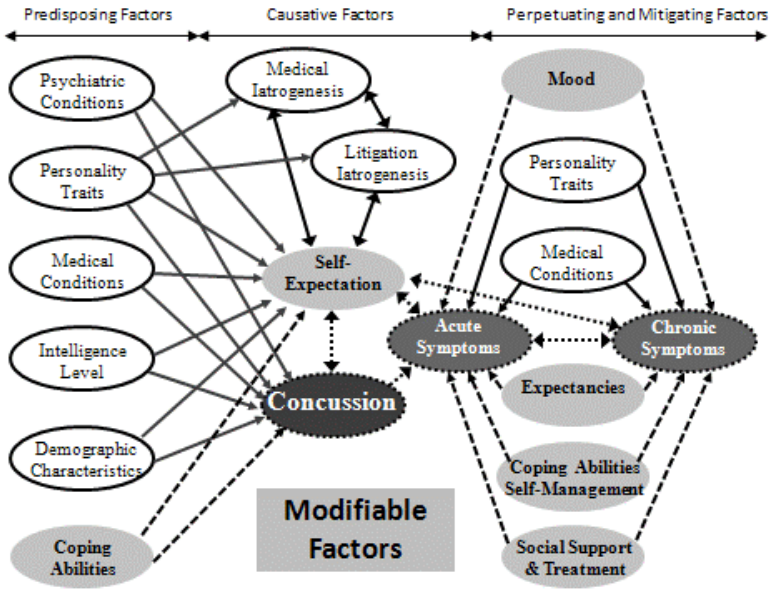
**Identification of Deployment-Related Mild TBI** – Due to population screening within the VHA since 2007, increasing numbers of patients have been identified who sustained a mild TBI and are currently symptomatic (i.e., have multiple complaints of PCS symptoms). A question for VHA is how best to effectively manage and treat these patients.

Misattribution of symptoms to a residual TBI when such symptoms are secondary to stress, chronic sleep deprivation, Post-Traumatic Stress Disorder (PTSD) or other factors can iatrogenically reinforce the misconception that these symptoms are permanent.[35]

A growing body of literature demonstrates the role of expectation in both cognitive performance and rate of symptom complaint. Simply drawing attention to the label “TBI” can cause increased symptom reporting and result in poorer cognitive performance.[36-38] If there is an expectation of post-injury problems, then in at least some individuals, such symptoms are more likely to occur.[37 39] In addition, since virtually everyone with a mild TBI experiences acute symptoms for minutes to hours, the mere presence of these symptoms can reinforce preexisting expectations and beliefs. In contrast, if there is no expectation of ongoing symptoms, then few or no ongoing

symptoms are reported.[36] Both brain dysfunction and expectation play independent and interactive causative roles.[40] Given the current political climate and the emphasis on TBI as the "signature injury" of the war on terror, research regarding patient self-expectation is particularly pertinent. Merely by screening individuals within the context of increased media attention on TBI, the stage is set for expectancies to exert an influence on the patient's belief system and to attribute many or all difficulties to TBI. In addition, there may be an inclination by the patient to attribute symptoms to TBI, rather than psychological diagnoses such as PTSD, given the perception that a physical brain injury is less "their fault" or under their control.

**Figure 1. Theoretical Model of PCS**




A Theoretical Model of PCS. Based on a thorough review of PCS literature, we posit a theoretical model of acute and chronic symptom etiology and maintenance, as depicted in Figure 1.[40] Factors that are likely most modifiable are shaded light gray.

**Providing Education to Reduce PCS in Civilians** - Psychoeducational interventions include giving patients information about common symptoms following mild TBI, typical time course of symptoms, expectancy effects, relation of symptoms to stress, and strategies for symptom management and reattribution. These educational interventions have been shown to result in significantly shorter average symptom duration and significantly fewer symptoms at follow-up in civilians.[41] [42] Several standardized, empirically supported treatment manuals are available.[43] [44] Even an early single session intervention can prevent the syndrome as effectively as traditional outpatient therapy.[41] We have extensively reviewed the studies published to date with regard to non-pharmacological approaches to the treatment of PCS.[45] The literature consistently demonstrates that psychoeducational interventions, with provision of education about mild TBI, typical recovery, and symptom management strategies are effective. However, as the existing literature is almost entirely civilian seen within days to weeks after injury, it is still unknown if Veterans with combat-related mild TBI seen months to years' post-injury and post-combat can benefit from this type of intervention.

Only one study utilized a chronic population. Tiersky et al.[46], studied patients with mild to moderate injuries who were an average of 5 years post-injury. Significant treatment effects for a

rehabilitation program consisting of psychotherapy and cognitive remediation were found for some psychological symptoms (e.g., anxiety and depression) but the treatment was much more involved than other studies that focused on acutely injured patients (i.e., 33 treatment sessions total). As such, it is currently unknown if brief psychoeducational interventions will be helpful in patients who are seen months to years after their injuries. The brief psychoeducational approach that has been successful with patients soon after injury has never been tested in a subacute or chronic sample.

## Mobile Technology

Within VHA, nearly a third of returning Veterans referred for an evaluation following a positive screen for mild TBI fail to arrive at the facility (Cifu, personal communication). Lindley et al. found,[47] in their analysis of mental health screening of OEF/OIF Veterans, that approximately 40% of those referred for care do not attend even one appointment. Some of the barriers to care are likely logistical, such as lack of transportation. In response, the VA has been at the forefront of finding new and creative ways to reach Veterans, such as MyHealtheVet, telehealth, mobile medical clinics, and most recently, "smart phone" technology.

Mobile phone applications have become a primary source of information and communication among many Americans, especially those of the OIF/OEF/OND generation. A Pew Research Center survey estimated that 79% of 18 to 29 year olds use mobile application technology.[48] Mobile phones now offer multiple functions such as calendar, photography, music, instant messages, video, and social networking. Furthermore, users can download applications (i.e."Apps") that serve a variety of functions. Smart phone technology is increasingly being used in medical settings[49] and for the provision of health-related education, including CPR instruction, communication skills, diabetes self-management, sex education, and other uses. Many apps allow for patients to track symptoms and receive messages.

The VA and Department of Defense are investing heavily in mobile technology. The VA has over 15 mobile apps in various stages of development to assist Veterans and their families with issues ranging from mild TBI to parenting. Julia Hoffman, is the lead author of the VA's new Concussion Coach, as well as the award-winning PSTD Coach.

**The VA's Concussion Coach is an interactive, self-management tool designed to address the modifiable 'causes' of PCS identified in our theoretical model.** Investigating the utility of the Concussion Coach smart phone application for increased self-management and PCS reduction is the primary focus of this study. Concussion Coach, which is described in the Methods section, is based on an evidence-based review of the PCS intervention literature but delivers it via an innovative, interactive, self-management platform. Randomized controlled trials have demonstrated the effectiveness of a self-management approach to chronic disease in improving self-efficacy, physical and psychological health, and reducing health care utilization in patients with arthritis, lung disease, stroke, heart disease, and multiple sclerosis.[1 2] We found no studies that applied a chronic disease self-management approach for treating PCS, though such an approach is clearly applicable given the longstanding presence of symptoms and multifactorial contributing predictors (many of which are potentially malleable), as outlined in our model above.

Interactive, computer-based patient education programs have demonstrated utility in a variety of different medical conditions.[3] They draw on constructivist learning theories that highlight the importance of active self-paced learning. In a recent review, interactive computer-based patient education programs were found to be as effective or more effective than education provided by healthcare professionals in 7 of 8 studies[3] in terms of various clinical outcomes, satisfaction, knowledge gain, and cost savings. Theories of self-management rely on social cognitive theory that posits behavior is influenced by personal factors, environmental factors, and behavior itself.[50 51] Key personal factors include self-efficacy (or confidence in one's ability), outcome expectancies, and mood. Beliefs that people have about themselves are key elements in the exercise of control and personal agency; individuals are viewed both as products and as producers of their own environments and of their social systems. Improved self-efficacy, expectancy effects, and improved mood, have all been linked to improved health outcomes across many different patient groups. We will attempt to answer the following research questions:

**Q1:** Is Concussion Coach effective in improving PCS and psychological distress in those with a history of mild TBI?

**Q2:** What are the moderators and mediators of the effectiveness of Concussion Coach?

(a) Is comfort with technology related to efficacy of Concussion Coach?

(b) Is perceived social support related to efficacy of Concussion Coach?

**Q3:** Does use of Concussion Coach (a) increase Veterans' knowledge about TBI and change Veterans' attribution of symptoms from mild TBI to less "pathological" explanations (e.g., stress, post-deployment re-adjustment, or other causes), (b) increase Veterans' self-efficacy in coping with symptoms?

More broadly, are the effects of Concussion Coach on PCS and psychological distress mediated through change (from T1 to T2) in Veterans' perceptions and knowledge of the illness and in self-efficacy?

**Q4:** What aspects of Concussion Coach are most associated with positive outcomes among recipients of Concussion Coach? Is more frequent use of specific components of Concussion Coach associated with greater improvement, relative to other components?

**Q5:** What are the factors associated with use of Concussion Coach or with deriving benefit from use of Concussion Coach that can be used to inform future modifications of the application and wide scale implementation?

## 3.0 Objectives

The proposed study is a 4-year randomized control trial investigating the utility of an interactive, self-management smartphone application, "Concussion Coach," one of a suite of mobile applications developed by VA. The primary goal of the proposed study is to evaluate the efficacy of Concussion Coach for improving clinical outcomes in those with a history of mild traumatic brain injury (mild TBI) and to determine what aspects of Concussion Coach are most

useful to Veterans. An overarching goal of this line of research is to improve access among Veterans with mild TBI who still have symptoms months to years after injury.

**Aim 1. Evaluate the efficacy of Concussion Coach for improving clinical outcomes among recipients of Concussion Coach.**

**Hypothesis 1 (Primary Hypothesis):** Patients randomized to receive Concussion Coach for 3 months will have (a) lower Post-Concussion Symptom severity (PCS) and, (b) lower psychological distress, compared to patients randomized to a no intervention control group, after adjusting for baseline severity and other potential confounders.

**Aim 2. Explore mediation/moderation of Concussion Coach effects on clinical outcomes among recipients of Concussion Coach.**

**Hypothesis 2:** The effects of Concussion Coach on PCS (and psychological distress) will be greater for Veterans who have (a) greater comfort with technology at baseline than for those who are less comfortable; (b) greater social support at baseline than for those with less social support.

**Aim 3. Determine the aspects of Concussion Coach most associated with positive outcomes.**

**Hypothesis 3:** If Concussion Coach improves Veterans' (a) knowledge about TBI and attribution of symptoms and/or (b) self-efficacy in coping with symptoms, Veterans will have less PCS and psychological distress.

**Aim 4. Obtain qualitative information on factors associated with use of Concussion Coach or with deriving benefit from use of Concussion Coach that can be used to inform future modifications of the application and wide scale implementation.**

**Hypothesis 4:** More time spent on (a) Concussion Coach use, and (b) specific interactive components of Concussion Coach (i.e., the "tools" section) will be associated with lower PCS symptom severity after adjusting for baseline PCS values and potential confounders.

**Research Question 1:** What barriers prevent patients from using the Concussion Coach and from improving on PCS symptom severity?

**Research Question 2:** Are there facilitators that support Concussion Coach's use and enhance its efficacy?

## 4.0 Resources and Personnel

The study will be conducted at two sites – Tampa VA and Bay Pines VA. Both sites will recruit from their primary hospitals, and also their respective CBOCs (outpatient clinics).

The key personnel's roles in the study are described in section 1.0. The only contractor is Vertical Product Development to create the explorer version of the App.

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- Include where and by whom the research will be conducted.
- Provide a brief description of each individual's role in the study. Be sure to indicate who will have access to protected health information and who will be involved in recruiting subjects; obtaining informed consent; administering survey/interview procedures; and performing data analysis.
- If applicable provide information on any services that will be performed by contractors including what is being contracted out and with whom.
- If applicable provide information on any Memoranda of Understandings (MOUs) or Data Use Agreements (DUAs) that are being entered into including with whom and for what reason.

# 5.0 Study Procedures

## 5.1 Study Design

- Describe experimental design of the study. Include sequential and/or parallel phases of the study, including durations, and explain which interventions are standard of care.
- Include a description of how anticipated risk will be minimized and include an analysis of risk vs. potential benefit.
- Provide description of the study population (delineate all categories of subjects – patients, providers, family members, employees, etc.). Include anticipated enrollment numbers
- As applicable, provide information on any added protections for vulnerable populations.
- If applicable include information on data.

Patients who meet eligibility criteria and consent to participate in the study are randomly assigned to one of two arms, either the Concussion Coach group, which will receive the Concussion Coach "Explorer" version either downloaded onto their own smart phone or via an iPod touch® given them for this purpose or the no mobile app control group. Study personnel will explain the purpose of the study, complete the informed consent process in person or over the telephone, obtain the random treatment assignment and introduce the participant to his/her baseline evaluator, if appropriate. The random assignment to intervention will be accomplished in blocks within each site. While small block sizes allow intervention group sizes to be very similar it may make the allocation process predictable. Therefore, to reduce selection bias and achieve balance across the intervention arms, a sequence list of individual assignments by random block sizes will be generated.

Both groups will be assessed in a pre/post intervention design and will be compensated for completing study questionnaires. During the time that they are involved in the study, the intervention group will be sent (via Concussion Coach) reminders to engage with the App. Their use (e.g., total time spent on each component of the App) will be collected electronically. Both

groups will receive care as usual (meaning their regularly scheduled VA appointments and medications). At the completion of the study, both groups will be encouraged to download the App for their own use, with assistance from the study team if needed (see Figure 2).

**Description of Intervention & Training**

The Concussion Coach is designed to provide psychoeducation, self-assessment, and treatment of PCS following a mild TBI. The PI and three of the co-investigators were co-developers of Concussion Coach. The public-facing Concussion Coach will be available for free download from a public marketplace and available for use with most mobile devices. The application has the advantage of privacy and anonymity, thus addressing the stigma often expressed as a barrier to seeking treatment. A mirror version of the public version, called Concussion Coach "Explorer Version", was developed and is being used for this study. Unlike the public version, it has the capacity to collect usage information, such as length of time spent on each part of the app, self-report ratings of symptoms and distress, and identification of "favorites" among the self-help tools. This data can be uploaded in a de-identified form to a HIPAA compliant server. Other than the ability to collect data, it will be exactly like the "real" Concussion Coach. The Explorer version will be developed by our collaborators, Vertical Product Development, which developed Concussion Coach, PTSD Coach, and PTSD Explorer version. Explorer versions are especially useful as they allow for unobtrusive, highly detailed, real-time data collection without relying on patient self-report. In addition, the Concussion Coach will be an 'opportunistic' exporter of data. It will upload data to the server whenever it has new data and is in a Wi-Fi zone; participants do not have to have a home wireless network. If they never enter a Wi-Fi area, we will collect the data from their smart phone or iPod device at the second and final study visit. We will utilize ohmage, an existing open source technology stack, to port the app to the server.

Concussion Coach has the following components in addition to a 'Resources' section:

- Psychoeducational content covering basic information about mild TBI, associated symptoms, and resources for additional help. The information is derived from various VA and DoD informational websites and is based on the scientific literature on TBI. There are approximately 10 headings (e.g., "What is TBI?") that can be clicked to receive educational information. Additionally, each answer includes an icon, visually represented by an ear that the user may tap in order to hear the information spoken aloud.
- Self-assessment using the Neurobehavioral Symptom Inventory (NSI), a validated measure of 22 PCS that is used broadly throughout VA, DoD, and civilian settings. Users are provided with interpretive feedback about the severity of their symptoms and information about their score relative to the last administration. Repeated self-assessment can be viewed in graphical form. Users can also schedule future assessments and reminders to complete the NSI.
- Portable skills are available to address the Veteran's symptoms, regardless of etiology. The user identifies and rates the distress from a list of symptoms. Depending on the problem and the severity, the user is routed to any of a number of helpful skills depending on the symptom and severity; the user is then asked to rate his/her distress following use of the stress management tool. Feedback and recommendations are provided based on the

change in score. Irritability, sleep problems, memory problems, and headaches are the four foci of this app. If a symptom is rated 9 or 10, crisis strategies are provided.

**Training**: Concussion Coach will be publicly available just as is the PTSD Coach. To facilitate its use, the developers will create a brief handout to provide basic instructions on its use. Dr. Julia Hoffman, the primary author of both the PTSD Coach and the Concussion Coach, will be responsible for this content. Therefore, we are testing Concussion Coach as it will be implemented outside of this trial, increasing applicability of our findings to the "real world."

**Safety Plan**: If participants voice suicidal ideation/plan either in person or via telephone to study staff, hospital policy will be followed. There are specific policies in place for crisis management both via telephone and in person. All research personnel with participant contact will be trained per this policy. In addition, interviewers and research assistants will be trained by the PI on how to identify and respond to participants in distress. This will occur through role play, readings, and other pre-study group trainings. All proposed pertinent study personnel have clinical training/experience and suicide/violence assessment experience. They will follow VA Suicide Prevention guidelines and are required to have had all VA research trainings which include Suicide Prevention guidelines.

**Data Collection Methods:** After informed consent and randomization, participants will complete baseline study measures. At follow-up, participants will be re-assessed using the same measures via mail, telephone or in person with telephone reminders, if needed. In addition, Concussion Coach will also collect the extent of their interaction with the application during their participation.

***Individual interviews*** will be conducted with at least 10% of the Concussion Coach users to evaluate their perception and satisfaction with other TBI-related education received within the VA to date, their overall satisfaction with Concussion Coach e.g. its ease of use, perceived barriers and facilitators to the use of the App, behavioral intention to use Concussion Coach in the future and recommendations for improving it. This 10% sample will not be random – rather we will solicit interviews from those who improved using PCS Concussion Coach, those who did not get better or became worse, and those who did not use the App during the study period or used it infrequently. In addition to qualitative questions about barriers and facilitators, interview questions will include quantitative assessment of satisfaction (e.g., rating scales of satisfaction). Interviews will be conducted by experienced trained interviewers (e.g., Delikat) and will be audio recorded. Participants will already be consented in person or over the telephone, so the interviewer will identify and briefly recap the consenting process, the project, and then ask permission for audio tape recording the interview. Interviews will be conducted by phone or in person based on participant convenience. The interviewer will use standard communication techniques to stimulate discussion such as generic prompts (tell me more), summarizing statements, silence, and eye contact. If the respondent exhibits adverse reactions, such as shame, during the interview, every effort will be made to encourage him or her and they will be reminded of their rights as participants.

**Risk Minimization Plan:**

The educational program is self-administered and participation is strictly voluntary. There are no known risks involved. The PI will inform participants of all methods used to maintain confidentiality of information. Participants will be assured of the confidentiality of the data and that no one outside of the research team will have access to the raw data.

A lack of privacy may be a potential risk; therefore, participants will be assured of the confidentiality of the data and that no one outside of the research team will have access to the raw data. The PI will inform participants of all methods used to maintain confidentiality of information.

All data will be coded by number and stored in locked computer files. Only the investigators will have access to the data. Individuals will be informed that they may be contacted in the future for continuing involvement in this research study if funding is maintained. The smart phone application will be encrypted and the encryption will be FIPS 140-2 validated.

De-identified data from the USF server will be sent to the PI via password protected email, using winzip software.

Data collection instruments will be collected using Microsoft Access Database or on paper and pencil instruments and will be collected on scannable forms using Teleform technology. We have used *Teleform* for five years in a variety of projects and have found it to be accurate, reliable, and efficient. Scanning allows the data to be directly placed into a database for subsequent data cleaning and analysis using SAS. Data will be housed in Tampa. Care will be taken to ensure that sufficient backup procedures are in place. To assure intact data files, we will copy the raw data file into a data file for computation and analysis so that if there are computational errors or computer problems, the raw data will remain unchanged. This system has been used in several previous studies, and it ensures confidentiality and adheres to all HIPAA guidelines.

Once data is either hand entered or scanned into databases, electronic data will be maintained on password protected VA servers in Tampa with two firewalls within a research building that is kept locked with an entrance manned by security personnel. Physical paper data will be housed at 8900 Grand Oak Circle, Room 183 at the James A Haley Hospital in Tampa, and will be kept in a locked file cabinet in a research building that is kept locked with an entrance manned by security personnel. At Bay Pines VAHCS, physical paper data will be stored in locked cabinets in a locked office located within a locked building.

Data from the Concussion Coach application will be electronically sent to the USF server. It will be de-identified (but matched to a study number that will identify the individual to the study coordinator who will need it for follow-up). It will be periodically emailed to study personnel at the Tampa VA via password protected email, using winzip software.

Finally, data from the recorded qualitative interviews will be transcribed by VA key personnel or by the Alpha Transcription Corporation and placed in the secure folder of the VA server as

described above. Alpha Transcription Corporation will be given access to a specific secure folder of the VA for the recorded qualitative interviews data to be transcribed.

The risk associated with this study is minimal. The only link between participant data and their identity is the study code (and the list matching the study code numbers to the individual will be securely held by the study coordinator). The research data will be kept on a secure VA shared drive. A secure folder will be set up, allowing access to only key personnel that need access to the data. Once a key personnel individual is no longer part of this study their name will be removed from the list of key personnel with access. They will no longer be able to open the folder. The ISO and Privacy Officer will be notified within one hour of any improper use or disclosure, as well as any other violations of local policies.

Providing education following a mild TBI is the most well researched and valid intervention for reducing overall post-concussion symptom severity. We postulate that mobile technology is likely to be an efficient delivery mode of this psycho-education and will enhance access for Veterans. The potential benefit of learning about expected recovery, learning self-management techniques, learning how to get support and assistance, as well as the ability to do these things at one's own pace and in one's home environment far outweigh the minimal risks associated with participation.

**Safety Plan:** If participants voice suicidal ideation/plan either in person or via telephone to study staff, hospital policy will be followed. There are specific policies in place for crisis management both via telephone and in person. All research personnel with participant contact will be trained according to this policy. In addition, interviewers and research assistants will be trained by the PI on how to identify and respond to participants in distress. This will occur through role play, readings, and other pre-study group trainings. All proposed pertinent study personnel have clinical training/experience and suicide/violence assessment experience. They will follow VA Suicide Prevention guidelines and are required to have had all VA research trainings which include Suicide Prevention guidelines.

## 5.2 Recruitment Methods

- State how many subjects will be needed.
- Describe when, where, how and by whom potential subjects will be identified and recruited.
- Describe materials that will be used to recruit subjects, e.g., advertisements. Include materials as an appendix or separate attachment.
- Describe any payments to subjects, including the amount, timing (at the end of the study or pro-rated for partial study participation), method (e.g., direct deposit or check), and whether subjects will experience a delay in receiving the payment.

**Study Population:** Approximately 600 patients with a history of mild TBI and current symptom complaints will be recruited. Participants will be recruited from both the Tampa VA (lead site) and the Bay Pines VA, which is located about 20 miles from the Tampa VA within VISN 8, and their respective outpatient clinics (CBOCs). Both sites are Polytrauma Network Sites (PNS) which are designated sites within the VA Polytrauma System of Care that assess TBI outpatients and see the majority of mild TBI patients.

To ensure that we capture a broad spectrum of Veterans with a history of mild TBI, we will also supplement recruitment from the VA with several methods aimed at recruiting potential community-based TBI participants. Primary recruitment will be through TBI-relevant clinics at both Bay Pines and Tampa VAs. Both facilities have active PNS clinics (Polytrauma Network Sites), Post-Deployment, PTSD and other clinics with patients identified to have a history of mild TBI. The recruiter and PI/Site PI and co-investigators will identify potential participants through their regular contact with patients. When a clinician determines that a patient is eligible (based on study inclusion/exclusion criteria), the clinician will either approach the patient to discuss his/her interest in research, or will refer the patient to a member of the research team. The recruiter, or other co-investigators, will approach potential participants, inform them of the study, and verify their eligibility. If potential participants are interested, the recruiter will obtain written informed consent and HIPAA authorization.

It is possible that potential participants will not be able to meet in person and will need to talk to a study investigator via telephone. In this instance, a study investigator will explain the study determine that the participant is interested in participating, and screen for eligibility. If eligible, an appointment will be scheduled for the participant to meet in-person with the study team members to complete the consenting process. Or, for interested participants who reside a distance away from the VA and would like to participate in the study the ICF will be done over the telephone. After the Telephone Consent process is complete, a copy of the study ICF/Information Sheet will be mailed to the participant for his/her file. Once the consent process is completed via telephone with those participants who are not able to physically be at either the Tampa or Bay Pines VA site location, they will be asked to complete the study Baseline questionnaires. When speaking to potential participants via telephone, the study team member will be physically located at the Tampa or Bay Pines VA.

To facilitate the recruitment process, we will hang flyers throughout the hospitals and catchment area (e.g., outpatient clinics) of each hospital, and provide the clinical team with hospital-based flyers and business cards to give to interested patients. (See the Appendix for the hospital-based flyer and business card.)

***Relevant Veteran Events:*** With permission from event organizer(s) and/or department manager(s), we will attend and/or contribute to relevant events around the Tampa/St. Petersburg area. Methods of recruitment during events may include but are not limited to, providing flyers, cards, and/or give-away recruitment materials. It may also involve giving a short presentation on the participation opportunities, collecting contact information from interested participants, or leaving a basket of give-away recruitment materials at a desk for interested participants to pick up at their leisure (the flyers, business cards, and give-away recruitment

materials are attached as an Appendix). Events and departments could include but are not limited to the University of South Florida's Veteran events and program, The Defense and Veterans Brain Injury Center events, Family Care events, Yellow Ribbon Reintegration Program Events, MacDill Air Force events, or Family/patient educational meetings. Interested participants will have the option to take recruitment materials away with them and make contact with a study team member at a later date themselves and/or leave their name, contact details, and preferred day/time with the study team member at the event who will contact them at a later date to initiate consent and enrollment. We will not be consenting participants at the Yellow Ribbon event.

***Publicizing though various forms of media:*** We will publicize the study through various forms of media. We will contact new organizations and include new forms of media as possibilities when they are brought to our attention or as recruitment needs change. We will not submit these new organizations for IRB review but will use approved methods. Future possibilities include but are not limited to the National Military Family Association, Stars and Stripes, or Military Base newspapers. Currently, we plan to publicize in Military Times, Veterans of Foreign Wars Magazine, and through social media of relevant organizations. A half page community based color advertisement (circulating between two Half Page Ads, see Appendix) will be placed in the Military Times Combined newspapers (militarytimes.com; militarytimesedge.com; Army Times, armytimes.com; Navy Times, navytimes.com, Air Force Times, airforcetimes.com; Marine Corps Times, marinecorpstimes.com). A fullpage advertisement (as per the community-based flyers) will also be placed in the Veterans of Foreign Wars Magazine (official publication of the Veterans of Foreign Wars of the United States). Additionally, the social media mangers of the following organizations (Wounded Warrior Project, Army, Marines, National Guard, Air Force, Navy, Brain Line) will post a brief advertisement (including a link to a PDF version of the flyer) on their Social Media sites (e.g., Facebook, Twitter feeds, press release, attached in the Appendix). Please see the attached Agreements to Support Publicizing Efforts and weblinks to social media pages from the related social media managers (Appendix). At Bay Pines VAHCS, efforts will also be made to contact Veterans who subscribe to Veterans Health via Email Blasts generated by the Public Affairs Officer.

Finally, we will send letters to potential participants, identified through VA national databases (with appropriate permissions), who have been screened and evaluated for concussion within the Bay Pines or Tampa VA systems of care and who were identified through that process as having a history of concussion.

Potential participants may respond to these various publicizing efforts via the study telephone contact details. For those recruited from the community, the study team member will explain the study over the telephone, determine that the participant is interested in participating, and screen for eligibility. If eligible, the participant will complete the consent process over the telephone or an appointment will be arranged for in-person consent at the VA. After the telephone consent a copy of the ICF/Information Sheet will be mailed to the participant for his/her file. When speaking to potential participants via telephone, the study team member will be physically located at Bay Pines or Tampa VA facilities.

Participants will be reimbursed for the time spent completing the questionnaires. Payment will be provided via a check sent to the Veteran's home or through direct deposit. We will compensate participants $20 for the time they spend completing the first assessment and $10 for the time they spend on the second assessment. In addition, 10% of participants who complete an interview will be compensated for their time ($10).

5.3 Informed Consent Procedures

Informed consent will be obtained from all participants. Potential participants will be approached by study personnel (recruiter or other study team member). This will either be done via mailed letter, in person or by phone. It is also possible that a potential participant will see one of our flyers or other marketing and call the recruiter. If recruited in person, the recruiter will ascertain eligibility and do informed consent in a private office. These particular participants will be identified by clinical study personnel or other approved means.

It will be explained to participants that if they choose not to participate they will receive the services that they would ordinarily receive and that is there is no penalty for not participating and that the study is entirely voluntary and that they are free to withdraw from the study at any time. All personnel involved in the informed consent process will be trained by the PI to ensure that the process is explained properly and that there is no undue coercion. The voluntary nature of the study will be emphasized and potential participants will be able to take home the consent document to read at their leisure if they prefer.

Primary recruitment will be through TBI-relevant clinics at both Bay Pines and Tampa VAs. Both facilities have active PNS clinics (Polytrauma Network Sites), Post-Deployment, PTSD and other clinics with patients identified to have a history of mild TBI. The recruiter and PI/Site PI and co-investigators will identify potential participants through their regular contact with patients. When a clinician determines that a patient is eligible (based on study inclusion/exclusion criteria), the clinician will either approach the patient to discuss his/her interest in research, or will refer the patient to a member of the research team. The recruiter, or other co-investigators, will approach potential participants, inform them of the study, and verify their eligibility. If potential participants are interested, the recruiter will obtain informed consent and HIPAA authorization. Or, if interested participants reside a distance away from the VA and would like to participate in the study the informed consent process will be done over the telephone.

It is possible that potential participants will not be able to meet in person and will need to talk to a study investigator via telephone. In this instance, a study team member will explain the study, determine that the participant is interested in participating, and screen for eligibility. If eligible, an appointment will be scheduled for the participant to meet in-person with the study team member to complete the consenting process. Or, if interested participants reside a distance away from the VA and would like to participate in the study the consenting process will be done over the telephone. ICF/Information Sheet will be mailed to participants consenting over the telephone. When speaking to potential participants via telephone, the study team member will be physically located at the Tampa or Bay Pines VA.

| Project Team Member | Degrees | Project Role | Obtaining Informed Consent? Yes/No |
|---|---|---|---|
| | | | |
| Gail Powell-Cope | PhD | Co-I | Yes |
| Tracy Kretzmer | PhD | PI | Yes |
| Peter Toyinbo | PhD | Statistician | No |
| Heather Belanger | PhD | Consultant | No |
| Sharon Haire | MA | Co-I | Yes |
| Sarah Bradley | Provisional CHP | Qualitative Data Manager | Yes |
| Emily King | PhD | LSI | Yes |
| Zoe Proctor-Weber | PhD | Co-I | Yes |
| Tanya Harris | MD | Co-I | Yes |
| Susan Horrigan | MA | Study Coordinator/Recruitment | Yes |
| | | | |
| Barbara McKenzie | MA | Project Manager | Yes |
| Blake Barrett | MSPH | Data Manager | Yes |
| Padmaja Ramaiah | MSBME | Research Assistant | Yes |
| Angel Klanchar | MS | Recruitment | Yes |
| Lee Augello | | Transcriptionist | No |
| Kevin Kip | PhD | Consultant | No |
| Tamara McKenzie-Hartman | PhD | Research Associate | Yes |

| | | | |
|---|---|---|---|
| Nina Sayers | PhD | Offsite Consultant/Co-I | No |
| Jemy Delikat | MOT OTR/L | Interviewer | No |

Study personnel, including all personnel collecting informed consent, will be trained by the study team members. The PI will lead a training session attended by all personnel involved in the informed consent process. All staff will have up-to-date required training.

## 5.4 Inclusion/Exclusion Criteria

Inclusion/Exclusion Criteria: To be eligible for the study, participants will be 18 or older with a history of mild TBI (DoD/VA criteria[66] as determined by trained, experienced staff via interview and medical record review via comprehensive evaluation process within PNS Clinic[65]) with current symptoms complaints (operationally defined as at least two symptoms on the NSI endorsed at the 'moderate' level or a total score on the NSI greater than 25. At least 93.5 percent of a sample of over 50,000 individuals with mild TBI within VA reported at least two NSI symptoms at a moderate level of severity or higher.[67] In addition, eligible participants must speak and read English, not have a history of moderate to severe TBI, not have a self-reported diagnosis of psychosis or be actively suicidal. Finally, potential subjects who report prior experience with Concussion Coach will also be excluded. We will attempt to recruit women and minorities to the extent possible. Our experience suggests that approximately 4% female and 30% ethnic minority will likely participate; they agree to participate in research at about the same rate as male and non-minority participants. Subjects who meet the inclusion/exclusion criteria and who agree to participate in the research study will sign an informed consent.

## 5.5 Study Evaluations

Table 1 outlines quantitative measures we propose to use. Examination of potential mediator and moderator variables will allow us to determine who is most likely to benefit from the intervention (e.g., people with limited social support, people who are less 'tech savvy') and qualify our findings. Justification for each of these included variables is contained in the description of each measure below the table.

**Table 1. Study Measures**

| Construct | Tool | Timepoint |
|---|---|---|
| **Primary Outcomes** | | |
| PCS | Neurobehavioral Symptom Inventory (NSI) | Baseline, up to 1 year later |
| Symptom Exaggeration | mBias | Baseline, up to 1 year later |
| Psychological Distress | Brief Symptom Inventory (BSI)<br>PCL-5 Strong Star (PCL) | Baseline, up to 1 year later |

| | | |
|---|---|---|
| Time Spent on Concussion Coach in total and on various components | Concussion Coach download | Duration of study i.e. a 3 month period for use of APP |
| PCS | NSI from Concussion Coach download (could be multiple NSIs depending on subject) | Duration of study i.e. a 3 month period for use of APP |
| Barriers and Facilitators of Concussion Coach use and effectiveness | Concussion Coach Interview<br>Follow-Up Data Form | Up to 1 year later for Follow-Up Form. Interview date is an undetermined time after the final study visit. |
| **Potential Mediators** | | |
| Perceptions and Knowledge of Illness | TBI Education Satisfaction, Knowledge, and Attributions | Baseline, up to 1 year later |
| Self-Efficacy | Self Efficacy for Symptom Management Scale (SEsx) | Baseline, up to 1 year later |
| **Potential Moderators** | | |
| Social Support | Social Support Questionnaire – Short Form (SSQSR) | Baseline, up to 1 year later |
| Comfort with Technology | eHealth Literacy Scale (eHEALS) | Baseline, up to 1 year later |
| Use of Apps during study period | Follow-Up Data Form | Up to 1 year after Baseline |
| Mental Health Treatment during study period | Follow-Up Data Form | Up to 1 year after Baseline |
| **Demographics, Health and Disability Status** | | |
| Age, gender, diagnosis, comorbidities, other injuries. | Medical Record:<br>Participant Information Form<br>Enrollment Participant Information Form | Baseline |

**Primary Outcome Measures**:

- Neurobehavioral Symptom Inventory (NSI) is a 22-item questionnaire developed to evaluate post-concussion symptoms following mild TBI.[52] It is used throughout the VA system of care to assess complaints associated with identified concussion. Patients are asked to rate each symptom on a scale of 0-4 (none, mild, moderate, severe, and very severe) with three different types of symptoms: affective/psychological/stress, somatic/physical, and cognitive reflecting three factors. The total score will be used in primary analyses. It is our primary outcome of interest because the civilian literature on interventions for mild TBI has focused (and found effects) on symptom-based measures.[41 53] Our own pilot data suggests that educational interventions have a significant impact on this measure.
- mBIAS is a 5-item measure of atypical symptoms. It is associated with symptom exaggeration following mild TBI (Cooper et al., 2011).
- Brief Symptom Inventory 18 (BSI 18) is a self-report measure with 18 items designed to measure psychological distress. It can be completed in approximately 4 minutes and is well-suited for helping measure symptom change due to treatment. It has good psychometric properties and has been used in the population of interest. It measures three primary dimensions: Somatization, Depression, and Anxiety, as well as a Global Severity Index (GSI). The GSI will be used in primary analyses as a measure of overall psychological distress. The Posttraumatic Stress Disorder Checklist (PCL-5) is a 20-item, self-rating scale that provides a quick and accurate measure of PTSD symptoms. Each item corresponds to current diagnostic criteria of PTSD, and each symptom is rated in terms of frequency and severity (Weathers, Huska, & Keane, 1991).Participant use of Concussion Coach will be collected electronically, including total time spent using the app as well as each component.
- Concussion Coach Interview (Tampa VA, unpublished). We have developed an interview that combines open-ended questions about use of the Concussion Coach with rating scales to assess satisfaction with the TBI app. Interviews will be conducted with a purposive sample of 10% of Concussion Coach users at study end to evaluate their satisfaction with Concussion Coach, ease of use, barriers and facilitators to use of Concussion Coach, behavioral intention to use Concussion Coach in the future and recommendations for improving it. We will use purposive sampling for participation in these interviews. We will solicit interviews from 10% of those who improved on PCS using Concussion Coach and 10% who did not improve or became worse. In addition to qualitative questions about barriers and facilitators, interview questions will include quantitative assessment of satisfaction (e.g., rating scales of satisfaction). Interviews will be conducted by experienced trained interviewers (e.g.,Delikat) and will be audio recorded. Participants will already be consented, so the interviewer will identify and briefly recap the project, and then ask permission for audio tape recording. Interviews will be conducted by phone or in person based on participant convenience. The interviewer will use standard communication techniques to stimulate discussion such as generic prompts (e.g. tell me more), summarizing statements, silence, and eye contact, if conducted in person. If the respondent exhibits adverse reactions, such as shame, during the course of the interview, every effort will be made to encourage him or her and they will be reminded of their rights as participants.
- Follow-Up Data Form

Potential Mediators:

- TBI Education Satisfaction, Knowledge, and Attributions Questionnaire is a 24 item modified version of the Brief Illness Perceptions Scale,[54] which assesses TBI education, knowledge, and attributions related to PCS. This measure is included due to the well known impact that

symptom attributions can have on outcomes following mild TBI [55-57] and to explore the relationship between outcomes and prior exposure and satisfaction with the VA's existing TBI education.

- Self Efficacy for Symptom Management Scale (SEsx) is a measure of confidence or perceived self-efficacy for managing chronic conditions. Perceived self-efficacy has been shown to influence a broad range of health-related and rehabilitation outcomes and may be particularly relevant in examining the effects of neuropsychological rehabilitation. Previous research has demonstrated an empirical relationship between generalized self-efficacy and outcomes after TBI.[58]

Potential Moderators:

- Social Support Questionnaire – Short Form (SSQSR) [59 60] is a 12-item questionnaire that measures both availability and satisfaction with social support. Social support is known to be associated with outcomes from TBI.[61 62]
- An adapted eHEALS, 10-item measure of eHealth literacy was developed to measure consumers' knowledge, comfort, and perceived skills at finding, evaluating, and applying electronic health information to health problems. Based on responses of 664 participants aged 13 to 21 internal consistency reliability was found to be .88. Test-retest reliability from baseline to 6-month follow-up (r = .68 to .40). Principal components analysis produced a single factor solution (56% of variance).[63]

Demographics, Health and Disability Status:

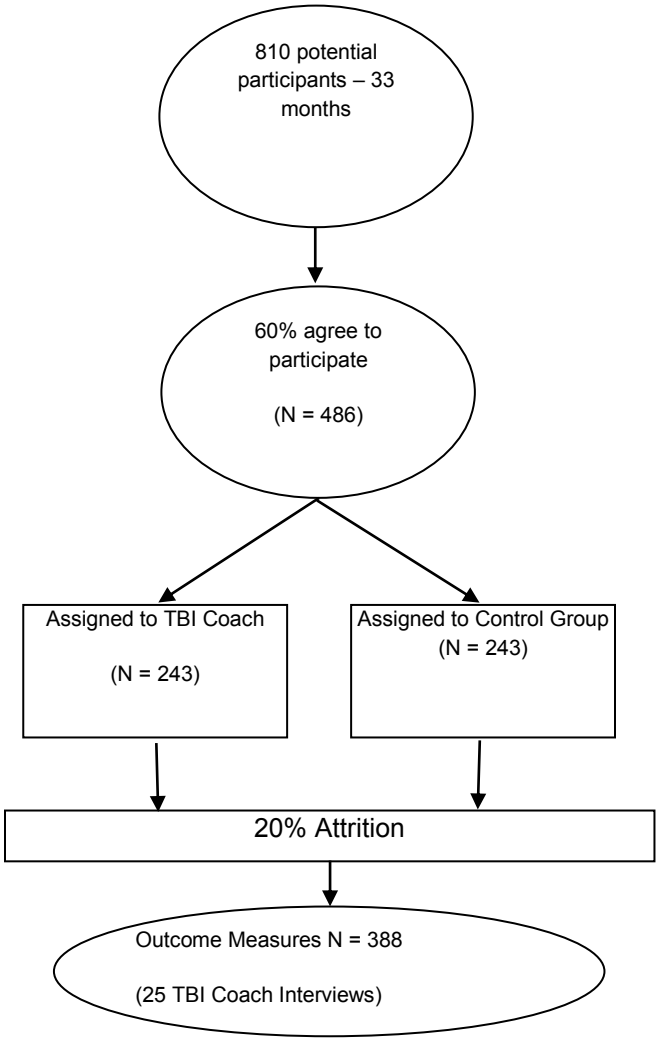
- The Participant Information Form gathers pertinent demographic data.
- Enrollment Participant Information Form

***Individual interviews*** (see Appendix for script) will be conducted with 10% of the Concussion Coach users at study end to evaluate their satisfaction with Concussion Coach, ease of use, their perception and satisfaction with other TBI-related education they have received within the VA to date, barriers and facilitators to use of Concussion Coach, and behavioral intention to use Concussion Coach in the future. This 10% sample will not be random – rather, we will solicit interviews from those who improved on PCS using Concussion Coach, those who did not get better or became worse, and those who did not use the App during the study period or used it infrequently. In addition to qualitative questions about barriers and facilitators, interview questions will include quantitative assessment of satisfaction (e.g., rating scales of satisfaction). Interviews will be conducted by experienced trained interviewers (i.e.,Delikat) and will be audio recorded. Participants will already be consented in person or over the telephone, so the interviewer will identify and briefly recap the project, and then again ask permission for audio tape recording. Interviews will be conducted by phone or in person based on participant convenience. The interviewer will use standard communication techniques to stimulate discussion such as generic prompts (e.g., tell me more), summarizing statements, silence, and eye contact, if conducted in person. If the respondent exhibits adverse reactions, such as shame, during the interview, every effort will be made to encourage him or her and they will be reminded of their rights as participants.

5.6 Data Analysis

**Sample Size Justification:** Below is a diagram of the expected subject recruitment and attrition (see Figure 2). Our recruitment estimates are based on our experience with prior trials (e.g., a recent pilot study of a web based intervention successfully recruited over 90% of potential participants) and our emphasis in the budget of recruitment personnel who will be embedded in our clinics. We conservatively estimate that 60% of potential participants will agree to participate and be successfully enrolled in the study. Our attrition estimate of 20% is based on our experience with an internet self-help intervention study, during which drop out was less than 20%. This was accomplished through continued outreach by the recruiter via letter and calls. Based on these conservative numbers and a recruiting period of 33 months we expect a minimum N=388 participants in the study [(20 newly identified participants per month over 33 months + 150 existing) *60% participation* (1-20% attrition)]. This is a conservative estimate because we have excluded the existing 1,332 potential participants living in our area (national dataset) to whom we will mail letters.

Figure 2. Expected Total Recruitment




For each regression model proposed for H1&2, results of sample size calculation using the application PASS v11 (Hintze, 2011) show that a much smaller N=148 (or N=194) achieves 80% (or 90%) power to detect an additional R-Squared of 0.05 (proportion of explained variation in the outcome) attributed to 2 independent variables (TBI Coach plus an interaction) using an F-Test with alpha of 0.05. This assumed the variables tested are adjusted for 10 independent variables with an R-Squared of 0.20.

We note that of all statistical models proposed in this study, the mediation model has the most stringent sample size requirement. With conservative total N=388, we expect to have greater than .80 power to detect a small to medium effect size of the mediated effect at alpha = 0.05. The two regression coefficients (beta1 & beta2) that jointly capture the mediated effects are critical in the power calculation for a mediation model. Using the parameter values of 0.14, 0.39, and 0.59, corresponding to Cohen's criteria68 for small (2% of the variance), medium (13% of the variance), and large (26% of the variance) effect sizes, respectively, Fritz and MacKinnon (2007) conducted empirical estimates of sample

sizes needed for .8 power at 95% confidence level. Their results showed that when bias-corrected bootstrap is used, N=462 is adequate to detect small effect size for each of alpha and beta while N=377 is adequate to detect small/medium effect size combination for both alpha and beta.69 Conservatively we expect to recruit N=388. We calculated directly the power for testing mediation effect based on Sobel's test (Sobel, 1982) using the R package 'power Mediation'. By specifying Cohen's small ES for each coefficient in the indirect pathway (beta1 = beta2 = 0.14) and with the following assumptions: both the predictor and the mediator have S.D. of 0.5 while the square of the correlation between both equal 0.3; and S.D. of the random error term is 0.2; the expected N=388 will provide 0.82 power to detect the small mediation effect size.

**Sample Size for Qualitative Research Questions:** In qualitative research, sample size relies on the quality and richness of information obtained.[70 71] Achieving conceptual saturation is the goal of qualitative research and is not dependent on sample size but on the ability of the data to support interpretations, i.e. saturation.[70 71] For this aim, we project saturation will occur within the first twelve interviews; meta-themes will present in six interviews.[72] Thus we will recruit 10% of Veterans to provide adequate data to represent sub-groups that may emerge from the sample and allow for an adequate sub-sample sizes; allowing for some attrition. For example, we expect low volume and high volume users; those who intend to have continued use and those who may not. This will also allow sampling groups for analysis by socio-demographics such as gender and race. We have budgeted to recruit 10% of Veteran participants to conduct the proposed interviews.

## Data Analysis:

Data from the Concussion Coach application will be electronically sent to the USF server. It will be de-identified (but matched to a study number that will identify the individual to the study coordinator who will need it for follow-up). It will be periodically emailed to study personnel at the Tampa VA.

Data from paper questionnaires will be obtained from the recruiter and study personnel and maintained by the study coordinator. Again, study numbers will be used to identify participants.

All data will be combined into a study database. The integrity of the database will be managed by our database manager. Analyses will be conducted by the statistician (Peter Toyinbo) and the PI (Tracy Kretzmer).

**Data Analysis Plan:** An intention-to-treat (ITT) analysis will be performed, that is analysis will be based on the groups to which participants are randomized regardless of whether they receive or adhere to the assigned intervention. This will allow us to test the effects of assigning TBI Coach in practice, separate from assessing effects of adherence and/or loss to follow-up. Those who are lost to follow-up and therefore are missing outcome measures (T2 assessments) will be included in separate comparison analyses that utilize multiple imputations of the missing data.

For each primary outcome and other measures consisting of multiple items, a summation score will be produced for each subject. Summary of each variable by intervention group will be cross-tabulated. The time spent on TBI Coach and its specific components on the average will also be tabulated. All primary outcomes will be analyzed as continuous variables. Exploratory bivariate plots will be used to investigate possible nonlinear relationships between baseline/covariates and each follow up outcome variable. In separate statistical models proposed, we will control for demographics and other covariates including the baseline values of the outcome under investigation. Where appropriate, nonlinear regression model will be utilized (e.g., generalized additive model).

**Hypothesis 1 (Primary Hypothesis):** Patients randomized to receive TBI Coach for 3 months will have (a) lower post-concussive symptom severity and (b) lower psychological distress, compared to patients randomized to a no intervention control group, after adjusting for baseline severity and other potential confounders.

Analysis: The two intervention groups (TBI Coach = 1; Control = 0) will be compared on each outcome (a) and (b) in separate regression models that include the group variable and control for the outcome at baseline and other potential confounders. A significant positive estimated coefficient of the group variable will indicate positive TBI Coach's effects on the outcome, with the standardized value of the coefficient as the standardized effect size.

**Hypothesis 2:** The effects of TBI Coach on PCS (and psychological distress) will be greater for Veterans who have (a) greater comfort with technology at baseline than for those who are less comfortable; (b) greater social support at baseline than for those with less social support.

Analysis: Two separate tests of moderated effects of TBI Coach will be performed with respect to each outcome. Each regression model in H1 (one per outcome) will be extended by adding a 2-way interaction term (between intervention and (a) eHealth Literacy Scale and (b) Social Support score; one at a time (i.e. two different moderation models per outcome). A significant coefficient of an interaction term will indicate presence of interactive effects. A co-plot using model fitted values will also be produced to further investigate the nature of any significant interaction.

**Hypothesis 3:** If TBI Coach improves Veterans' (a) knowledge about TBI and attribution of symptoms and/or (b) self-efficacy in coping with symptoms, Veterans will have less PCS and Psychological Distress.

Analysis: Single-mediator models[73] will test the indirect effects of the group variable (TBI Coach) on each outcome (separately) with respect to mediating variables: (a) knowledge and attribution, and (b) self-efficacy. Preliminary regression analyses will test whether (1) TBI Coach substantially changes the mediating variable, and (2) the mediating variable changes the outcome. Next, we will proceed to a full mediation model with simultaneous estimation of both direct and indirect effects of TBI Coach on the outcome. The mediated effect will be estimated as a product of the two path coefficients alpha and beta in the indirect pathway. The distribution of the product of coefficients is non-normal and this has implications for statistical inference as well as power calculation (see section on sample size justification). Therefore, the analysis will

be performed using the Mplus statistical application which offers alternatives that do not require the regular assumption of symmetric, normal distributions for parameter estimates. Bayesian estimation method with diffuse priors will be used with appropriate posterior simulation schemes based in Markov Chain Monte Carlo (MCMC) methods. One advantage of the MCMC estimation process is that it provides accurate tests of mediated effects for small samples; e.g. by simply taking the product of the two coefficients alpha and beta for every draw and compute its standard deviation across all draws to obtain standard errors of mediated effect. Also, unlike the normal-based ML confidence interval, inference will rely on Bayesian credibility interval based on the percentiles of the posterior, which easily allows for a strongly skewed distribution alpha-beta product[74]

**Hypothesis 4:** More time spent on (a) TBI Coach use, and (b) specific interactive components of TBI Coach (i.e., the "tools" section) will be associated with lower PCS symptom severity after adjusting for baseline PCS values and potential confounders.

Analysis: A regression model of PCS will be performed on the TBI Coach sample only, separately for (a) TBI coach use, and (b) each interactive component as the main predictor. First the PCS baseline score, demographics and other potential confounders will be included in the base model. Then a full model with addition of the time score for one TBI Coach aspect at a time will be fitted. Appropriate transformation (e.g. log) of all time variables will be done as suggested by their general distribution; a significant negative coefficient of the time variable will confirm a negative association between time spent on that component and symptom severity. Standardized coefficient estimates as well as R-sq estimates will be obtained so that all TBI Coach aspect-specific models can be compared on the relative strengths of the aspect-outcome relationships.

As an extension, secondary analysis will be performed on the TBI Coach components that show strong relationship in the expected direction. Each time spent (as a dependent variable) will be regressed on the predictors in the base model to identify both positive and negative contributory factors to the specific component usage.

### 5.7 Withdrawal of Subjects

We do not and cannot anticipate any circumstance under which subjects will be withdrawn from the research without their consent. There will be no consequences if a subject decides to withdraw from the study. Indeed, the voluntary nature of the study will be stressed during the informed consent process. Contact information for study personnel will be given to each participant.

## 6.0 Reporting

We do not anticipate any serious events. If the respondent exhibits adverse reactions, such as shame, during the interview portion of the study, every effort will be made to encourage him or her and they will be reminded of their rights as participants. A highly trained and experienced interviewer will conduct the interviews.

If participants voice suicidal ideation/plan this will be reported as a SAE or UAP.

We will inform the Central IRB of any unanticipated problems through information reporting and continuing reviews.

## 7.0 Privacy and Confidentiality

We are requesting a HIPAA waiver for identification of potential participants. Without identifying potential participants (with a medical history of concussion), we would need to screen all patients within our two sites somehow, and make them go through a redundant evaluation to determine that they've had a concussion. This would be incredibly inefficient, since we are only targeting people who have had a concussion. The VA has a screening and evaluation process in place that can help us hone in on participants who might benefit and are eligible for this study. Identifying subjects that meet inclusionary criteria and garnering contact information requires access to the protected health information. Without this information, there is no practical means of contact within the context of this study. Gaining consent from the entire VA patient population is impractical.

In addition to diagnosis, we will need name and mailing address since we would like to send letters, asking potentially eligible participants (those with history of concussion) if they would be interested in participating. We will get this information from CPRS data from both Tampa and Bay Pines VA. We will also request national data on the TBI evaluation results from the appropriate sources (VHA Support Service Center (VSSC), national PM&R office national data system).

After participants are identified, no longer will any PHI be tied to an individual participant. In other words, data will be linked to a specific subject by a code rather than a direct identifier. There will be no identifying information on the questionnaire data, the interview data, or in the electronic data that is transmitted from the smart phone application to the server.

Patient data will be kept on networked, password protected VA computers and on VA servers in files with access limited to study personnel. Hard copies of the Informed Consent Forms and other data collection instruments are kept in locked file cabinets in an office that is kept locked when unoccupied. HIPAA privacy rules will be strictly maintained. Data will not be shared with anyone other than who is named in the consent form. All paper records will be maintained in locked files within a locked office. All electronic study data will be stored on a password protected database with access limited to select research personnel and will be encrypted and protected by firewall per VA guidelines. The PI and all study personnel will be responsible for ensuring that the research is conducted in a manner consistent with the ethical principles outlined in the Belmont Report, and in compliance with USF policies and procedures. A similar smart phone application has already been developed by the VA. It will be encrypted and the encryption will be FIPS 140-2 validated.

## 8.0 Communication Plan

All local site approvals will be obtained and maintained by the Lead Site (Tampa)'s study coordinator. If there are any problems, this will be communicated to the PI who will work to resolve it with the site PI at Bay Pines.

The lead study coordinator at Tampa will be responsible for keeping the Bay Pines study staff informed of any changes to study procedures, any changes required in documentation, any serious adverse events or unanticipated problems. The PI will inform Bay Pines study staff of any interim results that may impact the conduct of the study.

Regular, scheduled communication will occur between Tampa and Bay Pines via email and telephone. In person meetings will occur as necessary. As the PI has worked with the site PI and co-investigator at Bay Pines in the past, we do not anticipate any problems with communication.

The study will be largely implemented at Bay Pines by the site coordinator at Bay Pines (Horrigan), with oversight from the site PI.

All personnel involved in the study will be trained by the PI to ensure that the study is faithfully carried out and implemented. Regular communication will also facilitate this. When the study is over, the PI and primary study coordinator will ensure that the Bay Pines site is aware.

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