

# Use of a multi-level mixed methods approach to study the effectiveness of a primary care progressive return to activity protocol after acute mild traumatic brain injury/concussion in the military☆

Emma Gregory<sup>a,b,\*</sup>, Therese A. West<sup>c</sup>, Wesley R. Cole<sup>a,b,d</sup>, Jason M. Bailie<sup>a,b,e</sup>, Karen L. McCulloch<sup>f,g</sup>, Mark L. Ettenhofer<sup>a,h,i</sup>, Amy Cecchini<sup>a,g</sup>, Felicia M. Qashu<sup>a</sup>

<sup>a</sup> Defense and Veterans Brain Injury Center, 1335 East West Highway, Silver Spring, MD 20910, United States

<sup>b</sup> General Dynamics Health Solutions, 8601 Georgia Ave Ste. 900, Silver Spring, MD 20910, United States

<sup>c</sup> US Army Medical Research and Materiel Command, Combat Casualty Care Research Program, 722 Doughten Street, Fort Detrick, MD 21792, United States

<sup>d</sup> Womack Army Medical Center, MCXC-TBI 2817 Reilly Road, Fort Bragg, NC 28310, United States

<sup>e</sup> Naval Hospital Camp Pendleton, 33 Area, Camp Margarita, Mental Health Building 33305, Camp Pendleton, CA 92055, United States

<sup>f</sup> University of North Carolina Chapel Hill, 321 S. Columbia Street, Bondurant Hall Ste 3024, Chapel Hill, NC 27599, United States

<sup>g</sup> Venesco LLC, 14801 Murdock Street Suite 125, Chantilly, VA 20151, United States

<sup>h</sup> Naval Medical Center San Diego, Department of Physical Medicine and Rehabilitation, 34730 Bob Wilson Dr. Ste #201 Bldg 3, San Diego, CA. 92134, United States

<sup>i</sup> American Hospital Services Group LLC, 1 E. Uwchlan Ave, Suite 407, Exton, PA 19341, United States

## ARTICLE INFO

### Article history:

Received 16 August 2016

Received in revised form 31 October 2016

Accepted 7 November 2016

Available online 9 November 2016

### Keywords:

Clinical study methodology

Outcomes research

Traumatic brain injury

Concussion

Knowledge translation

Military

## ABSTRACT

The large number of U.S. service members diagnosed with concussion/mild traumatic brain injury each year underscores the necessity for clear and effective clinical guidance for managing concussion. Relevant research continues to emerge supporting a gradual return to pre-injury activity levels without aggravating symptoms; however, available guidance does not provide detailed standards for this return to activity process. To fill this gap, the Defense and Veterans Brain Injury Center released a recommendation for primary care providers detailing a step-wise return to unrestricted activity during the acute phase of concussion. This guidance was developed in collaboration with an interdisciplinary group of clinical, military, and academic subject matter experts using an evidence-based approach. Systematic evaluation of the guidance is critical to ensure positive patient outcomes, to discover barriers to implementation by providers, and to identify ways to improve the recommendation. Here we describe a multi-level, mixed-methods approach to evaluate the recommendation incorporating outcomes from both patients and providers. Procedures were developed to implement the study within complex but ecologically-valid settings at multiple military treatment facilities and operational medical units. Special consideration was given to anticipated challenges such as the frequent movement of military personnel, selection of appropriate design and measures, study implementation at multiple sites, and involvement of multiple service branches (Army, Navy, and Marine Corps). We conclude by emphasizing the need to consider contemporary approaches for evaluating the effectiveness of clinical guidance.

© 2016 Elsevier Inc. All rights reserved.

**Abbreviations:** CPG, clinical practice guideline; CR, clinical recommendation; DVVIC, defense and veterans brain injury center; DoD, department of defense; mBIAS, mild brain injury atypical symptoms scale; mTBI, mild traumatic brain injury; NSI, neurobehavioral symptom inventory; PCMs, primary care managers; PRA CR, progressive return to activity; RCTs, randomized controlled trials; SSI, semi-structured interview; SMs, service members; TAU, treatment as usual; VA, veterans affairs.

☆ The views expressed in this manuscript are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, Department of the Army, Department of Defense, or the U.S. Government.

\* Corresponding author at: Defense and Veterans Brain Injury Center, 1335 East West Highway, Silver Spring, MD 20910, United States.

E-mail address: [emma.d.gregory2.ctr@mail.mil](mailto:emma.d.gregory2.ctr@mail.mil) (E. Gregory).

## 1. Introduction

Since 2000, over 300,000 service members (SMs) in the U.S. military have been diagnosed with at least one traumatic brain injury (TBI), with most of the injuries characterized as mild TBI (mTBI), also known as concussion [1]. Clinical guidance for how injured SMs and their providers can best manage concussion during the acute phase continues to evolve with emerging research [2–7]. The symptomatology of concussion may vary across patients, but often includes headache, fatigue, memory problems, dizziness and visual disturbances [8,9]. Symptoms can be exacerbated as a result of cognitive, physical and/or vestibular exertion too soon after the injury [10,11] or after prolonged or excessive rest [12,13]. Taken together these findings emphasize the importance of resuming activities at the right time and at an appropriate pace [10–14].

With the aim of accelerating recovery and reducing persistent symptoms, patients should be advised to gradually return to activities only once they are asymptomatic [8,9,15–17]. The Veterans Affairs (VA)/Department of Defense (DoD) Clinical Practice Guideline (CPG) for Management of Concussion/mTBI [18] provides such guidance for a graded return to activity after concussion for veteran and SM patients and providers. However, while this guidance is robust, it does not provide details for the return to activity process nor does it consider military requirements or operational environments.

In response to this knowledge gap, the Defense and Veterans Brain Injury Center (DVBIC) released recommendations for primary care providers detailing a step-wise return to unrestricted activity following concussion in January 2014 [19]. The DVBIC progressive return to activity clinical recommendation (PRA CR) was developed in collaboration with an interdisciplinary group of clinical, military, and academic subject matter experts using an evidence-based approach [20]. The rigorous development of the CR logically should be followed by systematic evaluation [21] to ensure positive patient outcomes, to understand barriers to implementation and adoption by providers, and to identify opportunities for improvement.

Accordingly, this study was developed to 1) to evaluate the effectiveness of the PRA CR in improving acute patient outcomes and 2) to assess the adherence to the PRA CR by primary care providers and their patients. It is hypothesized that greater adherence to the CR guidelines will be associated with better outcomes (e.g., quicker resolution of symptoms, return to activity, and return to duty) among patients with acute concussion. The first objective will be executed by comparing outcome and adherence measures for patients receiving treatment as usual (TAU) versus those receiving care according to the PRA CR. Data from these TAU and PRA CR patient groups will be collected from the acute injury stage to six months following injury to explore differences between groups of the trajectory of recovery. The second objective will be tackled by evaluating providers' knowledge of the PRA CR and their perception of patient change and compliance over time. Finally, an additional and important objective is to identify aspects of the PRA CR requiring improvement.

## 2. Design and methods

### 2.1. Participants

Patient and provider participants will be enrolled in the study from clinics and operational medical units at three U.S. military installations: one Army installation in the southeast, one Navy installation in the southwest and one Marine Corps installation in the southwest. The clinics and operational medical units involved in the study include concussion care clinics and primary care clinics where acutely concussed SMs receive care. Inclusion of multiple clinics across military service branches allows for assessment of variability in clinical practices throughout the Military Health System, as well as variability in levels of patient education regarding concussion symptoms and expectations for recovery.

Participants in the provider group will be approximately 100 primary care managers (PCMs) who treat concussed SMs at one of the three participating study sites. Providers may include physicians, physician's assistants, nurse practitioners and medically trained military personnel.

Participants in the patient group will be approximately 200 SMs who have sustained a concussion within 72 h preceding enrollment in the study, and who have received initial care from a provider enrolled in the study. Though the PRA CR is written to provide guidance within 24 h of the injury, for this study including patients who have sustained an injury within 72 h was deemed a suitable criterion, as many concussed SM do not seek care from their PCM immediately and there are no known differences in primary care initially received within 24 h versus 25 to 72 h. Therefore, this wider enrollment window

ensures the ability to enroll a sufficient number of acutely concussed SMs within the study timeframe.

Patients are eligible to enroll in the study based on a history of concussion that is verified via medical record review indicating a diagnostic code or the VA/DoD definition for mTBI/concussion [22]. The latter would require meeting one or more of the following criteria: a) loss of or a decreased level of consciousness for less than 30 min, b) loss of memory for events immediately up to one day after the injury, c) alteration of consciousness/mental state for 0–24 h after the injury, and/ or d) score of 13–15 on the Glasgow Coma Scale [18,23].

Other patient eligibility criteria are based on the characteristics of the patient group intended to receive care per the guidance in the primary care PRA CR. Of note, as we are recruiting adult active SMs, participants' ages, calculated for age at the time of injury, will fall within the age range of the US military population, which is 18 to 60 years of age. In addition, patients who have had a head injury in the 12 months preceding the index injury are not eligible for the study, as the PRA CR contains different guidance for such patients, and this guidance is not part of this evaluation. Otherwise, individuals are included regardless of lifetime history of TBI if those injuries were longer than 12 months immediately preceding the index injury. Additionally, because the PRA CR was devised to support patients diagnosed with concussion, regardless of symptomatology, patients are eligible to participate even if they are asymptomatic at baseline. Similarly, there are no exclusion criteria for demographic variables such as gender, age or rank. Table 1 provides an overview of eligibility criteria for patient participants.

### 2.2. Study design

Though randomized controlled trials (RCTs) are typically viewed as the gold standard for evaluating the efficacy of clinical interventions, this approach was determined to be inappropriate for use in evaluating the effects of implementing an existing/published CR among primary care providers. Instead, a two-phase mixed-method design was selected for the study. In this design, patient data and provider data are collected for two study phases of care (TAU, PRA CR) and data include both quantitative and qualitative elements.

Providers are enrolled at the start of the study, and provide TAU care in the first phase. At mid-study, a provider training serves as an educational intervention in order to compare the effects of TAU to the effects of acute concussion management and education according to the PRA CR. Specifically, after completion of the TAU phase, providers will receive in-person training on the PRA CR to include basic information on concussion management, detailed content of the PRA CR, and instructive case studies. The training will be followed by the PRA phase during which providers are instructed to follow guidance in the PRA CR when providing care for their patients. For the patient group this is a between-subjects design in which participants receive either TAU or PRA CR care but not both. The study group to which patients are assigned depends on the stage the study is in when the patient enrolls, with half of the target enrollment occurring during TAU phase and half during PRA phase. For provider participants the study entails a within-subject design such that the participant takes part in both the TAU and PRA phases of the study, with the difference being whether or not the provider cares for the patient according to TAU or PRA CR (i.e., before or after being trained on the PRA CR).

**Table 1**  
Patient eligibility criteria for study.

Inclusion	Concussion as defined by VA/DoD, sustained within the past 72 h, and verified in the medical record Receive care for current concussion at clinic participating in the study Age at time of injury of 18 to 60 years consistent with the US military population
Exclusion	Concussion or more severe head injury sustained in the 12 months preceding the index injury

To gather information on patient outcomes and adherence to provider recommendations, data collection for patient participants occurs at five time points: during the initial assessment within 72 h of injury, at one week, one month, three months, and six months after injury. The data collected and the timing of the collection is the same for patient participants, regardless of their assignment to TAU or PRA. Data from provider participants will be collected at three time points during the course of the study: at the beginning of the study, immediately after the TAU phase and prior to providers' receiving the PRA CR educational intervention, and at the end of the study after they have provided care according to the PRA CR. These time points are selected to track not only their knowledge of the PRA CR before and after the PRA CR training but also how their clinical care practices and their perception of patient change alters as a result of the PRA CR training they receive. See Fig. 1 for an illustration of the overall study timeline with provider participant assessment points (1A) and patient participant assessment points (1B).

The use of a TAU, sometimes called “usual care”, group poses some ethical concerns if the usual care is not in alignment with evidence-based recommendations for concussion management. The baseline provider interviews (before the TAU phase starts) will allow some assessment of how similar or different TAU is compared to current standards, such as the VA/DoD CPG [18].

2.3. Measures: patient participants

Data to be gathered from patient participants includes information on the individual's background and injury history, current symptoms, expectations following concussion, activities to determine adherence to clinical guidance in the PRA CR, and details of visits with providers following the injury. See Table 2 for descriptions of each data collection instrument. These measures entail a combination of already-established, commonly-used measures or outcomes and measures expressly developed to assess the CR. Examples of the former are demographics (e.g., education, gender), military variables (e.g., service branch, occupational specialty), and the Neurobehavioral Symptom Inventory (NSI; [24]). Inclusion of these standard metrics is critical, not only because of the value of each data point, but also because they allow comparisons of data from other studies of concussion. The study-specific data elements are equally critical as they directly evaluate the PRA CR. For example, an activity questionnaire will allow us to track the extent to which a patient is adhering to guidance in the PRA CR and progressing through the various PRA CR stages (see Appendix A for all of the non-published,

study-specific measures). Notably, each of the selected measures is intended to conform with the PRA CR, which recommends limited computer use or reading until stage 2. Therefore, computerized measures were excluded, and informed consent and data collection procedures and questionnaires are conducted with the study investigator mostly orally, allowing the SM to limit reading.

2.4. Measures: provider participants

Quantitative and qualitative data is obtained from providers via a semi-structured interview at three time points. The decision to include collection of qualitative data was made in part because of the likely variability in TAU practices across providers and the desire to understand “why” rather than just “what” or “how” related to the care they are providing. While the same questions are asked of all provider participants at all time points, the semi-structured measures allow for follow up to get more information depending on the participant's responses. This method allows a foundation of similar information to be obtained across all providers, with flexibility to account for the variability in the providers' experience level and approach to treatment. Moreover, the interviews are conducted in person to promote engagement in the study and minimize attrition.

The interviews contain questions on care provided to acute concussion patients, experience (e.g., number of patients seen, years in particular clinic settings, factors determining when a patient is considered ready to return to exercise, who is involved in the patient's recovery plan), perception of patient change as a result of the care, and perception of patient compliance with provider recommendations. The final interview, at the very end of the study, also asks about information in the PRA CR, how PRA CR guidance differs from their TAU and if/how they have changed their practices as a result of PRA training. Of note, explicit mention of the CR is avoided until the second interview, after the TAU phase is complete. Because the PRA CR product was made publicly available in January 2014, prior to the initiation of the study, the study team did not want to incidentally encourage the provider to seek out information on the PRA CR prior to the educational intervention. Questions in the second and third interviews gauge the extent to which the provider knew about the PRA CR prior to the training that is part of the study. Providers who report to have known about or used the PRA CR before receiving the educational intervention will not be excluded from the study. A driving reason for this decision is that the study's educational intervention, described below, is robust and aims to improve

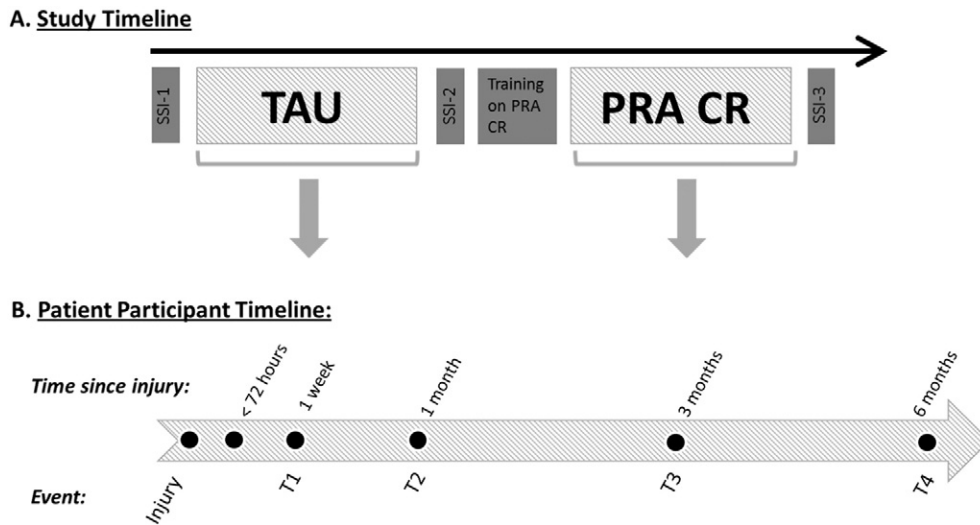


Fig. 1. A. Study timeline with key assessment points for patient and provider participants. Provider participants are recruited and enrolled at the start of the study and participate throughout the study. Provider participants complete three semi-structured interviews (SSI) and a study training on the PRA CR. Patient participants enroll in either the TAU group or the PRA CR group and complete assessments during either the TAU or PRA CR phase. B. Patient Participant Timeline for both the TAU and PRA CR patient participant groups. The five assessment time points are shown.

**Table 2**  
Patient participant data collection instruments.

Measure	Description	Reasoning	Time points collected*
Background	Basic demographic and military information to characterize patients	Track any influence of participant characteristics on patient outcomes and adherence to guidance	T0
Combat Exposure Scale [25]	A 7-item self-report measure to assess wartime stressors experienced by SMs	Track any influence of combat exposure on patient outcomes and adherence to guidance	T1
Ohio State University TBI Identification method [26]	A standardized instrument used to elicit the lifetime history of TBI for an individual	Document injury details (date of injury, loss of consciousness, agent of injury, etc) and history of head injury	T0
Patients' global impression of change scale [27]	A single-item, Likert-scale measure of domain global outcome or change	Quantify patient perception of change over time	T1, T2, T3, T4
NSI [24] embedded with Mild Brain Injury Atypical Symptoms Scale (mBIAS) [28]	A 22-item self-report measure of post-concussion symptoms and the mBIAS is a screening measure for symptom exaggeration	Symptomatology following injury is the key outcome both for the CR and for the effectiveness study.	T0, T1, T2, T3, T4
Injury diagnoses <sup>+</sup>	Confirm diagnosis or clinical description of self-reported TBI. Also to check for concurrent orthopedic injury	Evidence of TBI in the medical record is required for study eligibility. Orthopedic injuries will be factored into analyses.	After T0
Return to duty <sup>+</sup>	Date when cleared to return to duty	The date will be used to calculate time to return to duty, which is one of the key outcome measures of the study and CR.	After T4
Activity levels	A 60 item Likert-scale questionnaire targeting participant's engagement in physical, cognitive, and vestibular activities, based on guidance described for each stage of the PRA CR	Quantify adherence to CR, and time to return to physical, cognitive and vestibular activities	T0, T1, T2, T3, T4
Knowledge of concussion	An 11-item Likert-scale questionnaire assessing one's understanding of what to expect following a concussion (i.e., symptoms, recovery time)	Evaluate pre- and post-treatment education levels, as patient education is an integral part of the PRA CR	T0, T1, T2, T3, T4
Care received	Questions on care received for this mTBI (e.g., number of follow up visits, specialty referral, exertional testing, clearance to return to duty, receipt of education materials, patient reported monitoring of symptoms)	Explore the extent to which patient care is as prescribed by PRA CR, to include how and when they are returned to duty	T0, T1, T2, T3, T4

\* T0 or baseline occurs within 72 h of injury, T1 one week after injury, T2 one month after injury, T3 three months after injury, and T4 six months after injury.

<sup>+</sup> These data will be collected via medical record review.

understanding of the PRA CR for a variety of audiences, including individuals with knowledge of existing guidance and experience treating concussion patients. Therefore, the potential to see change in provider behavior remains, regardless of knowledge of the PRA CR prior to the training intervention. (See Appendix B for the three interviews.)

### 2.5. Provider intervention: PRA CR training

Education on the PRA CR involves a standardized, two-hour in-person training with enrolled providers. The training will occur at least 30 days after the last patient is enrolled in TAU phase to ensure that providers continue to offer acute care consistent with TAU to that patient group. Efforts will be made to have the same trainer conduct all group trainings with the same material and format across all sites. The primary trainer is a study team member with considerable experience providing education to military providers as well as working as a physician in DoD settings. In addition, each study site has a "champion" who will be available to providers as questions or comments arise during their application of the CR. To maximize provider attendance, the trainings are scheduled approximately two months in advance and to the extent possible around the providers' schedules. Along with providers enrolled in the study, attendance to the training will be open to and encouraged for non-enrolled providers at the installation. Continuing medical education units will be offered to both study enrollees and non-study enrollees attending the study trainings.

The curriculum for the interactive training includes a detailed overview of the guidance in the PRA CR, followed by case study-based activities, conducted in small groups, where implementation of the PRA CR is demonstrated. Providers receive workbooks with the case studies and questions for discussion to use in group problem-solving activities. In

addition, providers receive several formats of the PRA CR itself and other concussion diagnosis tools. Presenting the information using multiple mediums supports learning and increases the likelihood that the guidance will be implemented following the training [29,30]. Information on provider experience with concussion patients will be collected at the beginning of the training to equally distribute expertise and experience levels among the small groups of providers.

### 2.6. Statistical analysis

For the data collected from patient participants, the analyses of interest involve within-subjects analyses (e.g., comparing measures from the initial interview to the follow-up interviews) and between-subjects analyses (e.g., comparing those receiving TAU to those receiving treatment after PRA CR training). Stem-and-leaf plots, frequency distributions, and measures of central tendency and variability will be used to describe group sample characteristics. Multiple regressions will be conducted to explore relationships between NSI change scores and participant characteristics (e.g., age, rank, marital status, deployment history, education, concurrent orthopedic injury). Similar analyses will also be employed to investigate change in activity participation over time by group and factors related to those changes. For comparisons of the TAU and PRA groups, independent two sample t-tests will be carried out to identify differences on measures of interest at each time point. Analysis of variance (ANOVA) will be used to test for differences in symptoms (using NSI scores) between groups (TAU vs. PRA) and change in symptom reporting across the five assessment points. Other generalized linear model approaches such as multivariate analysis of variance (MANOVA) will be used as appropriate to effectively model within-subject correlations across time points. Sample size for



the patient participant groups was estimated using NSI differences from previous studies of mTBI [31] and based on the assumption of a moderate effect size, defined as a standard effect size of  $d = 0.5$  between outcome means in each arm. Sample size of 75 per group will provide power of 0.91 to detect an effect with a two-tailed alpha of 0.05. Moreover, based on conducting other research at the participating military installations, it is anticipated that attrition during the first three assessments, occurring within one month, will be minimal. Data from these initial three data assessment points will be valuable to address the study's main objectives. There will be expected 25–30% attrition during the three and six month follow-up time points. Missing data and any known reasons for missed follow-ups will be noted, with data included through that individual's last completed assessment.

For provider participants, the data gathered in the three interviews will be used to evaluate providers' knowledge of PRA and their perception of patient change and compliance. Qualitative analyses will be used to identify categories and subcategories of responses. Responses to questions that are identical across interview time points will allow us to track changes in provider responses over time. Interview responses will be characterized based on a coding frame developed by extracting key themes from a subset of the interviews and examined for acceptable inter-rater agreement between two independent qualitative raters.

### 2.7. Special considerations for study implementation within a military setting

Effectively and efficiently implementing a research study with human subjects is made significantly more complex when the study population primarily involves active duty SMs. This is due to a multitude of issues including military installation operational tempo and mission focus, support for research by the command, stability of personnel stationed at the chosen site (e.g., transfer to new duty stations, deployment, remote training exercises), accessibility and availability of the targeted population, and existence of a research infrastructure to implement the study methods. Study sites were selected because of the strong TBI research presence on each installation and because historical data indicate a high frequency of concussion among SMs at those sites. Additional efforts were undertaken to identify specific clinics and operational medical units within these large military installations where patients with concussion receive acute care, in order to target participant recruit. Strong collaborative relationships between researchers and commands of outlying medical clinics are required to successfully recruit research study participants from these locations. These relationships are necessary to pave the way for obtaining support and participation in new research efforts in an operationally-driven environment. Establishing clinical relevance of the research, with the ultimate goal to bolster SM wellness and mission readiness, is an essential message to convey to higher command levels to obtain support and approval, if required. Ultimately, commanders want to know if their personnel are “fit for duty” or “deployable.” Therefore, articulating that research efforts are aimed at force protection, force resiliency, and force readiness helps to develop reciprocal support to allow SMs and other personnel, both patients and providers, to participate in the research.

The military medical context also influences procedures for participant recruitment. As participant compensation is restricted per regulation for active duty and federal employees, it is understood that participants must be motivated by other factors to adhere to the multi-visit study schedule. Military providers must manage large numbers of patients (e.g., one physician's assistant and up to 14 medics per 750 person unit) while regularly briefing commanders regarding SM readiness for duty. Providers want to ensure they are providing appropriate, effective, and efficient care while commanders want to ensure force readiness. Therefore, the recruitment process must highlight the natural alignment of the goals of the research project with the providers' own interests in providing high quality care. A parallel source

of motivation also applies to patient participants, many of whom adhere to a “battle buddy” mentality of helping others in the broader SM community who may be similarly injured. Therefore, it is critical to emphasize the study's objectives on ensuring optimal post-concussion care for not only the SM him or herself but also for fellow SMs. Accordingly, in this research study, the patient is told during the consent process that while taking part in the study may not directly benefit him or her, it may lead to important information that could support future care for other patients.

### 3. Discussion

In order to provide specific guidance for the gradual return to activity process following concussion, DVBC developed the PRA CR for PCMs detailing a graded return to unrestricted activity following acute concussion, including specifics pertinent to military training and practices [19,20]. The PRA CR emphasizes patient education for activities to engage in and to avoid during each of the stages, when the SM should return to the provider, and generally what to expect in terms of recovery. The CR's education component is supported by previous work demonstrating that education via early intervention and the use of written information improves patient outcomes after concussion [32].

Systematic evaluation of the PRA CR is necessary to ensure positive patient outcomes, to identify barriers to use of the CR by providers, and to determine opportunities to enhance the CR. Here we have described a two phase, mixed-methods study evaluating the effectiveness of the PRA CR guidance for PCMs in the military medical system. Assessment of the PRA CR involves consideration of patient and provider perspectives with implementation of the guidance in ecologically valid military settings. While evaluation of clinical guidance can be considered at multiple levels (e.g., clinical content, product packaging, training on product, adoption into practice, patient outcomes), the focus of this study is on patient outcomes as a result of clinical guidance received. Because patient outcomes depend on the providers' understanding of the guidance and patient-provider interactions about the guidance, this study also tracks provider behavior as they use the guidance in their practice.

Design and implementation of a study to assess the PRA CR in a real-world military setting presents several complex challenges. The largest challenge is that the CR guidance is multi-dimensional and thus compels evaluation from several perspectives (i.e., providers and patients). Other challenges include conducting the study across different military service branches at multiple sites, recruiting a relatively transient population, obtaining support from research, clinical, and operational stakeholders, implementing the PRA CR across sites to influence adoption by providers, as well as upholding ethical standards. Many of the challenges are common in any clinical research trial, especially those with military populations, and therefore we attempted to describe ways in which we overcame or attempted to overcome some of those challenges. We argue that consideration of non-RCT approaches may be more appropriate depending on the needs of the study and the populations and material being evaluated. Also, there is abundant value in using standardized, validated data collection tools along with study-specific tools that more directly gather information about the product being evaluated, in combination with quantitative and qualitative approaches to analyses.

The resulting study design provides a number of advantages, including evaluation of the PRA CR within an ecologically-valid setting, minimal interference to the providers' clinical load, and valuable tracking of provider behavior over time to greatly increase our understanding of “treatment as usual” in these settings. Additionally, the study is designed to provide valuable information even if hypothesized differences were not observed. For example, the TAU phase of the study aims to understand each provider's approach to concussion care, which may or may not be different from recommended clinical guidelines, such as the PRA CR. If providers are consistently implementing approaches similar to the PRA CR (which was released in 2014), and no differences

between TAU and PRA CR are found, this could be considered indirect validation of the guidance in the PRA CR. Additionally, patient outcomes from injury to six months post-injury will be collected, and this information will further our understanding of recovery following concussion. The careful tracking of symptoms and activities will allow for identification of symptoms with the slowest resolution and whether those symptoms arose with participation in certain activities.

The data gathered will also provide useful information beyond assessing the PRA CR. First, patient data collected, including when and where they have follow up visits, could provide valuable information about typical patient flow during recovery from concussion or other medical conditions seen in military primary care settings. Second, data collected from providers in the TAU phase will provide information to better understand current patient care procedures and identify additional avenues for improvement of care after concussion. For example, preliminary data from baseline provider interviews suggests that a great deal of variation exists across PCMs in their knowledge of and experience and comfort level with treating concussion patients. Moreover, the interview data will yield a better understanding of providers' attitudes, including willingness to change their clinical practices. Taken together, this information could contribute to future development and dissemination of clinical practice guidelines or the development of tools that may foster implementation of such clinical practice guidelines. In addition, the feedback from patients and command could lead to enhanced means to bolster patient education about medical issues.

In sum, methods and rationale have been described for a study evaluating the effectiveness of the PRA CR for primary care of military SMs with acute concussion. We have hypothesized that training providers on the PRA CR will increase provider and patient adherence to PRA CR recommendations, and ultimately will improve patient outcomes. Due to challenges in evaluating acute concussion care, particularly within military settings, evidence for existing return-to-activity guidelines has been based primarily on correlational designs or expert consensus. If successful, this study will provide valuable evidence regarding the use of this PRA CR in military treatment facilities and operational medical units, as well as for the feasibility and effectiveness of implementing return-to-activity guidelines in others. Additionally, secondary data analyses will help identify targets for further clinical improvement, even if primary study aims are not met or study hypotheses are not confirmed.

## Funding

This work was supported by the Defense Health Program 6.7 and the Defense and Veterans Brain Injury Center.

## Supplementary material. Appendices A and B

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.cct.2016.11.005>.

## References

- Defense and Veterans Brain Injury Center, DoD worldwide numbers for TBI worldwide totals Retrieved from: [http://dvbic.dcoe.mil/files/tbi-numbers/DoD-TBI-Worldwide-Totals\\_2000-2016\\_Q1\\_May-16-2016\\_v1.0\\_2016-06-24.pdf](http://dvbic.dcoe.mil/files/tbi-numbers/DoD-TBI-Worldwide-Totals_2000-2016_Q1_May-16-2016_v1.0_2016-06-24.pdf) 2016.
- C.C. Giza, et al., Evidence-based guideline update: Evaluation and management of concussion in sports, Report of the Guideline Development Subcommittee of the American Academy of Neurology, *Neurology* 80 (24) (2013) 2250–2257.
- K.G. Harmon, et al., American medical society for sports medicine position statement: concussion in sport, *Clin. J. Sport Med.* 23 (1) (2013) 1–18.
- M. Makdissi, et al., Natural history of concussion in sport: markers of severity and implications for management, *Am. J. Sports Med.* 38 (3) (2010) 464–471.
- P. McCrory, et al., Consensus statement on concussion in sport—the 4th international conference on concussion in sport held in Zurich, November 2012, *J. Sci. Med. Sport* 16 (3) (2013) 178–189.
- Ontario Neurotrauma Foundation, Guidelines for concussion/mild traumatic brain injury & persistent symptoms: second edition Retrieved from: <http://onf.org/documents/guidelines-for-concussion-mtbi-persistent-symptoms-second-edition> 2013.
- T.A. West, D.W. Marion, Current recommendations for the diagnosis and treatment of concussion in sport: a comparison of three new guidelines, *J. Neurotrauma* 31 (2) (2014) 159–168.
- M. Lovell, M. Collins, J. Bradley, Return to play following sports-related concussion, *Clin. Sports Med.* 23 (3) (2004) 421–441.
- P. McCrory, et al., Consensus statement on concussion in sport—the 3rd international conference on concussion in sport held in Zurich, November 2008, *S. Afr. J. Sports Med.* 21 (2) (2009) 36–46.
- J.E. Meyer, P.A. Arnett, Changes in symptoms in concussed and non-concussed athletes following neuropsychological assessment, *Dev. Neuropsychol.* 40 (1) (2015) 24–28.
- N.D. Silverberg, G.L. Iverson, Is rest after concussion “the best medicine?”: recommendations for activity resumption following concussion in athletes, civilians, and military service members, *J. Head Trauma Rehabil.* 28 (4) (2013) 250–259.
- M. DiFazio, et al., Prolonged activity restriction after concussion: are we worsening outcomes? *Clin. Pediatr.* 55 (5) (2016) 443–451.
- T.C.V. McLeod, G.A. Gioia, Cognitive rest: the often neglected aspect of concussion management, *15* (2) (2010) 1–3.
- D.G. Thomas, et al., Benefits of strict rest after acute concussion: a randomized controlled trial, *Pediatrics* 135 (2) (2015) 213–223.
- M.B. Gaetz, G. Iverson, Sex differences in self-reported symptoms after aerobic exercise in non-injured athletes: implications for concussion management programmes, *Br. J. Sports Med.* 43 (2009) 508–513.
- K.M. Johnston, et al., Current concepts in concussion rehabilitation, *Curr. Sports Med. Rep.* 3 (6) (2004) 316–323.
- R.H. Lutz, S. Kane, J. Lay, Evidence based diagnosis and management of mTBI in forward deployed settings: the genesis of the USASOC neurocognitive testing and post-injury evaluation and treatment program, *J. Spec. Oper. Med.* 10 (1) (2010) 23–35.
- Management of Concussion/mTBI Working Group, VA/DoD clinical practice guideline for management of concussion/mild traumatic brain injury, *J. Rehabil. Res. Dev.* 46 (6) (2009) CP1–C68.
- Defense and Veterans Brain Injury Center, The progressive return to activity following mTBI clinical recommendations Retrieved from: <http://dvbic.dcoe.mil/resources/progressive-return-to-activity> 2014.
- K.L. McCulloch, et al., Development of clinical recommendations for progressive return to activity after military mild traumatic brain injury: guidance for rehabilitation providers, *J. Head Trauma Rehabil.* 30 (1) (2015) 56–67.
- IOM (Institute of Medicine), Clinical practice guidelines we can trust, The National Academies Press, Washington, D.C., 2011
- Department of Defense Instruction 6490.11, DoD policy guidance for management of mild traumatic brain injury/concussion in the deployed setting Retrieved from: <https://www.hsdl.org/?search&collection=public&fct&so=date&submitted=Search&offset=0&tabsection=US+Depts%2C+Agencies+%26+Offices&page=1&publisher=United+States,+Dept.+of+Defense> 2012.
- Management of Concussion/mTBI Working Group, VA/DoD clinical practice guideline for management of concussion/mild traumatic brain injury, Version 2.0 Retrieved from: <http://www.healthquality.va.gov/guidelines/Rehab/mtbi/> 2016.
- K.D. Cicerone, K. Kalmar, Persistent postconcussion syndrome: the structure of subjective complaints after mild traumatic brain injury, *J. Head Trauma Rehabil.* 10 (3) (1995) 1–17.
- T. Keane, et al., Clinical evaluation of a measure to assess combat exposure, *Psychol. Assess.* 1 (1989) 53–55.
- J.D. Corrigan, J. Bogner, Initial reliability and validity of the Ohio State University TBI identification method, *J. Head Trauma Rehabil.* 22 (6) (2007) 318–329.
- H. Hurst, J. Bolton, Assessing the clinical significance of change scores recorded on subjective outcome measures, *J. Manip. Physiol. Ther.* 27 (1) (2004) 26–35.
- D.B. Cooper, et al., Utility of the mild brain injury atypical symptoms scale as a screening measure for symptom over-reporting in operation enduring freedom/operation Iraqi freedom service members with post-concussive complaints, *Arch. Clin. Neuropsychol.* 26 (8) (2011) 718–727.
- M.D. Cabana, et al., Impact of physician asthma care education on patient outcomes, *Health Educ. Behav.* 41 (5) (2014) 509–517.
- D. Davis, et al., Impact of formal continuing medical education: do conferences, workshops, rounds, and other traditional continuing education activities change physician behavior or health care outcomes? *JAMA* 282 (9) (1999) 867–874.
- E.G. King, et al., Pilot of a novel intervention for postconcussive symptoms in active duty, veterans, and civilians, *Rehabil. Psychol.* 58 (3) (2013) 272.
- J. Ponsford, et al., Impact of early intervention on outcome following mild head injury in adults, *J. Neurol. Neurosurg. Psychiatry* 73 (3) (2002) 330–332.