

Study of Cognitive Rehabilitation Effectiveness

The SCORE clinical trial is a randomized controlled treatment trial evaluating the effectiveness of cognitive rehabilitation in post-deployment military service members who sustained a concussion.

*Chapter 1: Study
of Cognitive
Rehabilitation
Effectiveness
Clinical Trial:
Overview*

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Congress established DVBIC in 1992 after the first Gulf War in response to the need to treat service members with TBI. DVBIC's staff serves as the Defense Department's primary TBI subject matter experts. DVBIC is part of the U.S. Military Health System and is the TBI operational component of the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE). Learn more about DVBIC at dvbic.dcoe.mil.

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SCORE Disclaimer

The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Army, the Department of Defense, the Department of Veterans Affairs, or the U.S. Government.

Chapter 1:

Study of Cognitive Rehabilitation Effectiveness Clinical Trial: Overview

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Rationale and Significance

Establishing the effectiveness of cognitive rehabilitation is an important issue, with relevance both for providing optimal clinical care, as well as evidence to support the importance of reimbursement for appropriate clinical services within the healthcare industry. Currently, the basic military healthcare plan for active-duty service members does not cover cognitive rehabilitation for mild traumatic brain injury (mTBI). The basis for this policy, in addition to other factors, is a meta-analysis of existing literature conducted by the Emergency Care Research Institute (ECRI) for the Office of the Chief Medical Officer, TRICARE, which confirmed the efficacy of limited cognitive rehabilitative interventions for moderate and severe TBI, but not for mTBI.¹ However, differences in outcomes assessed and an insufficient number of studies negatively influenced the results of this meta-analysis.

A legislative response to this situation came in the form of Section 723 of House Resolution 2647, (National Defense Authorization Act for Fiscal Year 2010), which stated: “The Secretary of Defense shall provide for a clinical trial to assess the efficacy of cognitive rehabilitative therapy for members or former members of the Armed Forces who have been diagnosed with a traumatic brain injury (TBI) incurred in the line of duty in Operation Iraqi Freedom or Operation Enduring Freedom.”² The task of conducting this clinical trial of cognitive rehabilitation went to the Defense and Veterans Brain Injury Center (DVBIC), headquartered in Silver Spring, Maryland. DVBIC is the primary operational component of the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury, under the auspices of the TRICARE Management Authority and the Office of the Assistant Secretary of Defense for Healthcare Operations.

The goal of the resultant Study of Cognitive Rehabilitation Effectiveness (SCORE) trial was to improve the health and quality of life for wounded warriors with mTBI through the development of empirically validated rehabilitation interventions. An additional aim of this study was to inform recommendations on the advisability of including cognitive rehabilitation therapy for mTBI as a benefit under TRICARE and meet the requirements of House Resolution 2647.

The SCORE trial is a joint endeavor, with investigators and clinicians from the Traumatic Brain Injury Rehabilitation Clinic at Brooke Army Medical Center (BAMC), investigators in DVBIC, and consultants from the Department of Veterans Affairs (VA) Healthcare System and Walter Reed National Military Medical Center. A representative team met in San Antonio, Texas, in June 2010 to develop a research plan for the SCORE trial. Members of the executive committee included:

Amy O. Bowles, M.D. (Rehabilitation Physician, BAMC TBI Clinic)
Douglas B. Cooper, Ph.D. (Neuropsychologist; BAMC TBI Clinic)
Micaela V. Cornis-Pop, Ph.D. (Speech Language Pathologist; VA Central Office)

Louis M. French, Ph.D. (Neuropsychologist; Walter Reed Army Medical Center), Bethesda, Maryland

Jan E. Kennedy, Ph.D. (Neuropsychologist; DVBIC San Antonio)

Loretta C. Polite (DVBIC; Office of Regulatory Affairs), Silver Spring, Maryland

Rodney D. Vanderploeg, Ph.D. (Neuropsychologist; James Haley VAMC), Tampa, Florida

Investigators agreed upon a randomized controlled treatment trial (RCT) study, designed to optimally evaluate the efficacy of cognitive rehabilitation therapy (i.e., exercises or tasks to treat memory and attention) for service members diagnosed with mTBI sustained in the line of duty in Operation Enduring Freedom (OEF) or Operating Iraqi Freedom (OIF) and who have persistent cognitive symptoms. The following sections provide details about the study design, including study aims, research hypotheses, measures, and participants.

Research Design and Methods

The SCORE trial is a prospective, RCT of cognitive rehabilitation for mTBI conducted at BAMC. The BAMC Institutional Review Board approved the clinical trial, and it was registered at clinicaltrials.gov (ID# NCT01339806). The study underwent secondary regulatory review and approval from the U.S. Army Medical Research and Materiel Command before enrollment began.

Consecutive patient referrals to the Traumatic Brain Injury Service (currently known as the Brain Injury Rehabilitation Service, or TBI Clinic) at BAMC provided participants for recruitment. Patients who met eligibility criteria and consented to participate in the treatment trial received random assignments to one of four, six-week treatment arms of the study. Participants completed all dependent measures before treatment started and at 3, 6, 12, and 18 weeks following the initiation of the study. The four treatment arms were designated as:

Arm 1. Psychoeducational control group

Arm 2. Non-therapist directed computerized cognitive rehabilitation

Arm 3. Therapist-directed individualized cognitive rehabilitation

Arm 4. Integrated interdisciplinary cognitive rehabilitation combined with cognitive behavioral psychotherapy

A statistical power analysis completed before the study began provided an estimated 160 participants needed for the clinical trial, consisting of approximately 40 participants per treatment arm. During the three years of study enrollment, the number of potential participants who met eligibility criteria diminished considerably, primarily due to the drawback of military personnel deployed to Iraq (OIF) or Afghanistan (OEF) and the time since injury criteria required for inclusion in the study (i.e., three to 24 months post-injury). As a result, the trial was closed in January 2014 with a total enrollment of 143 participants.

Inclusion Criteria

1. Diagnosis of mTBI that occurred during deployment in support of OEF/OIF within 3-24 months of study enrollment
2. Presence of cognitive complaints (score of three or higher on any of the four cognitive symptoms on the Neurobehavioral Symptom Inventory, or NSI)
3. Ability to understand and communicate in English

Exclusion Criteria

1. Medical/psychiatric/neurologic co-morbidity: blindness/low vision; uncontrolled seizure disorder; psychosis; history of moderate or severe TBI; or spinal cord injury with no use of upper extremities
2. Active participation in treatment for amputation, orthopedic trauma, burns, substance abuse, or posttraumatic stress disorder which would preclude full participation in an intensive cognitive rehabilitation program
3. Daily use of narcotic pain medication(s)

Participant Intake

As part of normal clinic procedures, all individuals referred to the TBI Clinic complete intake measures on a computer kiosk during their initial appointment, prior to their first evaluation by a medical provider. These intake measures include the NSI. The results of the intake measures (including the presence of cognitive complaints on the NSI) are then available to the treating medical provider during the initial appointment. A cadre of medical providers, including rehabilitation physicians, physician assistants, and nurse practitioners, complete the initial intake in the BAMC TBI Clinic.

For this study, providers established diagnosis of TBI using information from a semi-structured clinical interview and review of medical records (Armed Forces Health Longitudinal Technology, commonly known as AHLTA) and combat theater medical records (Theater Medical Data Store, or TMDS). Determination of injury severity was consistent with the VA/DoD Clinical Practice Guideline for the Management of Concussion/mTBI.³ Treating providers had access to an inclusion/exclusion checklist during the intake to determine whether a service member was eligible for the study. Providers used the checklist solely as a reminder of the eligibility criteria for the study and did not enter individual identifying information on the form. Providers did not include individual identifying information in the research record.

Study Enrollment

As part of standard care, the provider discussed treatment options (e.g., individualized cognitive rehabilitation) with individuals who reported cognitive complaints and met eligibility criteria. These options included participation in the RCT. The provider referred individuals who expressed willingness to consider participation in the RCT to the study coordinator or principal investigator (PI) located in the clinic. The study coordinator/PI met with referred individuals, verified eligibility using the inclusion/exclusion checklist, discussed the purpose of the study, and initiated the informed consent process. The study coordinator/PI then randomly assigned the participant to one

of the four treatment arms of the study (see Randomization) and scheduled the participant for clinical treatment appointments and research evaluations. All participants had a follow-up appointment scheduled with their medical provider within a week of their initial appointment to implement or follow up on individualized treatment recommendations, regardless of whether they chose to participate in the RCT.

Randomization

Following consent and enrollment, investigators randomized participants to one of the four treatment arms according to the following procedure.

1. Investigators used true random number tables to manually generate randomization assignments *a priori*.
2. To preclude the participant or provider from guessing the next assignment, the investigators used blocked randomization, with randomly determined block size.
3. An associate investigator (AI) on the study whose office was physically located outside the TBI Clinic was responsible for the integrity of the randomization assignments. The study coordinator or PI obtained the randomization treatment assignment by telephone from the AI, or a staff member the AI assigned to this task.

Participants and providers were not blinded to the treatment.

Completion of Research Measures

The research team used a study ID number, assigned to each participant, to ensure protection of Personal Health Information (commonly known as PHI). A research psychometrician blinded to treatment assignments, and located outside of the TBI clinic but within the BAMC medical center, completed the research evaluations and outcome assessments. The research psychometrician administered all dependent measures (see Primary and Secondary Outcome Measures) prior to the start of treatment. The psychometrician repeated these measures at intervals of 3, 6, 12, and 18 weeks following the initiation of the study.

In addition to a dedicated research psychometrician and a study coordinator, the SCORE trial research staff included a research associate with part-time responsibilities for the SCORE trial to assist the study coordinator with coverage. Two additional psychometricians at BAMC, trained by the research team on the protocol, served as back-ups.

Primary outcome measures

1. **PASAT.** Paced Auditory Serial Addition Test, a measure of attention, concentration, working memory, and cognitive processing efficiency
2. **SCL-90.** Symptom Checklist – 90, a measure of general psychological functioning with subscales examining depression, anxiety, somatization, and other domains
3. **KBCI.** Key Behaviors Change Inventory, a measure of the key day-to-day cognitive, interpersonal, and functional adjustment behaviors commonly affected following TBI

Secondary outcome measures

1. **Fatigue Severity Scale (FSS).** Total score
2. **Neurobehavioral Symptom Inventory (NSI).** Total score

3. **Global Measure of Neuropsychological Functioning.** Average normative T-scores of CVLT, or California Verbal Learning Test, Sum Trials 1-5; D-KEFS, or Delis–Kaplan Executive Function System Verbal Fluency, (Letter and Category Fluency); Trail Making Test Parts A & B; and WAIS-IV, or Wechsler Adult Intelligence Scale-Fourth Edition, Processing Speed and Working Memory Index Scores
4. **WHOQOL-BREF.** Brief version of the WHO-Quality of Life measure
5. **Health Care Utilization.** Comparison of healthcare utilization 1 month prior to enrollment in the study with healthcare utilization, six months following study completion
6. **Work Status.** At study completion:
 - a. Returned to full duty
 - b. Attachment/Assignment to Warrior-in-Transition Battalion or rear detachment, but Medical Evaluation Board (MEB) proceedings have not been initiated
 - c. MEB proceedings have been initiated/completed

Please see SCORE Outcome Instruments for detailed information about the instruments.

Providers

Full-time clinical staff members within the BAMC TBI Clinic conducted all treatment interventions in the SCORE trial, including cognitive rehabilitation therapies, medical care, and behavioral health interventions. These providers carry licenses in their specialty area and have considerable experience in the treatment of mTBI in a military setting.

Staff members provided interventions in the SCORE trial according to the following disciplines:

- **Medical Care.** One rehabilitation physician; one nurse practitioner; two physician assistants
- **Behavioral Health.** Two psychologists; one postdoctoral fellow in neuropsychology
- **Cognitive Rehabilitation.** Three speech-language pathologists; two occupational therapists; one recreational therapist

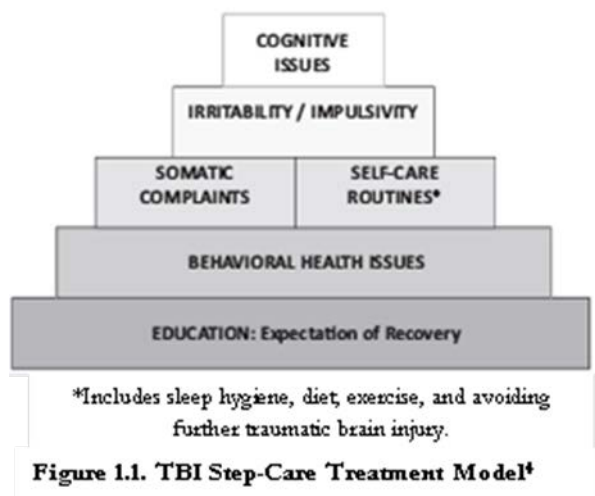
Treatment

All participants enrolled in the SCORE trial received the standard of care in management of chronic post-concussion symptoms, consistent with the VA/DoD Clinical Practice Guideline for the Management of Concussion/mTBI,³ regardless of treatment assignment. The standard of care includes provision of patient education materials adapted from existing studies to address more persistent rather than acute symptom management (see Chapter 2, Psychoeducational Interventions for Persistent Post-Concussion Symptoms Following Combat-Related Mild Traumatic Brain Injury (SCORE Arm 1); regularly scheduled follow-up with a medical provider every three weeks; and symptom-based treatment of post-concussion complaints (e.g., medication trials for headache and co-occurring psychiatric disorders, physical therapy for vestibular complaints, case management, and supportive counseling with social work for soldiers assigned to the Warriors-in-Transition Battalion).

Arm 1: Psychoeducational control group

Arm 1 of SCORE constituted standard of care treatment for patients with chronic post-concussion symptoms. Participants assigned to Arm 1 received written psychoeducational materials specifically

adapted for management of persistent symptoms and follow-up with medical providers every three weeks. The medical providers presented the psychoeducational materials to participants during their first visit, reviewed the materials, and answered participants' questions. Additionally, participants assigned to this group received medical care (e.g., psychopharmacological management of depression) and/or referral for symptom management (e.g., vestibular rehabilitation) of non-cognitive complaints, consistent with the current standard of care treatment model for managing post-concussion symptoms (see Figure 1.1). See Chapter 2 for details.



Arm 2: Non-therapist directed computerized cognitive rehabilitation

In addition to the standard of care treatment described in Arm 1, individuals assigned to Treatment Arm 2 received 10 hours of in-clinic, computerized treatment per week throughout the 6-week treatment trial. Participants received two hours of treatment per day, proctored by clinic staff (recreation therapist, medical staff, neuropsychologist) that was responsible for recording daily performance and providing positive reinforcement of participation and effort. Computer programs selected for this treatment trial included both skill-specific training (e.g.,

attention processes) and general cognitive activation.

Specific details about Treatment Arm 2 are available in Chapter 3, Computerized Cognitive Rehabilitation Interventions for Persistent Symptoms Following Mild Traumatic Brain Injury (SCORE Arm 2).

Arm 3: Therapist-directed individualized cognitive rehabilitation

In addition to the standard of care treatment described in Arm 1, participants assigned to Treatment Arm 3 received 10 hours per week of individual and group cognitive rehabilitation treatment, including homework assignments, conducted by speech therapists and/or occupational therapists. The weekly individual cognitive rehabilitation therapy consisted of five one-hour manualized (e.g., standardized) sessions, with two hours focused on compensatory strategies and three hours focused on restorative strategies. Participants had two hours per week of manualized group therapy, which were one-hour sessions focused on compensatory cognitive rehabilitation strategies. Finally, participants completed three hours per week of manualized, computer-based, cognitive rehabilitation “homework,” proctored by clinic staff responsible for recording performance and providing positive reinforcement for participation and effort. To ensure consistency, each participant received a treatment manual comprised of educational materials, integrated individual and group activities, and assignments.

Specific details about Treatment Arm 3 are available in Chapter 4, Traditional Cognitive Rehabilitation for Persistent Symptoms Following Mild Traumatic Brain Injury (SCORE Arm 3).

Arm 4: Integrated interdisciplinary cognitive rehabilitation combined with cognitive-behavioral psychotherapy

In addition to the standard of care treatment described in Arm 1, participants assigned to Treatment Arm 4 received 10 hours per week of manualized individual and group treatment, including homework assignments, conducted by credentialed speech therapists, occupational therapists, and doctoral-level psychologists. The weekly individual cognitive rehabilitation therapy consisted of four one-hour sessions, with two hours focused on restorative strategies, one hour focused on compensatory strategies, and one hour of individual psychotherapy targeting anxiety/combat stress symptoms through relaxation training, exposure therapy, and cognitive-behavioral principles.

Participants had three one-hour sessions per week of group therapy. Two hours focused on compensatory cognitive rehabilitation strategies, and the remaining hour of group psychotherapy targeted post-concussion and depressive symptoms through cognitive-behavioral psychotherapy principles.

Finally, participants completed three hours per week of “homework,” which included 30 minutes of relaxation training, 30 minutes of cognitive-behavioral psychotherapy homework, and two hours of computerized cognitive rehabilitation exercises proctored by clinic staff. To ensure consistency, each participant received a treatment manual comprised of educational materials, integrated individual and group activities, and assignments.

Specific details about Treatment Arm 4 are available in Chapter 5, Integrated Behavioral Health and Cognitive Rehabilitation Interventions for Persistent Symptoms Following Mild Traumatic Brain Injury (SCORE Arm 4).

Development of Manuals

One of the primary goals of the SCORE study included dissemination of study findings within the Military and VA Healthcare Systems. To this end, investigators collaborated to create detailed treatment and participant manuals as part of this research study. During a three-day workshop held in San Antonio, Texas, in September 2010, invited participants convened to develop the manual content. The workshop included BAMC TBI Clinic staff members participating in the SCORE trial, as well as invited subject matter experts in cognitive rehabilitation from the VA Healthcare System and DVBIC, including the following:

- **Medical Staff**
 - Amy O. Bowles, M.D. (BAMC TBI Clinic)
 - Michelle A. Lindsay, N.P. (BAMC TBI Clinic)
- **Behavioral Health**
 - Douglas B. Cooper, Ph.D. (BAMC TBI Clinic)
 - Jon Grizzle, Ph.D. (BAMC TBI Clinic)
 - Jan E. Kennedy, Ph.D. (DVBIC – San Antonio)
 - Laurence P. Perotti, Ph.D. (BAMC TBI Clinic)
 - Rodney D. Vanderploeg, Ph.D. (James Haley VAMC)

- **Speech Language Pathology**
 - Micaela V. Cornis-Pop, Ph.D. (VA Central Office)
 - Christine S. Fox, M.S. (BAMC TBI Clinic)
 - Melissa R. Ray, M.S. (BAMC TBI Clinic)
 - R. Kevin Manning, Ph.D. (BAMC TBI Clinic)
 - Linda M. Picon, M.C.D. (James Haley VAMC)
 - Donald L. MacLennan, M.A. (Minneapolis VAMC)
- **Occupational Therapy**
 - Christopher J. Gillis, M.A. (BAMC TBI Clinic)
 - M. Marina LeBlanc, M.S. (BAMC TBI Clinic)
 - Deborah Voydetich, M.S. (Minneapolis VAMC)

Workshop participants developed clinician guides and client manuals in Treatment Arms 3 and 4. Please see Chapters 4 and 5 for these manuals.

Research Aims, Hypotheses, and Measures

Before the clinical trial began, the research team developed the following research Aims.

Aim 1

Determine the effectiveness of cognitive rehabilitation for individuals with a history of mTBI and persistent cognitive symptoms. The SCORE study defines rehabilitation effectiveness as improvement in the following outcome areas: neuropsychological functioning; emotional, psychological and physical post-concussion symptoms, functional cognitive behavior in everyday life (KBCI), cognitive complaints, cognitive fatigue, quality of life, health care utilization, and work status.

Aim 2

Determine which of the following components of cognitive rehabilitation treatment are most effective:

1. Psychoeducational information regarding TBI, symptoms, and generally positive expectation of outcomes
2. Self-administered, computerized cognitive rehabilitation interventions
3. Therapist-directed and individualized cognitive rehabilitation interventions
4. Integrated interdisciplinary cognitive rehabilitation program combined with cognitive behavior psychotherapy

Aim 3

Determine the relationships between better treatment outcomes and the following participant characteristics: effort, treatment engagement/participation, psychiatric and substance use/abuse history, current psychiatric co-morbidities, current medical co-morbidities or injuries, multiple concussions, perceived self-efficacy, participant symptom attribution biases, and MEB status.

Hypotheses

The research team developed the following *a priori* hypotheses to assess the primary three aims of the SCORE trial. Descriptions of specific hypotheses and associated dependent variables follow:

Aim 1

- **Hypothesis 1.**
 - Groups will differ on Primary Outcome Measures following treatment
 - The effect size will be largest on the primary psychological outcome measure (SCL-90 Global Score)
- **Hypothesis 2.** Groups will differ on Secondary Outcome Measures following treatment.
- **Hypothesis 3.** The group differences in treatment outcomes attained at the end of treatment (six weeks) will be sustained at the 12- and the 18-week follow-up intervals.

Aim 2

- **Hypothesis 1.**
 - Treatment Arms 3 and 4 will have better Primary Outcomes than Arms 1 or 2
 - Arms 1 and 2 will be comparable on all Primary Outcome Measures
 - Arm 4 will have better Psychological Outcomes (SCL-90) than the other treatment Arms
- **Hypothesis 2.**
 - Treatment Arms 3 and 4 will have better Secondary Outcomes than Arms 1 or 2
 - Arms 1 and 2 will be comparable on all Secondary Outcome Measures

Aim 3

- **Hypothesis 1.** Those with clinically diagnosed psychiatric conditions (i.e., depressive disorder, anxiety disorder, posttraumatic stress disorder [PTSD], substance abuse) will benefit more (as assessed by the SCL-90 Global Severity Index) from psychological versus cognitive interventions.
- **Hypothesis 2.** Those with better effort will benefit more.
- **Hypothesis 3.** Those with multiple concussions will do more poorly than those with only one concussion.
- **Hypothesis 4.** Those participants who initiated a MEB prior to enrolling in the treatment study will do worse than those participants who did not initiate a MEB before beginning the study.

SCORE Outcome Instruments

Providers evaluated study participants at baseline (pre-treatment) and at follow-up intervals of 3, 6, 12 and 18 weeks following the initiation of treatment. Baseline assessment included collection of demographic information (e.g., age, education, rank), medical/psychiatric history (e.g., childhood history of attention deficit hyperactivity disorder, typically referred to as ADHD, and injury-specific characteristics (e.g., mechanism of injury; associated injuries).

In addition, the investigators administered the Test of Memory Malingering (TOMM) and Wide Range Achievement Test –Fourth Edition (WRAT-IV; Word Reading subtest) only at baseline. Every week, each clinician working with study participants enrolled in Arms 3 and 4 provided an independent rating of the Rehabilitation Intensity of Therapy Scale (RITS) for those participants. Investigators subsequently created a composite treatment engagement score by averaging the RITS scores. The AHLTA medical record system provided healthcare utilization information, which did not include any treatment that participants may have received at civilian facilities.

SCORE trial research team members did not share information obtained from outcome measures with either the study participants or the treating providers. The only exception was an independent review of the Alcohol Use Disorders Identification Test (AUDIT) score by the treating medical personnel, who provided interventions for individuals reporting significant alcohol use disorders, as recommended in the AUDIT manual. Table 1.1 provides detailed descriptions of outcome instruments, along with approximate administration times, and associated research aims and hypotheses.

Table 1.1. Outcome Instruments, Administration Times, Specific Aims and Hypotheses

| | Outcome Instruments | Admin. Time (min.) | Aim/Hypothesis |
|---------------------------------|--|--------------------|---|
| <i>Primary Outcome Measures</i> | Symptom Checklist – 90- Revised (SCL-90-R). The SCL-90-R is a self-report measure of a broad range of psychological problems and psychopathology that is commonly used in studies of treatment outcome, including cognitive rehabilitation for mTBI. ⁵ There is an extensive body of literature confirming the instrument's reliability and validity. ⁶ <i>Reliability:</i> Internal consistency ranging from .77 (Psychoticism) to .90 (Depression). Test-retest reliability ranges from .8 to .9, with time intervals as short as 1 week. <i>Variables:</i> Global severity Index and 9 subscales (Somatization; Obsessive-Compulsive; Interpersonal Sensitivity; Depression; Anxiety; Hostility; Phobic Anxiety; Paranoid Ideation, and Psychoticism). | 12 | Aim 1, Hyp 1a, 1b; Hyp 3 Aim 2, Hyp 1a, 1b, 1c Aim 3, Hyp 1 |
| | Paced Auditory Serial Addition Test (PASAT). The PASAT is a serial-addition test used to assess information processing speed, sustained attention, and divided attention. It consists of four trials with 50 items per trial. <i>Reliability:</i> The PASAT's split-half reliability is .9, implying high internal consistency. ⁷ Test-retest reliability following short intervals (7-10 days) are high (>.90), ⁸ although practice effects have been observed in several studies including studies with brain injury populations. <i>Variables:</i> Number correct per trial; Summed total across 4 trials. | 15 | Aim 1, Hyp 1a, 1b Aim 2, Hyp 1a, 1b |

| | Outcome Instruments | Admin. Time (min.) | Aim/Hypothesis |
|----------------------------------|--|--------------------|--|
| Primary Outcome Measures (cont.) | Key Behaviors Change Inventory (KBCI). The Key Behaviors Change Inventory (KBCI) is an instrument designed to assess cognitive and behavioral changes following traumatic brain injury (TBI). Patients, caregivers or relatives of individuals who have sustained a TBI can easily complete it. It consists of 64 items (8 scales of 8 items each), rated on a 4-point scale. The eight scales are: Inattention, Impulsivity, Apathy, Unawareness of Problems, Interpersonal Difficulties, Communication Problems, Somatic Difficulties, and Emotional Adjustment. Coefficients alpha for these scales ranged from .82 to .91. ⁹ Users can sum the scores to obtain a Total KBCI score (a measure used in the SCORE study). The KBCI has good criterion-related validity, discriminating effectively between 30 TBI survivors, 20 multiple sclerosis (MS) patients, and 50 normal control subjects equated on age and gender. ⁹ The KBCI effectively measures awareness problems following TBI ¹⁰ and can effectively assess executive functioning in elderly individuals. ¹¹ | 8 | Aim 1, Hyp 1a, 1b Aim 2, Hyp 1a, 1b |
| Secondary Outcome Measures | Fatigue Severity Scale (FSS). The Fatigue Severity Scale is a 9-item self-rated scale examining the impact of fatigue on motivation, activity level, and social participation. ¹² The psychometric properties are well-established and validated in multiple clinical populations, including traumatic brain injury. ¹³ <i>Reliability:</i> Test-retest: 10 weeks = .84. <i>Validity:</i> The instrument has excellent internal consistency (Cronbach's alpha =.90) and demonstrated construct validity in TBI patients, with moderate correlations with other measures of fatigue. ¹³ <i>Variable:</i> Total summed score. | 2 | Aim 1, Hyp 2 Aim 2, Hyp 2 |
| | Neurobehavioral Symptom Inventory (NSI). The NSI is a 22 item self-report checklist that has been validated in individuals with persistent post-concussion symptoms, ¹⁴ as well as in OEF-OIF service members and veterans. ¹⁵ Given the mixed constellation of symptoms that make up post-concussion syndrome, examination of the psychometric properties of the NSI has focused on factor-analysis of the instrument rather than examination of internal consistency. Studies have demonstrated and validated a 4-factor solution in the OEF-OIF population, once controlling for PTSD symptoms. ^{16,17} There are no known published studies on the test-retest reliability of this instrument. <i>Variables:</i> Cognitive Cluster; Physical Cluster; Individual items from the four cognitive items. | 3 | Aim 1, Hyp 2 Aim 2, Hyp 2 |
| | World Health Organization Brief Quality of Life Scale (WHO-QoL BREF). The WHOQOL-BREF is a 26 item self-report instrument measuring perceived quality of life in five domains (Overall Functioning, Physical Capacity, Psychological, Social Relationships, and Environment). Users score each domain on a scale of 0-100, which represents the percentage of the total possible score achieved for that domain. The psychometric properties of the instrument are well-established, ¹⁸ although, to date, there is limited information about its use in individuals with acquired brain injury. <i>Reliability:</i> Test-retest: range = .83-.96. <i>Validity:</i> Cronbach's alpha range: .65-.93. <i>Variables:</i> Total transformed score and total score for each of the 5 subscale domains. | 3 | Aim 1, Hyp 2 Aim 2, Hyp 2 |

| | Outcome Instruments | Admin. Time (min.) | Aim/Hypothesis |
|---|---|--------------------|------------------------------|
| Secondary Outcome Measures (cont.) | Neuropsychological Global Composite Score. The Neuropsychological Global Composite Score encompasses the average normative T-scores for five neuropsychological measures: CVLT-2 sum trials 1-5; D-KEFS Verbal Fluency (letter + category fluency); Trail Making Test Parts A&B; WAIS-IV Processing Speed, and WAIS-IV Working Memory indices. These five instruments are among the most common and well-studied neuropsychological instruments in use; the TBI Clinical Trials Network group ¹⁹ selected them as recommended outcome measures for TBI treatment trials. <i>Reliability:</i> All of these instruments have well-established internal consistency and test-retest reliability ranging from .75 to .96. <i>Variables:</i> Average normative t-score of CVLT-2 sum trials 1-5, D-KEFS Verbal Fluency total score; Trail Making Test – part B only; WAIS-IV Processing Speed and Working Memory (using Digit Span and Letter Number Sequencing subtests) Indices. | 25 | Aim 1, Hyp 2 Aim 2, Hyp 2 |
| | | | |
| Covariate and Tertiary Measures | Test of Memory Malingering (TOMM). This is a 50-item forced-choice recognition memory test developed to assess suboptimal effort on neuropsychological testing. It has been validated in several populations, including mild traumatic brain injury. ²⁰ <i>Reliability:</i> Coefficient alphas = .95 for Trial 2. Test-retest reliability is not known, although there is no concern regarding practice effects due to the intent of the instrument. <i>Variables:</i> Total raw score correct for Trial 2. | 15 | Aim 3, Hyp 2 |
| | Wide Range Achievement Test – Fourth Edition (WRAT-IV; Word Reading subtest). This is a 55-item word reading measure assessing basic reading achievement that can be used to determine grade-level reading skill performance. SCORE investigators used it to establish baseline reading level, which helped to determine inclusion in the treatment outcomes study. <i>Reliability:</i> Cronbach’s alpha ranges from .90 to .95, depending on the version and age range. <i>Variable:</i> Word Reading Grade Equivalent score (Blue). | 5 | None |
| | Alcohol Use Disorders Identification Test (AUDIT). AUDIT is a 10-item self-report screening measure for identifying individuals with harmful patterns of alcohol consumption. This is an extensively studied instrument, created by the World Health Organization. SCORE investigators used it as a covariate to examine the effects of alcohol disorders on treatment outcomes (Research Aim 3). <i>Reliability:</i> Test-retest reliability rates were high (.86) in a mixed substance abuse sample. ²¹ <i>Variable:</i> AUDIT total score. | 2 | Aim 3 |
| | Posttraumatic Stress Disorder Checklist-Military Form (PCL-M). The PCL-M is a 17-item self-report inventory for assessing the symptoms of Posttraumatic Stress Disorder. It has been validated in several populations, including motor vehicle crash victims. <i>Reliability:</i> Cronbach’s alpha = .93. ²² <i>Variables:</i> Total raw score. | 3 | Aim 3, Hyp 1 |
| | Headache Impact Test – 6 (HIT-6). The Headache Impact Test- 6 is a brief, 6-item questionnaire measuring headache severity and its impact on daily functioning. Weighted raw scores yield a total score ranging from 36-78. In a study of 540 individuals with recurrent headaches, estimates of HIT-6 were .89 for internal consistency, .90 for alternate forms, and .80 for test-retest reliability. ²³ <i>Variables:</i> Total raw score (weighted). | 2 | None |

| | Outcome Instruments | Admin. Time (min.) | Aim/Hypothesis |
|---|--|--------------------|----------------|
| Covariate and Tertiary Measures (cont.) | <p>Multidimensional Health Locus of Control Scale (MHLCS – Form C). This is an 18-item self-report inventory for assessing an individual’s perception of an internal or external locus of control regarding his/her health condition (cognitive difficulties, for the purposes of SCORE). Clinical studies have validated this instrument in numerous clinical populations, and its psychometric properties are well-established.²⁴ <i>Reliability:</i> Internal consistency range .85-.87. Test-retest reliability range .54-.80. <i>Variables:</i> Total raw score for each of the five subscales (internal, chance, powerful others, doctors, other people).</p> | 4 | None |
| | <p>Self-Efficacy for Symptom Management Scale (SEsx). The Self-Efficacy for Symptom Management Scale²⁵ is a 13-item scale that incorporates three subscales relating to self-efficacy to perform self-management behaviors that had the highest inter-correlations among a large sample of persons with diverse disabilities, and contained items that appear most meaningful for people with a neurological disability. The first subscale (Items 1 – 4/SEsoc) reflects self-efficacy for obtaining help from community, family and friends to perform everyday activities and get emotional support. The second subscale (Items 5 – 9) relates to self-efficacy to manage symptoms; for the SCORE study, investigators modified four of the five items from the original emphasis on managing self-efficacy after physical symptoms to emphasize the management and compensation for cognitive symptoms (SEcog). The investigators also modified the third subscale, self-efficacy for managing depression (Items 10 – 13), in order to reflect a more general emphasis on management of emotional symptoms, such as feeling frustrated or overwhelmed (SEemot). The question “How confident are you that you can...” precedes each item, with responses on a 1 to 10 point scale from “not at all confident” to “totally confident.” Users sum the items from each subscale to obtain a subscale score, and calculate a total score by summing all three subscale scores. Within a brain injury sample, the total scale demonstrated an internal reliability (Cronbach’s alpha) of .93 with subscale reliabilities between .77 and .93, with similar findings obtained for the non-injured participants. Correlations of the total SE and subscale scores with measures of satisfaction with cognitive functioning ($r = 0.73$) and patients’ ratings of general health status ($r = 0.50$) demonstrated construct validity.²⁵ <i>Variables:</i> SEsx total score; SEsoc, SEcog, and SEemot subscale scores.</p> | 3 | None |
| | <p>Cognitive Symptom Attribution Scale This is a one-item, self-report, Likert scale used to assess the subject’s perception of the etiology for his/her cognitive symptoms. SCORE investigators developed the scale specifically for this study; thus, its psychometric properties are not known. <i>Variables:</i> Total score ranging from 1-5.</p> | 1 | None |
| | <p>Rehabilitation Intensity of Therapy Scale (RITS). RITS is a 1-item Likert scale that rates patient effort and engagement in his/her rehabilitation therapies. The psychometric properties of this instrument are currently under investigation by the author.²⁶ However, studies have examined and validated similar instruments in the brain injury population.²⁷ <i>Variables:</i> Average weekly rating by therapists.</p> | 1 | Aim 3, Hyp 2 |

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Appendix A: Acronyms

| | |
|--------|---|
| ADHD | attention deficit hyperactivity disorder |
| AHLTA | Armed Forces Health Longitudinal Technology |
| AI | associate investigator |
| AUDIT | Alcohol Use Disorders Identification Test |
| BAMC | Brooke Army Medical Center |
| CLVT | California Verbal Learning Test |
| D-KEFS | Delis–Kaplan Executive Function System |
| DoD | Department of Defense |
| DVBIC | Defense and Veterans Brain Injury Center |
| ECRI | Emergency Care Research Institute |
| FSS | Fatigue Severity Scale |
| HIT-6 | Headache Impact Test – 6 |
| KBCI | Key Behaviors Change Inventory |
| MEB | Medical Evaluation Board |
| MHLCS | Multidimensional Health Locus of Control Scale |
| NSI | Neurobehavioral Symptom Inventory |
| OEF | Operation Enduring Freedom |
| OIF | Operation Iraqi Freedom |
| PASAT | Paced Auditory Serial Addition Test |
| PCL-M | Posttraumatic Stress Disorder Checklist-Military Form |
| PHI | personal health information |
| PI | principal investigator |
| PTSD | posttraumatic stress disorder |
| RCT | Randomized, controlled (treatment) trial |
| RITS | Rehabilitation Intensity of Therapy Scale |
| SAMMC | San Antonio Military Medical Center |
| SCL-90 | Symptom Checklist – 90 |
| SCORE | Study of Cognitive Rehabilitation Effectiveness |

Chapter 1: Study of Cognitive Rehabilitation Effectiveness Clinical Trial: Overview

| | |
|-------------|---|
| SEsx | Self-Efficacy for Symptom Management Scale |
| TBI/mTBI | traumatic brain injury/mild traumatic brain injury |
| TOMM | Test of Memory Malingering |
| TMDS | Theater Medical Data Store |
| VA | Veterans Affairs |
| WAIS-IV | Wechsler Adult Intelligence Scale – Fourth Edition |
| WHOQoL-BREF | World Health Organization Quality of Life measure (brief version) |
| WRAT-IV | Wide Range Achievement Test – Fourth Edition |