

APPENDIX A: SEARCH STRATEGY

Our study search coordinator, in consultation with our evidence synthesis team, developed the following search strategy. The PubMed and PsycINFO databases were searched for the following terms:

TBI – brain injury (and variants of injury); coma; coma, post-head injury; Glasgow Coma Scale; head injuries, closed; post-concussion syndrome; brain concussion; post-concussive; and brain injury, chronic.

PTSD - combat disorders (and variants of disorder); posttraumatic stress; posttraumatic stress disorder (and variants of disorder); post-traumatic stress disorder (and variants of disorder); stress disorders, post-traumatic; anxiety; and anxiety disorders.

The results from the TBI and PTSD searches were merged attempting to identify studies that included participants with both TBI and PTSD. The search was limited to English language studies of human subjects published between 1980 and 2009.

Sample Search Strategy:

-
- 1 brain injur*.mp. or exp Brain Injuries
 - 2 coma.mp. or Coma, Post-Head Injury/ or Coma/ or Glasgow Coma Scale
 - 3 Head Injuries, Closed/ or Post-Concussion Syndrome/ or Brain Concussion/ or post-concussive.mp. or Brain Injury, Chronic
 - 4 combat disord*.mp. or exp Combat Disorders
 - 5 (posttraumatic stress or posttraumatic stress disorder* or post-traumatic stress disorder* or ptsd).mp. or exp Stress Disorders, Post-Traumatic
 - 6 anxiety.mp. or exp Anxiety/ or exp Anxiety Disorders
 - 7 or/1-3
 - 8 or/4-6
 - 9 7 and 8
 - 10 limit 9 to English language
 - 11 limit 10 to yr="1980 - 2009"
 - 12 limit 11 to human

In addition, the REHABDATA database was searched as follows:

From the advanced search page at www.naric.com/research/rehab/advanced.cfm,

Used “All the words” field,

Searched for “brain injuries posttraumatic.”

[Provided by Jessica Chaiken of the National Rehabilitation Information Center (NARIC)]

Results of the database searches were combined and duplicate entries eliminated.

APPENDIX B: DATA ABSTRACTION FORM

TBI/PTSD Review Article Abstraction Form

Author (first): _____

Journal: _____

Year Publication: _____

Country: _____ (where study performed)

Reviewer: _____

VERIFICATION/SELECTION OF STUDY ELIGIBILITY

Article published after 1980	Yes	No	Unclear
English-language	Yes	No	Unclear
Adult Population	Yes	No	Unclear
Subjects with probable TBI	Yes	No	Unclear
Subjects with probable PTSD	Yes	No	Unclear
Report peer-reviewed	Yes	No	Unclear
Other reason for exclusion? (if yes, specify) _____			

DESIGN (circle)

Systematic review
 Randomized controlled clinical trial
 Non-randomized controlled clinical trial
 Historical clinical trial
 Cohort study
 Case-control study
 Cross-sectional study
 Case series
 Case report
 Qualitative
 Editorial/opinion piece/letter
 Undefined

KEY QUESTION(S) (circle)

KQ1: Epidemiology
 KQ2: Assessment
 KQ3: Treatment
 Background

NOTES:

- Study contains/may contain same data as another study (specify: _____)
- Study described high-quality RCT involving ASD

PARTICIPANTS

Single site or Multi-center? (circle one) Number of sites _____
 Setting: DoD VAMC Other (circle one)
 Total # of participants _____
 Total # eligible _____
 Reported response rate _____
 Participants excluded from analysis _____ (Why? _____)

	n and %				Total
	TBI/PTSD	TBI only	PTSD only	Neither	
# Participants:					
# with PTSD					
# with TBI					
Mild TBI (How defined?)					
Moderate TBI (How defined?)					
Severe TBI (How defined?)					
Age (M, SD)					
Men					
Women					
Race: white					
Race: black					
Race: other					
Ethnicity: Hispanic					
Ethnicity: non-Hispanic					
Active Duty					
Veteran					
Community					

	n and %				Total
	TBI/PTSD	TBI only	PTSD only	Neither	
Education: <HS					
Education: HS grad					
Education: Some college/Associates					
Education: College grad					
Education: Other (specify)					
Years of Education (M, SD)					
Service-connected/ disabled					
Seeking SC/ disability					
Trauma: Combat					
Trauma: Terror					
<i>(If combat or terror, specify blast vs. non-blast and any data on distance from blast)</i>					
Trauma: MVC					
Trauma: Assault					
Trauma: Other (specify)					
Time since trauma (M, SD) in months					
Number of traumas (M, SD)					
Previous head injury					
Comorbid: Depression					
Comorbid: SUD					
Comorbid: Pain					
Comorbid: Other (specify)					

NOTES:

METHODS OF ASSESSMENT

When were assessments made relative to trauma? _____

TBI Assessment	How defined (cut-off score)	n (%)	If measured:		
			Gold-standard test; cut-off score	Blinded rater?	Measure of diagnostic accuracy (and statistical uncertainty)
Self-report (specify)					
Clinic screening (specify: ie, VA screen)					
Diagnosis (specify: ie, clinical interview, neuropsych based, etc.)					
Administrative data					
Other (specify)					
PTSD Assessment					
Self-report (specify)					
Clinic screening (specify: ie VA 4-item screen)					
Diagnosis (specify: ie, structured interview)					
Administrative data					
Other (specify)					

NOTES:

(i.e., any indication of poorer performance of assessment method when conditions are co-occurring?)

METHODS OF ASSESSMENT

Neuropsych Tests	Check if used:	Notes
Wechsler Adult Intelligence Scale (WAIS-III)		
Stroop Color/Word		
Aphasia Tests (multiple)		
Wechsler Memory Scale – III		
Rey Osterieith Complex Figure		
Wisconsin Card Sorting		
Rey Auditory Verbal Learning Test		
MMPI		
Controlled Oral Word Association (COWA)		
Trail Making Test		
Boston Naming		
Finger Tapping		
Other (<i>specify</i>)		
Other (<i>specify</i>)		
Other (<i>specify</i>)		
Imaging		
EEG		
CT		
MRI		
fMRI		
PET		
SPECT		
Other (<i>specify</i>)		

TREATMENT OUTCOMES (use additional pages for each outcome)

Note additional KQ3 eligibility criteria:			
at least 80% with both TBI/PTSD	Yes	No	Unclear
- or -			
outcome stratified by comorbidity	Yes	No	Unclear

Treatment/intervention(s) of interest:

Outcome of interest and how measured:

	Treatment group 1 <i>(specify)</i> <i>(n =)</i>	Treatment group 2 <i>(specify)</i> <i>(n =)</i>	Treatment group 3 <i>(specify)</i> <i>(n =)</i>	Comparator <i>(specify)</i> <i>(n =)</i>
Baseline (mean, SD/SE)				
0 - 6 mos. posttreatment (mean, SD/SE)				
6 mos. - 1 year posttreatment (mean, SD/SE)				
1+ year posttreatment (mean, SD/SE)				
Other time frame <i>(specify)</i> (mean, SD/SE)				

NOTES:
(i.e., any evidence of adverse events/harms?)

APPENDIX C: PEER REVIEWER COMMENTS

Reviewer Comments	Authors' Responses
1. Are the objectives, scope, and methods for this review clearly described?	
Strengthen review by using "history of TBI" and "sequelae of TBI" or "symptoms associated (or possibly associated) with history of TBI."	Done.
Consider clarifying comorbid and comorbidity – maybe simpler to say that we meant PTSD in those with history of TBI or TBI in those who meet criteria for current PTSD.	We have defined and clarified our use of the terms "TBI," "PTSD," and "comorbidity" in the background section and throughout the revised report.
Use "other mental health conditions and anxiety disorders other than PTSD or anxiety symptoms unspecified" (PTSD is an anxiety disorder so use of terms "mental health comorbidities" and "anxiety" can be confusing at first read).	Changed statements throughout the revised report to read as recommended.
Add more rationale for focus on mTBI given the political context in which it takes place.	We have included a brief additional statement regarding the political importance and rationale for focusing on mTBI.
Explicitly state the reason for including the RAND study given that it is not peer-reviewed and not meeting inclusion criteria. Were other reports rejected?	A statement has been inserted. This study was peer reviewed. Though not published in a peer-reviewed journal, it is published by RAND and readily available on the RAND website. Additional rationale were provided in the draft report indicating that this was one of the largest and most nationally representative studies assessing TBI and PTSD in military personnel who had served in Iraq and Afghanistan. Therefore, it provides key evidence in examining TBI/PTSD prevalence.
We should be clear that this literature search is about people with a history of mTBI who are currently diagnosed with PTSD.	We have attempted to clarify this. Our search was broad. We included any study that assessed reported prevalence of individuals with mTBI and PTSD. Authors frequently referred to these individuals as having "comorbid" TBI and PTSD. However, we agree that the more accurate term for mTBI is "history of..." and have clarified this in our revised report.
Use Hoge review to clarify language – use post-concussive symptoms rather than TBI – for lasting symptoms that result from TBI; consider including paragraph about "language" or "terminology" at the beginning of the review.	We appreciate this suggestion and have been more clear throughout the report in terms of "TBI history," "symptoms related to a TBI," and "comorbidity."
2. Is there any indication of bias in our synthesis of the evidence?	
Inclusion of the RAND report without more justification may give impression of bias (note statement on pg. 30 that RAND report may provide the most reliable estimate ...) – consider how study is weighted given that it is not peer reviewed; perhaps findings should be classified as secondary findings?	We have reworded the referenced statement on pg. 30 and provided further rationale for our inclusion of this report. As noted above, the RAND report includes a statement that it underwent peer review with multiple reviewers. The nature of comments and authors' responses to these comments are not available. However, in our experience, the extent of peer review and number of reviewers on evidence reports (as witnessed by this VA ESP report) are typically greater than with most manuscripts submitted for publication in refereed journals. The final report is published on the RAND website. Whether it would have been accepted by a traditional paper journal is not known but we suspect condensed versions would have met journal publication criteria.
Some indication (in introduction) of belief that mTBI is associated with negative outcomes when this is the case in the minority of cases.	We have modified the introduction to include more information on the natural history of mTBI, including evidence that the majority of cases do not have long-term sequelae.

Reviewer Comments	Authors' Responses
<p>No; wondered why CH was a reviewer when he was a contributor with study; probably wanted unbiased reviewer; CH's research is controversial as noted on pg. 2.</p>	<p>Reviewers frequently have a bias. Often our goal is to seek a selection of reviewers that will ensure a broad range of opinions and comments. Prior publication history does not disqualify a reviewer. In general, we select reviewers without disclosure of the names of other reviewers, including the TAP members.</p>
<p>3. Are there any studies on the epidemiology, assessment, or treatment of TBI/PTSD that we may have overlooked?</p>	
<p>Suggest including Bryant study (Ref #83) in Exec. Summary (80% TBI subjects go on to develop PTSD).</p>	<p>The referenced study was included under secondary findings because it did not meet the study inclusion criteria (did not include participants with probable or diagnosed PTSD), which were developed <i>a priori</i> in consultation with our TAP. Consistent with previous ESP report formats, we did not include secondary findings in our Executive Summary.</p>
<p>Terrio et al. paper.</p>	<p>The suggested paper did not meet the study inclusion criteria (did not include data on probable or diagnosed PTSD).</p>
<p>Terrio (if PTSD).</p>	<p>We have updated our search through June, 2009. The following additional studies met inclusion criteria and were added to the evidence synthesis review: Brenner et al., 2009; Chalton et al., 2009; and Mora et al., 2009.</p>
<p>4. Additional comments</p>	
<p>Question 1 re comorbid TBI and PTSD is flawed; TBI is acute injury event while PTSD requires symptoms and impairment existing for a defined period of time AFTER the traumatic event; it would be correct to ask how often a TBI injury event may precede the onset of PTSD and whether TBI is a risk factor for PTSD; association may or may not be causal; it also would be correct to ask about comorbidity between PTSD and the sequelae or persistent symptoms/impairment resulting from TBI injury event; need accepted and valid case definition of sequelae attributed to mTBI/concussion; need to examine how strong the evidence is for causal association between mTBI/concussion and persistent symptoms, sequelae, or impairment (see recent IOM report).</p>	<p>The questions addressed in this evidence synthesis review were developed with considerable input from the VA ESP and specifically our TAP, with the purpose of addressing key questions of clinical and health policy importance and to inform the work of a VA consensus conference on this topic. We agree with the reviewer that the term "comorbid TBI and PTSD" is problematic especially when referring to mTBI. We had discussed the controversy surrounding this issue in our Introduction, Discussion and Future Research Recommendations sections. We have reviewed and further clarified these issues in the revised report. We strongly believe, and included in both our oral presentation at the consensus conference and in this report, that future research is needed to address the issues described by the reviewer.</p>
<p>It is correct to ask about how PTSD may affect, mediate, or confound the expression of symptoms attributed to an mTBI/concussion event (see 2008 NEJM); requires case-definition for dependent variable under study (e.g., symptom sequelae).</p>	<p>We agree and have spoken to this in our Limitations and Future Research Recommendations sections.</p>
<p>Report incorrectly applies the term prevalence; prevalence cannot be determined using the current definitions; technically correct to present the prevalence of PTSD in study participant <i>who had a history</i> of TBI (should not use present tense – see Figure 3); never correct to present prevalence of PTSD in those <i>with</i> TBI since TBI definition refers to past injury event (see Figure 2); figure should show prevalence of comorbid PTSD and persistent symptoms/sequelae attributed to TBI; lack of clarity by not separating mTBI from moderate and severe TBI for Question 1; inconsistent with Questions 2 and 3.</p>	<p>We have clarified throughout the revised report our intent to examine the prevalence of PTSD in individuals with a history of TBI. Our background clarifies that we addressed TBI with an emphasis on mTBI. For KQ1, we sought to examine prevalence of PTSD in individuals with a history of mTBI versus moderate or severe TBI. As such, our figures denote (when authors provided such information) the prevalence of mTBI history separate from moderate or severe TBI. For KQ2 and KQ3, we sought to assess diagnostic accuracy and treatment effectiveness versus harms for adults specifically with mTBI history who have PTSD.</p>

Reviewer Comments	Authors' Responses
<p>Questions 2 and 3 are flawed for the same reasons; the mTBI/concussion (past injury event) cannot (and should not) be the focus of diagnosis and treatment at time PTSD is diagnosed; questions would only be valid if asked about accuracy or diagnosis and treatment of sequelae of mTBI/concussion in presence of PTSD (with definition of sequelae)</p>	<p>We disagree.</p>
<p>Need consistent and accurate terminology in characterizing the sequelae attributed to concussion/mTBI; "post-concussive symptoms" encompasses the entire spectrum of physical, neurocognitive, and behavioral symptoms attributed to concussion/mTBI; need agreement on the nature of the symptoms – medical, functional somatic syndromes, or related conditions.</p>	<p>We agree and have clarified our wording throughout the report.</p>
<p>Report addresses questions that cannot be answered; questions are ill-conceived; need to first address limitations of current concussion/mTBI definition, derive valid case definition for sequelae attributed to concussion/mTBI, and broaden the focus beyond PTSD.</p>	<p>We agree that future research is needed to address limitations of current case definitions of mTBI. This has been discussed in the report. As noted above, we disagree that the key questions were ill-conceived.</p>
<p>Classification or designation of TBI as an event, diagnosis, sequelae confusing; suggest careful editing, defining of terms, and rephrasing/ reframing of results to address these concerns.</p>	<p>We thank the reviewer and have edited the report to address these concerns.</p>
<p>- EXECUTIVE SUMMARY</p>	
<p>Restate key questions in results section.</p>	<p>We attempted to follow a standard VA ESP report format and have not restated key questions in the results section of the Executive Summary. However, key questions are restated in the Results section of the main report.</p>
<p>8% cut-off for <18 years old unclear – need to state rationale (make change in full report also).</p>	<p>We have edited the report to reflect our 10% cut-off for children <18 years of age.</p>
<p>- INTRODUCTION/BACKGROUND</p>	
<p>Acknowledge that symptoms associated with mTBI in civilian cases generally resolve within weeks to months (1st paragraph of intro gives impression that mTBI is typically associated with negative outcomes).</p>	<p>We have edited this section to include evidence on the natural history of mTBI.</p>
<p>First sentence of 4th paragraph in background is inaccurate ("making an accurate diagnosis ..."); think what was meant was "determining etiology of presenting problems in individuals who have a history of TBI and PTSD"; paragraph gives impression that symptoms are needed for TBI diagnosis and that persistent symptoms are common in mTBI (suggest reworking).</p>	<p>We appreciate the reviewer's suggestion and have reworked the referenced paragraph.</p>
<p>Research on usefulness of education for mTBI is limited to education within a relatively short time period post-injury.</p>	<p>We have edited the relevant paragraph to address this comment.</p>
<p>Page 5 second paragraph difficult to follow.</p>	<p>We have clarified this paragraph.</p>
<p>May want to include DoD/VA definition of TBI in addition to CDC definition (Policy Memo October 2007).</p>	<p>Because the operational definitions are similar, we have retained the CDC definition in the report.</p>
<p>Did it matter whether diagnosis of mTBI was first followed by PTSD? Does it matter where initial evaluation starts ... mental health or neurology?</p>	<p>We noted in the report that the reported prevalence of TBI/PTSD was highly dependent on the construction of the cohort, method and timing of ascertainment, and definitions of disease/injury. The current literature is insufficient to determine whether timing of event/diagnosis influences outcomes or if there are clinically important differences according to where the initial evaluation starts.</p>

Reviewer Comments	Authors' Responses
Comparison chart (pg 3) – several items are controversial.	Unclear comment. We have included the chart as a direct extraction from a published article that we reference. We believe it is important for the reader to have a full range of information. We have included in the text some background on the controversies surrounding case definitions.
Page 4, nice discussion between screening measures and clinician confirmed diagnosis; also important to mention that VA TBI screening is symptomatic probable TBI (true incidence is difficult to ascertain because positive TBI should be designated as such with or without continued symptoms); VA/ DoD report a positive TBI screen as a symptomatic positive patient with probable TBI.	We thank the reviewer and have included a statement about the VA/DOD screening.
- METHODS	
Add special section outlining and addressing some of the issues CH raises.	We have added further information to the Discussion section. Our Future Research Recommendations section had previously discussed these issues.
- RESULTS	
More interested in prevalence of PTSD in a particular group of veterans who have suffered TBI than the overall prevalence of comorbid PTSD and TBI in the overall sample.	We reported the findings according to our key questions where data were available from published evidence. We have included a separate figure presenting data on prevalence of PTSD specifically in veterans with a history of mTBI.
RAND study and additional 5 studies not published? If published, why not included with other studies/manuscripts?	See our comment above regarding our rationale for including the RAND study. There were 31 unique published studies and the RAND report included in the evidence review. The other 5 publications met inclusion criteria but described the same study population as one of the 31 “unique” studies.
Flow diagram (fig 1) – what does “probable TBI/PTSD not included” mean? (clarify or reword).	We have clarified this in the diagram. This meant that individuals with a probable history of TBI and/or probable PTSD (as defined in our Methods section) were not included in the study and thus the study did not meet our evidence report inclusion criteria.
Would like to see table of 28 included studies earlier, including study design, quality rating, and population studied (perhaps grouped by population studied as in Table 2); this would be more helpful than current Table 1.	We placed the table in the appendix consistent with the ESP report template. The quality ratings did not directly apply to these studies and we discussed issues regarding applicability.
Would like to see more description and summarization of the findings from higher quality or more relevant studies rather than limited information including ranges across all studies	We have attempted to do this through our emphasis on the RAND report. Relevant to the military and veteran population, this study was the most population-based as investigators attempted to contact a random sample of military veterans across the United States. Additionally, investigators used detailed, previously-established methods for conducting phone interviews. We disagree that providing ranges across studies is not helpful. These help to show the variation in the literature that may result from studies employing different methods for cohort creation, case ascertainment and timing, and definitions of disease/injury. Therefore it is instructive in establishing future research recommendations.
- ACTIVE RESEARCH	
Did not identify any RCTs rather than state that there are none	We have edited accordingly.
More info on methods for Active Research – How many e-mails (effort to secure responses?); type of response from non-VA investigators; portfolio mgrs other than HSR&D?	A brief statement has been inserted. We acknowledge that our methods likely do not achieve rigorous scientific quality measures. This was an attempt to identify with limited resources high profile active research. The purpose was to guide policy makers, funders, and researchers to ongoing studies and assist in future research planning.

Reviewer Comments	Authors' Responses
- FUTURE RESEARCH	
Add to future research (pg 31) the need to review "systems issues" and coordination with different specialties – there is a real need to figure out ways to get the various specialties together to do treatment planning (Batten & Pollack, 2008 discuss this need).	We appreciate this suggestion and have added this suggestion to our Discussion.
Explicit recommendations that researchers come to a consensus as to measures to be used in this research so that findings can be pooled/ compared more easily.	We agree with this suggestion and have clarified this section in our Discussion.
Don't understand ascertainment bias; term "overlapping conditions" is confusing; don't understand 1 st sentence of last paragraph (p 31).	We have attempted to clarify these parts of the Discussion section. Ascertainment bias refers to problems with how the cases were defined, identified, and enrolled in a given study that could systematically skew the association(s) under investigation. This could occur because of selection of non-representative study populations, non-representative study participants, timing of the case assessment relative to the injury event, or individuals being aware of the purpose of the assessment and potential gains/harms from a certain response. Each of these alone could potentially result in study outcomes that are biased and not truly reflective of the actual prevalence of TBI/PTSD.
- OVERALL	
Overall, the manuscript is very well written. Thanks for doing this.	We thank the reviewers for their guidance and positive feedback.
I am impressed with this comprehensive report and I found the figures and tables very useful!	Thank you.

APPENDIX D: EVIDENCE TABLES

TABLE 1. Details of published studies evaluated in Key Question 1

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Brenner 2009 ⁸⁰ United States	Cross-sectional Veterans receiving services related to TBI and/or PTSD	N=72; 82% (n=59) with TBI; 63% with PTSD (n=45)	<i>Data for all study subjects</i> Trauma etiology: NR TBI severity: 46% mild; 17% moderate; 36% severe Time of assessment or since trauma: Median = 23 years (1-53) Mean age: 52 (9.7) years Women: 10% Race: Caucasian 65%; Hispanic 19%; African American 10%; Other 4% Education: Less than high school 3%; high school graduate 26%; more than high school 71% Pain: NR Other mental health conditions: NR	44% (n=32) of all subjects [89% of subjects with mild TBI; 36% of subjects with moderate TBI; 19% of severe TBI]	Interview and chart review.	Structured Clinical Interview for DSM-IV (SCID-IV).
Chalton 2009 ⁸¹ United Kingdom	Cross-sectional Patients recruited from a hospital outpatient head injury clinic	N=21; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 43%; fall 29%; assault 24%; work-related accident 5% TBI severity: 19% mild; 19% moderate; 62% severe Time of assessment or since trauma: 3-359 mos (median = 14) Mean age: 42.90 (10.98) Women: 33% Race: NR Education: 12.61 (2.85) years Pain: NR Other mental health conditions: 60% anxious (30% mild; 30% moderate or severe); 35% depressed (15% mild; 15% moderate)	14% (n=3) of all subjects [0% of subjects with mild TBI; 50% of subjects with moderate TBI; 8% of subjects with severe TBI]	Retrospective assessment of post-traumatic amnesia.	Clinician Administered PTSD Scale (CAPS).

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Mora 2009 ⁸² United States	Cross-sectional Record review of OEF/OIF soldiers with and without blast injuries treated at the United States Army Institute of Surgical Research Burn Center	n=119 22% with PTSD; 18% with TBI (all but one mTBI)	<i>Data for all study subjects</i> Trauma etiology: Military 100% TBI severity: Mild 95%; severe 5% (n=1) Time of assessment or since trauma: 193.7 (171.9) days for blast injury group; 189.7 (175.2) days for no blast injury group Mean age: 26.3 (6.1) for blast injury group; 25.9 (6.0) for no blast injury group Women: 15% blast injury group; 4% no blast injury group Race: NR Education: NR Pain: NR Other mental health conditions: NR	6% (n=7) of all subjects; 35% of mTBI subjects (PTSD status for 1 severe TBI case not reported)	Record review, loss of consciousness served as definition for mTBI.	Self report through PCL-M (> 44 required for PTSD diagnosis).
Gaylord 2008 ⁵² United States	Cross-sectional Service members identified through Trauma Burn Registry	n=76, 31 with TBI	<i>Data for all study subjects</i> Burned veterans, TBI vs. no TBI Trauma etiology: Combat (blast and burn) 100% TBI severity: mild 100% Time of assessment or since trauma: NR Mean age: 26 Women: 4% Race: NR Education: NR Pain: NR Other mental health conditions: NR	18% (n=14) of all subjects; 45% of TBI subjects	Medical records and clinical interviews. Glasgow Coma Scale (≥ 13), loss of consciousness (< 30 mins) and/or post-traumatic amnesia (≤ 24 h).	Self-report through PTSD Checklist (PCL-M). Score of 44+ indicative of PTSD.
Ruff 2008 ⁵³ United States	Cross-sectional Subjects evaluated as part of care in VA Medical Center	n=126; all TBI	<i>Data for all study subjects</i> OEF/OIF war veterans Trauma etiology: Combat (blast) 100% TBI severity: mild 100% Time of assessment or since trauma: 30 mos (range 8 mos - 4.5 years) Mean age: NR Gender: NR Race: NR Education: NR Pain: 63% (headache) Other mental health conditions: NR	66% (n=83) of all subjects	Administrative data based on positive Veterans Affairs (VA) 4-item TBI screen, including loss of consciousness (< 30 mins) and/or post-traumatic amnesia (< 24 h) and/or alteration of consciousness (< 24 h).	Self-report through PCL. Score of 50+ indicative of PTSD.

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Hoge 2008 ²² United States	Cross-sectional Army infantry soldiers surveyed while on duty	n=2525 819 injured; 384 with TBI. 1706 not injured	<i>Data for all study subjects</i> Iraq war veterans Trauma etiology (subjects with TBI, can have more than one source of injury): Blast/explosion 75%; fall 29%; MVC 22% TBI severity: mild 100% Time of assessment or since trauma: 3-4 mos post-deployment Mean age: NR Women: 5% Race: NR Education: less than HS 42%; HS grad 58% Pain: 30% (arm, leg, or joint pain; most frequently endorsed pain); 11% (headache) Other mental health conditions: Depression 11%	5% (n=125) of all subjects; 33% of TBI subjects	Self-report, a) loss of consciousness (n=124 subjects); and b) altered mental status (dazed, confused loss of memory) (n=260 subjects).	Self-report through PCL. Score of 50+ indicative of PTSD.
Koenigs 2008 ⁵⁴ United States	Cohort Vietnam veterans in the Vietnam Head Injury Study	n=245; 193 with TBI	<i>Data for all study subjects</i> Vietnam veterans Trauma etiology: Combat 100% TBI severity: penetrating 100% Time of assessment or since trauma: NR Mean age: NR Gender: NR Race: NR Education: NR Pain: NR Other mental health conditions: NR	25% (n=62) of all subjects; 32% of TBI subjects	NR.	Structured clinical interview (SCID), based on DSM-IV criteria.
Schneiderman 2008 ⁵⁵ United States	Cross-sectional Surveyed OEF/OIF veterans who served prior to October 2004 and lived in geographic catchment area	n=2235; 275 with TBI	<i>Data for all study subjects</i> OEF/OIF war veterans Trauma etiology (could have more than 1): Combat 34% (blast 74%, non-blast 26%); falls 39%; sports/physical training 28%; MVC 20% TBI severity: mild 100% Time of assessment or since trauma: NR Age groups: 18-25 18%; 26-30 15%; 31-35 16%; 36-40 17%; 41+ 38% Women: 13% Race: NR Education: NR Pain: NR Other mental health conditions: NR	5% (n=109) of all subjects; 39% of TBI subjects	Self report, Brief Traumatic Brain Injury Screen.	Self report through PCL. Score of 50+ indicative of PTSD.

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Schwartz 2007; ⁵⁷ Schwartz 2008 ⁸⁸ Israel	Case-control, terror vs. non- terror Patients treated in hospital PM&R unit	n=144; 38 with TBI	<i>Data for all study subjects</i> Trauma etiology: Terror subgroup - blast 70%, gunshot 30%. Non-terror subgroup – MVC 82%; fall 17% TBI severity: mild 32%; moderate 21%; severe 47% Time of assessment or since trauma: end of rehab stay – terror 218 ± 131days, non-terror 152 ± 114 days Mean age (range): 30 (9-76) Women: 33% Race: NR Education: Less than HS 15%; HS grad 47%; "student" 8%; college grad 29% Pain: NR Other mental health conditions: NR	11% (n=16) of all subjects; 42% of TBI subjects in terror subgroup; 42% of TBI subjects in non- terror subgroup [Prevalence not reported by TBI severity]	Based on Glasgow Coma Scale scores and brain computed tomography (CT).	Semi-structured interview; Revised PTSD Inventory (Solomon et al., 1993). Instrument based on Brief Symptoms Inventory.
Bombardier 2006 ⁵⁸ United States	Cohort Subjects recruited from trauma hospital	n=125; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 49%; assault 7% TBI severity: mild 44%; moderate 30%, severe 27% Time of assessment or since trauma: NR Mean age: 43 Women: 23% Race: white 92%; black 6% Education: HS grad 85% Pain: NR Other mental health conditions: 71% of TBI/ PTSD subjects had a history of depression or anxiety symptoms unspecified	11% (n=14) of all subjects [9% (n=5) with mild TBI; 8% (n=3) with moderate TBI; 18% (n=6) with severe TBI]	Medical record, based on Glasgow Coma Scale score.	PCL administered as a structured interview. Score of moderate severity on one intrusive, three avoidant, and two arousal symptoms indicative of PTSD.
Greenspan 2006 ⁵⁹ United States	Cohort Subjects identified from TBI databases after discharge from trauma hospitals	n=198; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 70%; fall 16%, pedestrian injury 6%; other 8% TBI severity: mild 19%; moderate 21%; severe 60% Time of assessment or since trauma: 3 years Mean age: 35 Women: 34% Race: white 74%; black 23%; other 3% Education: Less than HS grad 32%; HS grad 34%; at least some college 34% Pain: NR Other mental health conditions: NR	11% (n=22) of all subjects at 6 mos post-injury; 16% at 12 mos post- injury [Prevalence not reported by TBI severity]	Received treatment for head injury at hospital.	Self-report through the IES. Score of 35+ indicative of PTSD.

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Creamer 2005 ⁶⁰ Australia	Cohort Subjects were consecutive admissions to a level 1 trauma hospital	n=307; 189 with TBI	<i>Data for all study subjects</i> Trauma etiology: NR TBI severity: mild 100% Time of assessment or since trauma: mean 8 days Mean age: 37 Women: 24% Race: NR Education: NR Pain: NR Other mental health conditions: NR	8% (n=24) of all subjects; 15% of TBI subjects	Loss of consciousness of ≤ 30 minutes, PTA ≤ 24 hours, and GCS of ≥ 13 30 minutes post-trauma.	CAPS, amnesia eliminated as a symptom.
Gil 2005 ⁶¹ Israel	Cross-sectional Recruited from 2 surgery wards after treatment for TBI	n=120; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 90% TBI severity: mild 100% Time of assessment or since trauma: within 24 h after hospitalization; 7-10 days, 4 weeks, 6 mos Mean age: 31.4 Women: 42% Race: NR Education: 13 years (mean) Pain: NR Other mental health conditions: NR	14% (n=17) of all subjects at 6 mos post-injury	Presenting to hospital/ clinic for TBI (all had GCS 13-15).	CAPS.
Jones 2005 ⁶² England	Cohort Subjects were consecutive patients in hospital Accident and Emergency Department	n=131; 66 with TBI 118 at 6 weeks; 56 with TBI 74 at 3 mos; 58 with TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 100% TBI severity: mild 100% Time of assessment or since trauma: 6 weeks and 3 mos Mean age (range): 37 (18-65) Women: 60% Race: NR Education: NR Pain: NR Other mental health conditions: NR	14% (n=17) of all subjects at 6 weeks; 30% of TBI subjects 14% (n=10) of all subjects at 3 mos; 17% of TBI subjects	Post-traumatic amnesia (< 24 h), as described by Gronwall and Wrightson (1980).	PTSD Symptom Scale (PSS). Amnesia eliminated as a symptom.
Sumpter 2005 ⁶³ United Kingdom	Cross-sectional Subjects recruited from community outpatient and rehabilitation services, and volunteer organizations	n=34; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 47%; fall 32%; assault 18%; sports injury 3% TBI severity: severe 100% Time of assessment or since trauma: 6 year (0.6-34) Mean age (range): 40 (20-60) Women: 12% Race: NR Education: NR Pain: NR Other mental health conditions: NR	3% (n=1) of all subjects	NR. Subjects with severe TBI recruited from community out-patient and rehabilitation services and voluntary organizations.	CAPS, requiring clinical judgment of symptoms being related to trauma. (compared to 3 other methods of assessment.)

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Ashman 2004 ⁶⁴ United States	Cohort Subjects recruited from medical centers, brain injury associations, newspaper and website advertisements, and word-of- mouth	n=188; all TBI 83 at 24 mos; all TBI	<i>Data for all study subjects</i> Trauma etiology: NR TBI severity: mild 29%; moderate-severe 62%; 9% unknown Time of initial assessment or since trauma: 3mos - 4 years Mean age (range): 40 (18-87) Women: 47% Race: white 72%; black 12% Education: Less than high school 27%; HS/some college 38%; college graduate 25% Pain: NR Other mental health conditions at time 1: Depression 35%; Anxiety symptoms unspecified 27%; Substance use disorder (SUD) 14%	30% (n=56) of all subjects at time 1 (initial assessment between 3 mos and 4 years post- injury) 18% (n=34) of all subjects at time 2 (12 mos after initial assessment) 21% (n=17) of all subjects at time 3 (24 mos after initial assessment) [Prevalence not reported by TBI severity]	Self-reported; severity determined using ACRM loss of consciousness criteria.	SCID, based on DSM- IV criteria.
Williams 2002 ⁶⁵ United Kingdom	Cross-sectional Subjects recruited through brain injury services	n=66; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 45%; falls 18%; assault 3% TBI severity: severe 100% Time of assessment or since trauma: mean 5.9 years (range 1-26 years) Mean age (range): 38 (17-70) Women: 24% Race: NR Education: mean 12 years (range 9-19 years) Pain: NR Other mental health conditions: NR	18% (n=12) of all subjects	Self-report, based on loss of consciousness (+6 hrs) and/or post- traumatic amnesia (≥ 1 day).	Self-report through IES, corroborated by relative or caregiver. Score of 26+ indicative of PTSD.
Berthier 2001 ⁶⁶ Spain	Case series Consecutive referrals to Behavioral Neurology Unit of a single University Hospital; all patients diagnosed with OCD after TBI	n=10; all TBI (all OCD)	<i>Data for all study subjects</i> Trauma etiology: MVC 100% TBI severity: mild 60%; moderate 20%; severe 20% Time of assessment or since trauma: > 51 mos Mean age: 30 Women: 60% Race: NR Education: mean 11 years Previous head injury: 0% Pain: NR Other mental health conditions: Obsessive- compulsive disorder 100%; depression 90%	70% (n=7) of all subjects [60% (n=6) with mild TBI; 10% (n=1) with moderate TBI; 0% with severe TBI]	Glasgow Coma Scale score, determined at hospital admission.	SCID, based on DSM- III-R criteria.

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Hoofien 2001 ⁶⁷ Israel	Cohort Participants from a larger longitudinal study of patients from a single neuropsych rehab center with medically documented TBI at least 5 years before study	n=76; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 64%; combat 25%; work-related 9% TBI severity: severe 100% Time of assessment or since trauma: 14± 5.8 (SD) years Mean age (range): 25 (17-50) <i>age at injury</i> Women: 83% Race: NR Education: NR Pain: NR Other mental health conditions: Depression 45%	10% (n=7) of 68 responding to PTSD items	Subjects were in a coma for an unspecified long period of time.	Post-Traumatic Stress Disorder Inventory, based on DSM-III criteria. "Probable PTSD" diagnosis assigned to subjects meeting 4 criteria: traumatic event, re-experiencing, numbing, and hyperarousal symptoms.
McCauley 2001 ⁶⁸ United States	Cohort Participants recruited from Emergency Center or inpatient unit of a single Level-1 trauma center	n=200; 115 with TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 69%; assault 15%; other 16% TBI severity: mild 83%; moderate 17% Time of assessment or since trauma: 88 days Mean age: 34 Women: 78% Race: Hispanic 52%; black 32%; white 16% Education: mean 11 years Pain: NR Other mental health conditions: Depression 9%	8% (n=15) of all subjects; 13% of TBI subjects [12% (n=11) of subjects with mild TBI; 15% (n=4) of subjects with moderate TBI]	Hospital admission logs ("non-penetrating head injury" based on Glasgow Coma Scale scores 9-15).	SCID, based on DSM-IV criteria.
Turnball 2001 ⁷⁹ United Kingdom	Cross-sectional Subjects attended an Accident and Emergency Unit following a traumatic event and had evidence of TBI in medical record	n=53; all TBI	<i>Data for all study subjects</i> Trauma etiology: assault 58%; MVC 30%; fall 11% TBI severity: mild 58%; moderate 21%; severe 17%; none 2 subjects Time of assessment or since trauma: 5 mos Mean age: 35 Women: 13% Race: NR Education: NR Pain: NR Other mental health conditions: NR	17-27% of all subjects [Prevalence not reported by TBI severity]	Based on history of post-traumatic amnesia.	Those with IES-R score ≥ 20 administered the CAPS, with amnesia excluded as a symptom. Results reported using the most strict and most lenient cutoffs as recommended by scale authors on the CAPS.

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Bryant 1999a; ⁶⁹ Bryant 2000; ⁸⁹ Bryant 2000; ⁹⁰ Bryant 2001; ⁹¹ Bryant 2004 ⁹² Australia	Cohort Consecutive admissions to single site major brain injury rehab unit	n=96; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 73%; industrial injury 15%; assault 13% TBI severity: mild 100% Time since trauma: 6 mos Mean age: 34 Women: 20% Race: NR Education: NR Pain: 58% report daily pain; M = 6.90 (2.65) on a 1-10 severity scale Other mental health conditions: NR	27% (n=26) of all subjects	Medical records based on Glasgow Coma Scale score and post-traumatic amnesia (Westmead PTA scale).	Post-traumatic Stress Disorder Interview (PTSD-I; Watson et al., 1991), based on DSM-III-R criteria.
Bryant 1999b; ⁷⁰ Australia	Cohort Consecutive admissions to single site major trauma hospital following MVC	n=105; 46 with TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 100% TBI severity: mild 100% Time of assessment or since trauma: 6 mos Mean age: 31 Women: 40% Race: NR Education: NR Pain: Headaches in 100% of subjects with mTBI/PTSD Other mental health conditions: NR	9% (n=9) of all subjects; 20% (n=9) of TBI subjects	Hospital admissions, post-traumatic amnesia < 24 h, loss of consciousness.	Composite International Diagnostic Interview (CIDI).
Bryant 1998 ⁷¹ Harvey 2000 ⁹³ Australia	Cohort Consecutive MVC victims treated at a single site major trauma hospital with evidence of TBI	n=79; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 100% TBI severity: mild 100% Time of assessment or since trauma: mean 7.15 days (range 2-28); PTSD assessed 6 mos and 2 years post-trauma Mean age (range): 29 (16-60) Women: 30% Race: NR Education: NR Pain: NR Other mental health conditions: NR	24% (n=15) of 63 subjects assessed at 6 mos; 22% (n=11) of 50 subjects assessed at 2 years	Hospital admission, post-traumatic amnesia < 24 h.	Composite International Diagnostic Interview (CIDI).

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Hibbard 1998 ⁷² United States	Cross-sectional Participants randomly selected from 431 individuals with TBI involved in a larger quality of life survey	n=100; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 62%; assault 8%; other 30% TBI severity: NR Time of assessment or since trauma: mean 7.6 years Mean age: 40 Women: 47% Race: white 73%; black 14%; Hispanic 9% Education: HS grad or less 29%; some college/ college grad 49% Pain: NR Other mental health conditions: Depression 61%; SUD 28%; obsessive-compulsive disorder (OCD) 15%; panic disorder 14%; phobias 10%; general anxiety disorder 9%	19% (n=19) of all subjects	Self-reported loss of consciousness.	SCID, based on DSM- IV criteria.
Hickling 1998 ⁷³ United States	Cross-sectional Subjects were recently in and sought medical treatment within 2 days for MVC	n=107; 16 with TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 100% TBI severity: NR Time since trauma: 1-4 mos Mean age: 35.9 Women: 69% Race: 9.3% "minorities" Education: NR Pain: NR Other mental health conditions: NR	8% (n=9) of all subjects; 56% of subjects with TBI (9 of 16)	Clinical screening – rates of TBI stratified across multiple types of injury that varied in likelihood of producing TBI – only strictest criterion (e.g., loss of consciousness) used in the present review as evidence of TBI.	Clinician- Administered PTSD Scale (CAPS).
Trudeau 1998 ⁷⁴ United States	Cross-sectional Outpatient male combat veterans from a PTSD treatment program and/ or addictive disorders treatment program with a diagnosis of PTSD	n=43; all PTSD	<i>Data for all study subjects</i> Trauma etiology: Combat 100% (27 with a blast concussion and 16 without) TBI severity: mild 60%; moderate 40% Time of assessment or since trauma: NR Mean age (range): 52 (26-72) Women: 0% Race: NR Education: NR Pain: NR Other mental health conditions: SUD 42%; Attention-deficit/hyperactivity disorder (ADHD) 16%	60% (n=25) of 42 respondents [Prevalence not reported by TBI severity]	Self-report, either a) being in the presence at a detonation of ordnance, often resulting in death or serious injury to others closer to blast, b) experiencing unconsciousness for ≤ 20 mins or dazed for ≥ 1 hour without loss of consciousness, or c) requiring medical attention for concussive episode.	Not described, all subjects were enrolled in a PTSD recovery program and/or addictive disorders treatment program and had a clinical diagnosis of PTSD.

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Warden 1997 ⁷⁵ United States	Cohort Consecutive active duty service members with a moderate TBI at Walter Reed Army Medical Center	n=41; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 70%; fall 19%; assault 9% TBI severity: moderate 100% Time of assessment or since trauma: 4-29 mos Mean age: 27 Women: 2% Race: NR Education: NR Pain: NR Other mental health conditions: NR	11% (n=3) of 28 subjects at 8 weeks post-injury; 20% (n=3) of 15 subjects at 6 mos post-injury; n=0 of 18 subjects at 12 mos post-injury; 14% (n=1) of 7 subjects at 24 mos post-injury	Based on history of post-traumatic amnesia and Rancho Los Amigos scale.	Present State Examination, additional PTSD questions added to assess full spectrum of PTSD symptoms (e.g., added symptoms about re-experiencing and avoidance). Memory of event not required. Administered by clinicians.
Powell 1996 ⁷⁶ United Kingdom	Cohort Participants recruited from a hospital who were admitted for observation following mild/moderate TBI	n=35; all TBI	<i>Data for all study subjects</i> Trauma etiology: MVC 34%; dom. assault 29%; assault 14%; sport/other 14%; industrial 3% TBI severity: mild 69%; moderate 31% Time of assessment or since trauma: 3 mos Mean age: 35 Women: 34% Race: NR Education: NR Pain: NR Other mental health conditions: Depression 9%	34% (n=12) of all subjects [25% of subjects with mild TBI; 55% of subjects with moderate TBI]	Based on Glasgow Coma Scale, subjects admitted to hospital for minor head injury.	Self report through IES (>26 required for a positive screen for PTSD).
Sbordone 1995 ²¹ United States	Cross-sectional Participants diagnosed with post-concussive syndrome or PTSD prior to study recruitment; No information provided on method or location of recruitment	n=70; 28 with TBI, 42 with PTSD	<i>Data for all study subjects</i> Trauma etiology: MVC 66%; blunt head trauma 14%; fall 10%; other 10% TBI severity: mild 100% Time of assessment or since trauma: TBI 20.8 ± 16.4 mos; PTSD 29.1 ± 32.7 mos Mean age: 37 Women: 41% Race: NR Education: NR Pain: NR Other mental health conditions: NR	0 TBI subjects had PTSD	Unstructured interview by first author.	Unstructured interview by first author.

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
Middelboe 1992 ⁷⁷ Denmark	Cohort Consecutive patients admitted to a hospital Neurology Department with clinical evidence of TBI	n=28; all TBI	<i>Data for all study subjects</i> Trauma etiology: NR TBI severity: mild 100% Time since trauma: 3 mos & 1 year Mean age: 37 Women: 46% Race: NR Education: NR Pain: 32% reported headaches at 1 year post- TBI Other mental health conditions: NR	0 subjects had PTSD; 11% with "high" IES scores (above 19) 1 year post- trauma	Through neurologic exam (not specified).	Self-report through IES and unspecified symptom checklist. Information regarding how PTSD diagnosis was established not provided.

TABLE 2. Details of RAND study evaluated in Key Question 1

Study/ Country	Study design and population	n	Characteristics of participants	Prevalence of TBI history with PTSD	Traumatic brain injury definition/ measure	Post-traumatic stress disorder assessment
RAND 2008 ⁵ United States	Cross-sectional OEF/OIF service members and veterans identified through random digit dialing using telephone exchanges encompassing 24 geographic areas	n=1965; 19.5% with TBI (weighted percentage)	<i>Data for all study subjects</i> Trauma etiology: Military 100% TBI severity: NR Time of assessment or since trauma: NR. Time since deployment was 35% 0-17 mos, 33% 18- 35 mos, 33% 36 mos or greater Median age: 30 Women: 12% Race: white 66%; non-white 34% Education: NR Pain: NR Other mental health conditions: Probable major depression 14%	6.6% of all subjects; 34% of TBI subjects (weighted percentages)	Self report, Brief Traumatic Brain Injury Screen.	Self report through PCL.-M.

APPENDIX E: ACTIVE RESEARCH FINDINGS

TABLE 1. Ongoing research: Epidemiology of TBI/PTSD (Key Question #1)

Principal Investigator	Project Title/Status	Main Objective(s)	Study Characteristics
Copeland, L.	Tracking OEF/OIF Transition from DoD to VA Status: Completed, article in preparation	1. Determine feasibility of DoD-to-VA transfer of PHI on a local level 2. Determine rate of transition of Wounded Warriors from Brooke Army Medical Center to VA healthcare system 3. Determine use of VA mental healthcare NOTE: TBI diagnosis obtained from medical records	Study Design: Observational cohort Population: OEF/OIF deployed personnel treated and discharged from Brooke Army Medical Center (BAMC) FY02-FY07 Intervention: None Comparator: None Outcomes: Prevalence of PTSD at BAMC and at VA; delay from discharge at DoD to diagnosis/treatment of PTSD in VA system Timing: From discharge at DoD to treatment at VA Setting: Army Medical Center and VA sites
Donnelly, K. (See Appendix E, Table 2)	Cognitive Assessment of Veterans after Traumatic Brain Injury Status: In progress	1. Describe war-related cognitive and affective symptoms and patterns of substance abuse in OEF/OIF veterans 2. Construct cognitive and affective profiles of OEF/OIF veterans over time 3. Describe the temporal relationship between composite stress index and cognitive profiles of OEF/OIF veterans 4. Describe the temporal relationships among TBI, cognitive symptoms, patient outcomes, and health services outcomes	Study Design: Prospective cohort Population: 500 OEF/OIF veterans Intervention: None Comparator: None Outcomes: TBI identified with structured diagnostic interview; PTSD identified with PTSD checklist Timing: Baseline, 6, 12, and 18 mos Setting: 5 outpatient VA sites (VISN 2)
Griffin, J.	Understanding and Meeting the Needs of Informal Caregivers to Improve Outcomes for TBI patients with Polytrauma Status: In progress	Assess the relationship between caregiving and patient, caregiver, and family health outcomes, including the physical, emotional, and financial burden of caregiving and the resources available to caregivers	Study Design: Observational Population: Family caregivers of all OEF/OIF patients with a TBI discharged from a Polytrauma Rehabilitation Center (PRC) Intervention: None Comparator: None Outcomes: Caregiver-report of patients' TBI and PTSD diagnoses Timing: At least 3 mos post-discharge from PRC Setting: Surveys administered by mail

Principal Investigator	Project Title/Status	Main Objective(s)	Study Characteristics
Kang, H. (See Appendix E, Table 2)	National Health Study for a New Generation of U.S. Veterans Status: In progress	<ol style="list-style-type: none"> 1. Determine if the health status of OEF/OIF veterans is better, worse, or the same as non-deployed veterans 2. Characterize healthcare utilization and VA disability compensation patterns of OEF/OIF veterans 3. Describe the natural histories of psychological disorders, mTBI, musculoskeletal problems, and other health conditions over time among veterans 4. Obtain prevalence figures for mTBI and PTSD from a population-based sample 	Study Design: Longitudinal Population: 30,000 deployed OEF/OIF veterans and 30,000 non-deployed OEF/OIF era veterans Intervention: None Comparator: None Outcomes: TBI and PTSD identified with screening instruments used in VAMCs Timing: 10 year follow-up with assessment every 3 years Setting: Surveys administered by mail, on-line, and by telephone
Polusny, M.	Mild TBI/PTSD Comorbidity and Post-Deployment Outcomes in National Guard Soldiers Status: Completed, manuscripts in preparation	<ol style="list-style-type: none"> 1. Describe the scope of mTBI/PTSD among returning National Guard OIF veterans 2. Identify the extent to which these problems impacted veterans' psychosocial functioning, physical health, and quality of life over time 3. Examine variation in new OIF veterans' experiences with VA by mTBI and probable PTSD status 	Study Design: Two-wave longitudinal cohort Population: OIF National Guard soldiers Intervention: None Comparator: None Outcomes assessed: <i>In-theater</i> : blast exposure, mTBI, PTSD symptoms; <i>Post-deployment</i> : combat exposure, exposure to explosive blasts and injuries sustained, mTBI and post-concussive symptoms, current psychosocial functioning, physical health, access and use of VA healthcare services Timing: In-theater screening one-month before returning home; mailed survey at 1 year post-deployment Setting: In-theater and home
Rao, V.	Post-Traumatic Brain Injury Depression Status: In progress	To identify risk factors for depression among patients with first time TBI (all severity levels) (NOTE: PTSD assessed with full structured interview)	Study Design: Prospective, observational Population: 140 consecutive TBI patients; recruited soon after injury Intervention: None Comparator: None Outcomes: Major depression; also assessing PTSD Timing: Follow-up at 1 year post-injury Setting: Clinical (2 university-affiliated trauma units)
Tupler, L. (See Appendix E, Table 2)	TBI Severity and Associated Neurocognitive findings in OEF/OIF Veterans Status: Data collection complete; analysis in progress	To examine the epidemiology of TBI in OEF/OIF veterans and the relationship between self-reported severity of TBI and level of PTSD symptomatology and neurocognitive performance (NOTE: results to be analyzed by severity of TBI)	Study Design: Prospective, observational Population: Approximately 850 OEF/OIF veterans; TBI and PTSD status unknown by investigators at time of enrollment Intervention: None Comparator: None Outcomes: Neurocognitive and psychological test battery (including PTSD Checklist) findings examined in relation to TBI history (chart review or self-report) Timing: Post-deployment; time from TBI assessed Setting: One Polytrauma Rehabilitation Center, three Level III Polytrauma Support Clinic Teams

TABLE 2. Ongoing research: Assessment of mTBI/PTSD (Key Question #2)

Principal Investigator	Project Title/Status	Main Objective(s)	Study Characteristics
Donnelly, K. (See Appendix E, Table 1)	Cognitive Assessment of Veterans after Traumatic Brain Injury Status: In progress	Describe the psychometric properties of the VA TBI screening tool	Study Design: Prospective cohort Population: 500 OEF/OIF veterans Intervention: None Comparator: None Outcomes: Item analysis of the VA TBI screening tool; test-retest reliability and sensitivity/specificity with structured diagnostic interview for TBI probability/severity as criterion Timing: Baseline, 6, 12, and 18 mos Setting: 5 outpatient VA sites (VISN 2)
Kang, H. (See Appendix E, Table 1)	Markers for the Identification, Norming, and Differentiation of TBI and PTSD (MIND) Status: Planning stage	1. Clarify differential diagnoses between TBI and PTSD 2. Build objective, consistent, and operator-independent diagnostic criteria	Study Design: Cross-sectional Population: Subset of OEF/OIF veterans from New Generation study with TBI and/or PTSD and a comparison group Intervention: None Comparator: None Outcomes: Advanced diagnostic tests (neuroimaging, sleep studies, neuroendocrine measures) Timing: One-time testing; patients continue enrollment in New Generation study Setting: VA War Related Illness and Injury Study Centers
Rao, S. Levin, H.	Neural and Behavioral Sequelae of Blast-Related Traumatic Brain Injury Status: In progress	Identify the similarities and potential differences in the neural and behavioral sequelae of blast-related TBI compared to mechanically-induced TBI occurring in civilians	Study Design: Prospective, cross-sectional observational Population: n=120 in 4 groups – military with mild to moderate TBI, military with mild to moderate orthopedic injury (OI), civilian with mTBI, civilian with OI Intervention: None Comparator: None Outcomes: Advanced MRI findings, neuropsychological test results, post-concussion symptoms, PTSD symptoms, depression, pain and fatigue scales Timing: Assessment at 12-24 mos post-injury Setting: Cleveland and Houston VAMCs; community hospital trauma/rehabilitation centers

Principal Investigator	Project Title/Status	Main Objective(s)	Study Characteristics
<p>Tupler, L. (See Appendix E, Table 1)</p>	<p>TBI Severity and Associated Neurocognitive findings in OEF/OIF Veterans Status: Data collection complete; analysis in progress</p>	<p>Examine the relationship between self-reported severity of TBI and level of PTSD symptomatology and neurocognitive performance on a measure of premorbid intellectual functioning and prefrontal verbal abstraction (NOTE: results to be analyzed by severity of TBI)</p>	<p>Study Design: Prospective, observational Population: Approximately 850 OEF/OIF veterans; TBI and PTSD status unknown by investigators at time of enrollment Intervention: None Comparator: None Outcomes: Neurocognitive and psychological test battery (including PTSD checklist) findings examined in relation to TBI history (chart review or self-report) Timing: Post-deployment Setting: One Polytrauma Rehabilitation Center, three Level III Polytrauma Support Clinic Teams</p>
<p>Tupler, L.</p>	<p>Posttraumatic Stress Disorder with and without Traumatic Brain Injury: Comorbidity and Longitudinal Course of Recovery Status: Preparing for data analysis</p>	<p>Examine neurocognition in OEF/OIF post-deployed and active-duty personnel with TBI alone, PTSD alone, and comorbid TBI and PTSD compared with combat controls and non-combat controls (NOTE: same population as in study described below)</p>	<p>Study Design: Prospective, observational Population: Approximately 170 OEF/OIF veterans and active-duty personnel Intervention: None Comparator: None Outcomes: Neurocognitive and psychological test battery (including PTSD checklist) findings examined in relation to TBI history (chart review or self-report) Timing: Continuous recruitment since 2006 Setting: One Polytrauma Rehabilitation Center, two Level III Polytrauma Support Clinic Teams</p>
<p>Tupler, L.</p>	<p>Can Olfaction be used to Discriminate Traumatic Brain Injury from Posttraumatic Stress Disorder? Status: Preparing for data analysis</p>	<p>Examine the utility of the University of Pennsylvania Smell Test (UPSIT) as a means of discriminating TBI from PTSD (NOTE: same population as in study described above)</p>	<p>Study Design: Prospective, observational Population: Approximately 170 OEF/OIF veterans and active-duty personnel Intervention: None Comparator: None Outcomes: UPSIT and PTSD Checklist in relation to TBI history (chart review or self report) Timing: Continuous recruitment since 2006 Setting: One Polytrauma Rehabilitation Center, two Level III Polytrauma Support Clinic Teams</p>
<p>Vanderploeg, R. Fitzgerald, S.</p>	<p>TBI Screening Instruments and Processes for Clinical Follow-up Status: In progress</p>	<p>Evaluate the reliability and validity of the existing Traumatic Brain Injury (TBI) Clinical Reminder Screen for OEF/OIF Veterans controlling for comorbidities and demographics</p>	<p>Study Design: Diagnostic test evaluation Population: OEF/OIF veterans Intervention: None Comparator: None Outcomes: Reliability and validity Timing: Not stated Setting: VA Polytrauma Rehabilitation Centers, Network Sites, and Support Clinic Teams</p>

TABLE 3. Ongoing research: Treatment of mTBI/PTSD (Key Question #3)

Principal Investigator	Project Title/Status	Main Objective(s)	Study Characteristics
Beckham, J.	Rehabilitation Strategies to Reduce Violence and Anger in TBI and PTSD Status: Proposal under review	<ol style="list-style-type: none"> 1. Identify risk and protective factors empirically related to violent behavior among veterans who have returned from Iraq and Afghanistan 2. Examine the link between specific factors related to violence among veterans from previous conflicts and post-deployment violence risk among Iraq and Afghanistan veterans 3. Develop an evidence-based risk assessment instrument to administer to Iraq and Afghanistan veterans in order to identify those most in need of services 	Study Design: Prospective cohort Population: 300 OEF/OIF veterans and a member of their family Intervention: None Comparator: None Outcomes: Modality of psychotherapy, dosages and classes of psychiatric medications Timing: Interview at baseline and 6 mos Setting: VA, outpatient NOTE: although the direct aim of the study is not to evaluate particular rehabilitation strategies, the investigators believe that information yielded from the study may be useful in sequencing treatment efforts
Epstein, D.	Pilot Test of Preference-Based Insomnia Treatment for OEF/OIF Veterans Status: Proposal under review	Pilot test a brief, preference-based insomnia intervention augmented by audio files (MP3) and web-based resources	Study Design: One group, pre-post Population: 26 OEF/OIF veterans, history of blast exposure or other injury resulting in period of altered consciousness AND insomnia complaint of ≥ 1 mo. duration with daytime impairment, Insomnia Severity Index (ISI) ≥ 10 , phone and internet access, ability to listen to audio files on MP3 player Intervention: Multi-component – relaxation therapy, mindfulness exercise, stimulus control instructions, sleep restriction therapy, and sleep education and hygiene Comparator: None Outcomes: ISI, Pittsburgh Sleep Quality Index-Addendum for PTSD (PSQI-A), daily sleep diary, treatment feasibility Timing: 4 week treatment phase, assessed pre-treatment, during treatment, and 2 weeks post-treatment Setting: VA, outpatient
Nichols, L. Martindale-Adams, J.	Team Based Initiative: Support (Pilot) Status: Completed, report in development	<ol style="list-style-type: none"> 1. Determine the feasibility of implementing volunteer support teams with TBI families 2. Identify the obstacles and opportunities in implementation 	Study Design: Case series Population: Family members of 6 Guard/Reserve service members (OEF/OIF veterans) with mild-complicated TBI and co-occurring PTSD Intervention: Project coach for needs assessment, team formation, training Comparator: None Outcomes: Qualitative data on family issues and concerns Timing: Returning to community post-injury Setting: Outpatient (family homes), rural

Principal Investigator	Project Title/Status	Main Objective(s)	Study Characteristics
Harch, P.	<p>Pilot Study of Hyperbaric Oxygen Therapy (HBOT) in Chronic Traumatic Brain Injury (TBI)/Post-Concussion Syndrome (PCS) and TBI/Post-Traumatic Stress Disorder (PTSD)</p> <p>Status: In progress</p>	<p>Determine if one or two 40-treatment courses of low pressure HBOT can improve cognition and brain imaging in subjects with either chronic mild-moderate TBI (also known as PCS), or chronic TBI with PTSD secondary to blast injury</p>	<p>Study Design: Open-label, single group Population: 30 patients (15 with TBI, 16 with TBI and PTSD), 18-45 years old, blast-induced injury resulting in mTBI/concussion with loss of consciousness; able to manage self-care Intervention: 40 (or 80) HBOT sessions; 2 sessions per day for 20 days (4 weeks) Comparator: None Outcomes: Psychometric and neuropsychological tests, brain imaging Timing: Injury 1 to 4 years prior to enrollment; baseline assessment, post-treatment assessment, and follow-up at 6 mos and 1 year post-treatment Setting: Non-VA clinic</p>
Ruff, R.	<p>Improving Sleep: Initial Treatment in OIF/OEF Veterans with Blast-Induced Mild TBI</p> <p>Status: Completed, publication in development</p>	<p>Determine if treating impaired sleep would reduce headache frequency and severity</p>	<p>Study Design: Case series Population: OIF/OEF veterans with headaches associated with mTBI and persisting neurocognitive deficits Intervention: Education in sleep hygiene and prazosin to reduce nightmares associated with PTSD Comparator: Patients who do not complete prazosin protocol or who discontinued prazosin after intervention period Outcomes: Headache frequency and severity, cognitive assessment, sleep assessment Timing: Assessment at baseline, after 9 week intervention, 6 mo. follow-up Setting: Outpatients from VAMC</p>